Diagnostic management of maxillofacial trauma patients:

clinical considerations and radiological advancements

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ISBN: 978-94-6419-450-0
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Printing: Gildeprint Enschede, gildeprint.nl
Layout and (cover) design: Harma Makken, persoonlijkproefschrift.nl

The research presented in this thesis was performed at the Department of Oral and Maxillofacial Surgery, University Medical Center Groningen, The Netherlands.

Printing of this thesis was financially supported by the Wetenschapsfonds Medisch Specialisten Isala (WMI), University Medical Center Groningen (UMCG), The Graduate School of Medical Sciences of the University of Groningen (GSMS), Nij Smellinghe hospital, Nederlandse Vereniging voor Mondziekten, Kaak- en Aangezichtschirurgie (NVMKA), Nederlandse Vereniging voor DentoMaxilloFaciale Radiologie (NVDMFR), Nederlandse Vereniging voor Traumachirurgie (NVT), Koninklijke Nederlandse Maatschappij tot bevordering der Tandheelkunde (KNMT), Nederlandse Wetenschappelijke Vereniging van Tandartsen (NWVT), Straumann Group, KLS Martin Group and Noord Negentig.

rijksuniversiteit
groningen

Diagnostic management of maxillofacial trauma patients: clinical considerations and radiological advancements

Proefschrift

ter verkrijging van de graad van doctor aan de
Rijksuniversiteit Groningen
op gezag van de
rector magnificus prof. dr. C. Wijmenga
en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op

woensdag 30 maart 2022 om 14:30 uur

door

Romke Rozema

geboren op 20 juni 1991
te Dongeradeel

Promotor
Prof. dr. F.K.L. Spijkervet

Copromotores
Dr. B. van Minnen
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Psalm 119:105

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CHAPTER 1

General introduction

Maxillofacial trauma

Globally, trauma is of one of the leading causes of death, constituting nearly 8% of all deaths annually [1]. Maxillofacial trauma is estimated to occur in 25% of the trauma patients [2]. In the United States, maxillofacial trauma patients are a significant cause of morbidity and the total emergency department charges are approximately $1.04 billion annually [3]. Based on epidemiological data, most of the patients are male and 40 years of age or younger [4–9]. Most common causes of injury include assault, sports, motor vehicle accidents and falls, but the order of importance varies among the different studies [3,5,6,8]. Maxillofacial trauma patients are known to suffer concomitant injuries associated with the head and neck region, including intracranial injury, skull fractures and cervical spine injury [3,10–12].

Anatomy of the maxillofacial skeleton

Conventionally, the maxillofacial anatomy is divided into a tripartite system including an upper, middle, and lower horizontal third. The midfacial region is defined as the upper and middle third, including the frontal bone, maxilla, zygoma, orbits, nose and naso-orbital ethmoidal complex, whereas the mandible is the lower third.

Midfacial anatomy

The anatomy of the midface is known for its complexity and is composed of the following individual bony structures: nasal bones, lacrimal bone, ethmoid, sphenoid, maxilla, zygomatic bone, and palatine bone (Figure 1). The midfacial skeleton is often conceptualized as a framework of buttresses that is responsible for the width and height of the facial profile, and to establish functional support for the dental arch and globe [13]. The horizontal buttress is divided into an inferior buttress made up of the inferior orbital rims and the zygomaticomaxillary complex, and a superior buttress made up of the frontal bone and superior orbital rims. The vertical buttress is composed of the naso-orbito-ethmoidal, zygomaticomaxillary and pterygomaxillary complex. The midface contains a collection of air-containing cavities that are hypothesized to function as a crumple zone to protect the globe, brain and other critical structures [14].

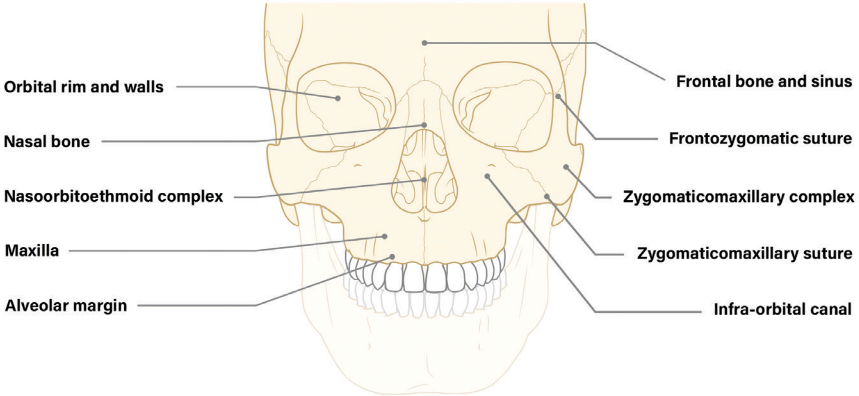

Figure 1: Skeletal anatomy of the midface.

Mandibular anatomy

The mandible is the largest bone of the skull and consists of a body and two rami (Figure 2). The body is horseshoe-shaped and contains the alveolar ridge in which the lower teeth reside. The superior aspect of the ramus is known as the condylar process that articulates with the temporal bone bilaterally. This junction is known as the temporomandibular joint which plays an essential role in mastication, breathing and speech.

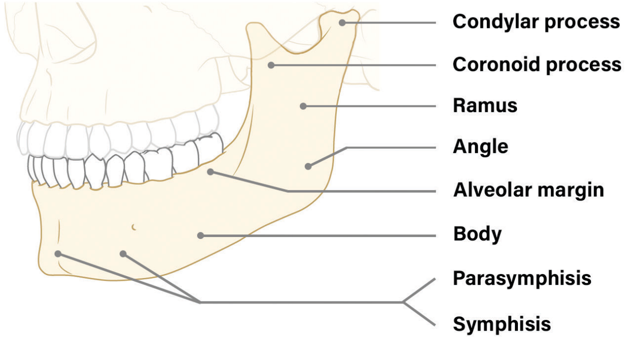

Figure 2: Skeletal anatomy of the mandible

Fractures of the maxillofacial skeleton

Midfacial fractures

Numerous systems have been proposed to classify midfacial fractures. In the late 19th century, René Le Fort (1869-1951), a French military surgeon, devoted his career to teaching at the University of Lille in northern France. He published papers regarding the classification of facial fractures in the Revue de Chirurgie [15]. In his studies, Le Fort conducted a series of infamous and somewhat macabre experiments where he inflicted fractures on cadaver heads. He hypothesized that fractures were dependent on the point of impact, the direction of the wounding agent, and the position of the head during trauma [16]. The experiments were conducted to mimic various traumatic conditions including wounding agents, a kick, a metal shaft, a wooden club, and the corner of a marble table [17]. The heads were sawn coronally and boiled to remove the soft tissues to subsequently examine the fractures [17]. Le Fort noticed three distinct groups of fracture types going in horizontal, pyramidal or transverse directions, currently known as Le Fort I, II, and III fractures [18].

Since then, various classification systems have been proposed for midfacial fractures. The Arbeitsgemeinschaft für Osteosynthesefragen CranioMaxillofacial Fracture (AOCMF) system is an image-based classification system in which anatomic modules are arranged into a hierarchy of three levels focusing on complexity and detail [19,20]. Classification systems have also been proposed by various other authors over the last few decades, focusing on either midfacial fractures or specific subtypes of fractures [21–28]. From a clinical perspective, midfacial fractures are classified according to the prevalence of common fracture patterns. For example, zygomaticomaxillary fractures are the result of a disruption to the anchoring of the complex, emanating through distinct fracture components of the orbital wall, the zygomatic arch, the zygomaticomaxillary suture and zygomaticofrontal suture [29]. These are often referred to as tripod or tetrapod fractures. Together with orbital and nasal fractures, they are the most common fracture types of the midface [5]. Other fracture types include frontal sinus, maxillary sinus, nasal bone, nasoorbitoethmoid complex, Le Fort I, II, III, and maxillary dentoalveolar complex fractures.

Mandibular fractures

To date, various authors have sought to classify fractures of the mandible by focusing on anatomical location, dentition involvement, fracture characteristics and displacement [30–32]. From a clinical perspective, the AOCMF topographical distribution is used most frequently and it classifies fractures according to symphyseal area, parasymphyseal area, ramus, angle, coronoid- and condylar process [19]. Mandibular fractures occur most commonly in the symphyseal and condylar region, accounting for 19.2% and 27.4% of the fractures, respectively [9], whereas those in the mandibular body account for 18.1% of the fractures and angular fractures accounting for 16.2% of the total. Depending on the specific mechanisms of injury, fractures of the mandible occur in specific patterns. For example, the 'guardsman' or 'parade ground' fracture is defined as a tripartite fracture of the bilateral condylar and symphyseal region [33,34]. The terms are used because these specific fractures are commonly seen among soldiers who faint and fall on their chin after standing upright on the parade ground for a long time. They are also seen in epileptic and elderly patients.

Clinical approach of maxillofacial trauma

The management of a maxillofacial injury is particularly challenging with respect to a multitrauma patient [35]. In the emergency department, each trauma patient is subjected to a systematic approach according to the principles of Advanced Trauma Life Support to identify and resuscitate all potential injuries [36]. During the primary survey, severe maxillofacial injury can be a threat to the management of the patient's airway [37,38]. However, the majority of maxillofacial trauma patients do not require immediate resuscitation and full physical examination of these injuries is conducted during the secondary survey.

Physical examination findings

Fractures of the facial skeleton often have characteristic signs and symptoms. For instance, zygomaticomaxillary and orbital fractures are associated with infra-orbital paraesthesia [39,40] The infra-orbital nerve emerges from the inferior orbital fissure and opens below the margin of the orbit via the infra-orbital foramen and, especially in displaced fractures, compression of the infra-orbital nerve may cause sensory innervation disturbances of the lower eyelid, the side of the nose, the upper lip, upper incisor, canine, premolars, or first molar. Orbital fractures can also be associated with extra-ocular movement limitations [41,42]. In orbital floor or "blow-out" fractures, any inferior rectus muscle entrapment leads to upward gaze limitations and diplopia (Figure 3).

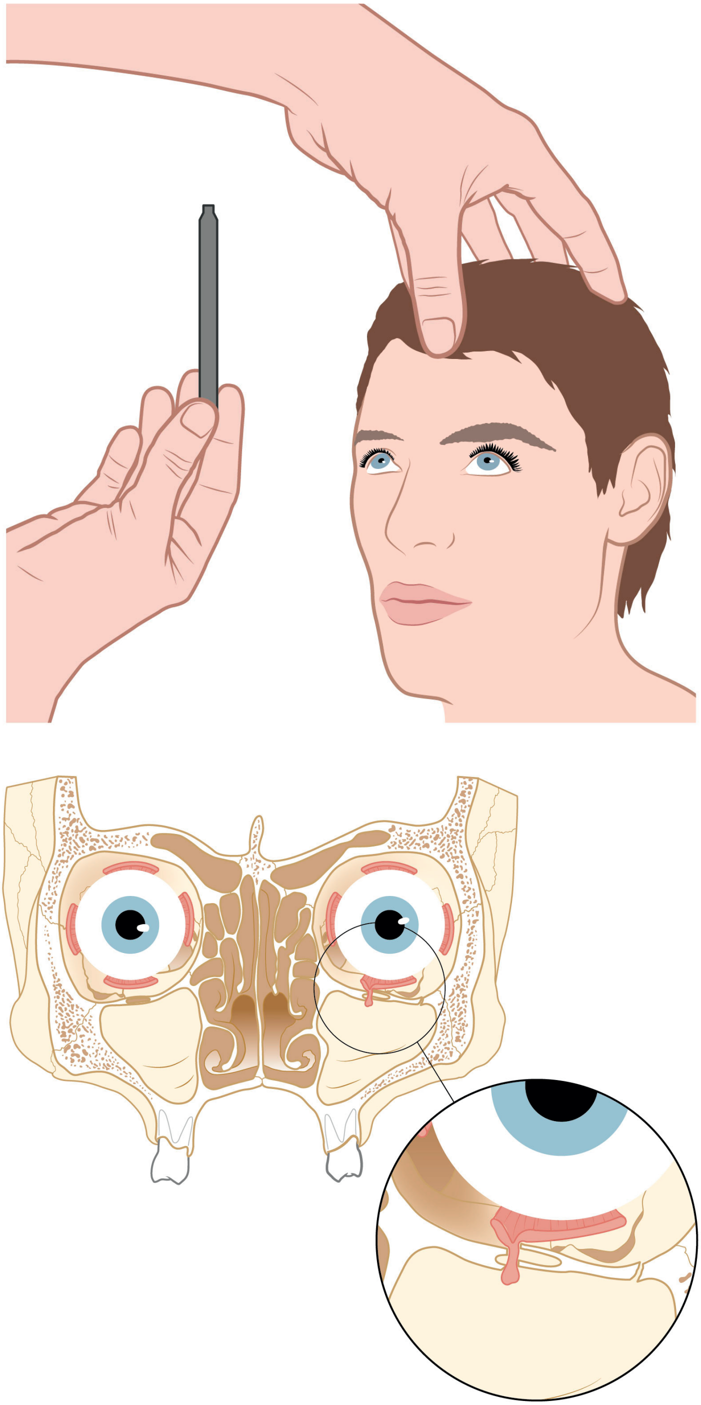

Figure 3: (a) Physical examination of eye movement limitations. (b) Visualisation on how entrapment of the inferior rectus muscle leads to upward gaze limitations.

Mandibular trauma patients also present with characteristic examination findings including abnormal mandibular movements, gingival laceration, sublingual hematoma and malocclusion [43,44]. Fractures of the condylar process, body and symphyseal region are especially associated with altered occlusion [45]. Comparable with the altered skin sensations following midfacial trauma, mandibular fractures may damage the inferior alveolar nerve resulting in loss of sensation in the lower lip, chin, anterior tongue and mandibular teeth on the injured side [46]. All these physical examination findings should be carefully considered to justify the need for diagnostic imaging.

Imaging modalities for the diagnosis of maxillofacial fractures

Computed Tomography (CT), Cone Beam Computed Tomography (CBCT) and orthopantomography (OPG) are the imaging methods of choice for maxillofacial traumas [47–51]. Orthopantomography is a single imaging technique where panoramic projections of the mandible are produced by positioning the patient in a natural head position while both the x-ray source and film rotate around the patient [51]. Although OPG is a well-established method for the diagnosis of mandibular fractures, it is prone to the typical disadvantages of two-dimensional imaging including superimposition, geometric distortion, x-ray angulations and artifacts [52]. These drawbacks are not found in three-dimensional imaging techniques like CBCT whereby a cone-shaped x-ray beam is centred on a detector which is involved in rotational data acquisition of two-dimensional images to reconstruct a three-dimensional dataset [49]. These datasets are particularly appreciated because of the high spatial resolution [53]. However, most CBCT systems do not allow data acquisition of trauma patients who have to remain supine due to cervical spine stabilisation or other traumatic conditions. Hence, emergency department patients suffering maxillofacial trauma are mostly scanned using CT, as it allows the patients to be scanned in a supine position.

Computed Tomography

CT, originally known as computerized axial tomography, was developed by Sir Godfrey Newbold Hounsfield in 1967 [54,55]. He was an English electrical engineer working for the Electrical and Musical Instruments (EMI) in south-eastern England where he designed a computer that could calculate the x-ray absorption patterns of biological tissues [56,57]. This technique would eventually evolve to a system that is nowadays known as CT (Figure 4).

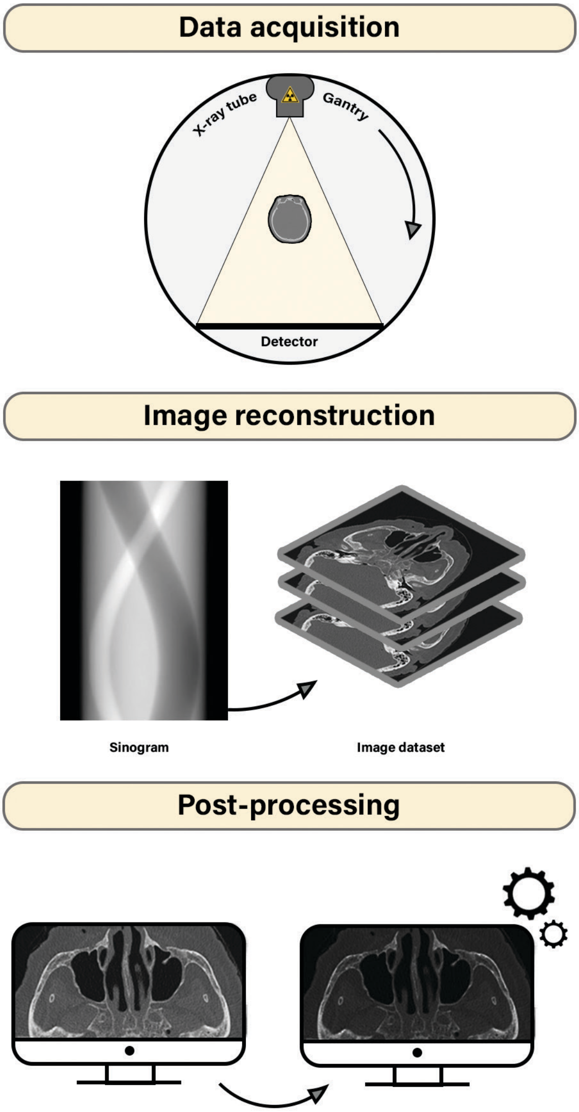

Figure 4: Basic concept of Computed Tomography dataset reconstruction

The geometry of a CT allows for continuous data acquisition of multiple body parts in one go while transporting the patient through the gantry [58]. Since its introduction a few decades ago, CT technology has evolved significantly and multiple generations of scan systems have been introduced. The first CT system generation was designed as a rectilinear pencil beam acquiring data by linear shift, followed by a rotation of the x-ray tube and detector to measure the next projection [59]. The second-generation CT system used multiple narrow beams that covered a fan angle of approximately 10 degrees and each detector actually acquired its own complete view at a different angle. One of the most important advantages was the substantial reduction in scanning time. In the third generation, the x-ray beam was widened into a fan beam encompassing the entire patient's width and the detectors were linked to the tube so that they could rotate together around the patient in full synchrony. This generation also introduced the slip-ring design to pass the electrical signals across sliding contacts to allow continuous rotation instead of having to rewind the gantry after each rotation of acquisition. The fourth-generation CT scanners incorporated a rotating fan beam with a 360-degree stationary ring of detectors. Although these scanners had the potential to generate short acquisition times per slice due to the very fast rotation speeds, the system was abandoned because of the high costs due to the large number of detector elements [60].

Nowadays, the CT market is dominated by systems using the third generation geometry, including clinical practices. In the past two decades, multiple CT vendors introduced multidetector (or multislice) systems that implement multiple detectors in the longitudinal axis, enabling simultaneous acquisition of multiple slices of the patient [61]. The longitudinal resolution and scanning speed of these scanners have been improved substantially [62–64], with up to 80mm or more of longitudinal coverage [65]. Current research is focusing on Dual Source CT (DSCT), where the temporal resolution is reduced by incorporating multiple tubes and corresponding detectors, and Dual Energy CT (DECT), where the different mean energies of the CT datasets allow for the identification of a material by means of a characteristic change in attenuation [66,67].

Radiation dose

Exposure to ionizing radiation is associated with the induction of cancer in humans and, therefore, the radiation dose received during diagnostic imaging procedures is a topic of major concern [68]. This topic is still very relevant as the increased utilization of CT is inherent to an increased source of radiation exposure [69]. Regarding the maxillofacial region, the effective dose for clinical CT protocols is estimated to be between 0.9 to 3.48 mSv [70]. The lifetime attributable risk of cancer per millisievert (mSv) is estimated to be 0.012% whereas the risk of mortality from all cancers is estimated to be 0.006% [71]. A variety of strategies have been introduced to reduce the radiation dose for individual patients.

Radiation dose reduction strategies

Automatic Exposure Control (AEC) is commonly used in modern CT acquisitions and designed to adjust the radiation dose according to the size and attenuation characteristics of the patient’s body [72–74]. AEC operates on the concept that different-sized patients require different levels of noise to maintain adequate image quality [73]. It is performed by modulating the tube current based on the patient’s size, z-axis and rotational variation. Regarding patient size AECs, the topogram suggests a milliamperage to be used throughout the examination to reduce the variation in image quality between small and large patients [74]. The aim of a z-axis AEC is to maintain the standard deviation of the milliamperage throughout the examination. Consequently, the milliamperage for the head is lower than that for the facial region. In rotational AECs, a topogram is used for sinusoidal modulation of the milliamperage during the 360° rotation to equalize the x-ray absorption around the patient [73]. These AEC concepts do not only reduce radiation dose, but also avoid photon starvation artifacts, reduce the load on the x-ray tube and maintain image quality despite the different attenuation values [75]. Various studies of this technique have provided low dose protocols for facial CTs [76,77].

Iterative reconstruction

Radiation dose reduction results in a deterioration of image quality due to an increase in image noise and artifacts. Thus, Iterative CT Reconstruction techniques (IR) have been proposed to maintain diagnostic image quality while reducing radiation dose [78]. Although these algorithms were initially proposed to reconstruct the data from the first CT systems, the demanding computational requirements hampered their use for clinical purposes [79]. The primary goal of data reconstruction is to assign an attenuation value to each voxel of a three-dimensional volume. This process was originally performed by filtered back projection (FBP) in which the attenuation profile at each gantry angle was ‘back-projected’ across the image space [78,80]. IR algorithms have been designed to reconstruct the image data to correspond accurately to the scanned projection data using backward and forward projection [81,82]. The process consists of a multitude of iterations in which repeated transitions are performed from the projection data to the image space to improve the constructed image data [83]. To date, different generations of IR algorithms have been presented by all the major CT vendors which can be used fully today in clinical practice. The most recent and more complex so called ‘model- based’ IR algorithm provides a more exact and detailed modelling of the CT imaging process by correcting factors such as the system’s geometry, physics modelling, detector element size and electronic noise from the system [81,83]. Although these IR algorithms are superior in optimizing the image quality, the images are also associated with motion artifacts and unfamiliar image textures which are often referred to as 'blotchy', 'pixelated' or 'plastic like' appearance [83].

Artificial intelligence

Recently, artificial intelligence (AI) has gained substantial interest because of the potential to improve the image quality of the CT datasets [82,84]. These algorithms, often referred to as a Non-iterative Technique Artificial Neural Network (NiTANN), are used as noise reduction techniques on low dose scanned datasets [85]. The algorithms use a complex arrangement of computational steps to achieve a mathematically defined goal such as to train the software to "reconstruct" a normal dose image from a low dose acquisition [85]. Preliminary research suggests that the algorithms have the potential to reduce radiation dose without adversely affecting the diagnostic image quality [86–88]. To date, a few of these AI algorithms have been approved by the Food and Drugs Administration (FDA) [84,89]. One of them is the PixelShine algorithm which is a software technology trained at pixel level to detect voxel patterns at different resolution scales to determine whether a pattern is noise or a relevant structure. One of the main advantages of these algorithms is that the training is performed a priori on a multitude of iterations and that no computation is needed for the implementation. Also, in contrast to other techniques, the AI algorithms can be used post-processing and can therefore be applied to datasets that are already reconstructed using FBP and IR. Although research data is still scarce, these characteristics provide the potential to decrease radiation doses further while preserving or even improving the image quality.

Maxillofacial injury is a frequent presentation in the emergency department which means physicians are faced with making a decision regarding the necessity of diagnostic imaging for each patient. Although various radiological imaging modalities are widely accessible in today's emergency departments, a full physical examination of each maxillofacial injury patient is required to optimize the clinical workflow and to reduce unnecessary radiation exposure and health care costs. If radiological imaging is necessary, the "as low as reasonably achievable" (ALARA) principle should be adhered to and, with respect to CT, the various technological advances should be considered to minimize each individual patient's exposure to radiation.

Aim and outline of the thesis

The overall aim of this thesis is to provide evidence-based clinical and radiological recommendations for the diagnostic management of maxillofacial trauma patients. Our goal was to evaluate the diagnostic accuracy of physical examination findings to produce a clinical decision aid for maxillofacial trauma and to elaborate the potential of novel reconstruction algorithms for image quality optimization of CT datasets.

Part I: Clinical considerations

The first part of this thesis focuses on the predictive value of physical examination findings for patients suspected of midfacial or mandibular fractures. In **Chapter 2**, a systematic review is described on the best available evidence on how individual physical examination findings and clinical decisions aids can be used to identify patients at risk of midfacial fractures. In **Chapter 3**, we aim to study the diagnostic accuracy of physical examination findings from a large retrospective cohort of patients suspected of midfacial or mandibular fractures and had undergone radiological imaging of the maxillofacial region. **Chapter 4** focuses on the identification of emergency department patients with a low at risk of midfacial and mandibular fractures. The aim was a prospective multicentre observational cohort study of all consecutive emergency department patients with a midfacial or mandibular trauma in which the physical examination was standardized for each patient. This group was referred to as REDUCTION cohort which stands for "*RED*ucing *U*nnecessary *C*omputed *T*omography *I*n *M*axill*O*facial I*N*jury". Consequently, **Chapter 4a** presents a clinical decision aid constructed specifically for midfacial and mandibular trauma patients, with the focus being on ruling out patients with midfacial or mandibular fractures. Such a clinical decision aid could help in reducing unnecessary radiological imaging and, thereby, radiation dose and associated health care costs. **Chapter 4b** presents a clinical decision aid constructed to single out patients with midfacial or mandibular fractures that require treatment. This category of patients is especially important because of the significant functional and aesthetic consequences when these particular fractures are missed. In **Chapter 5**, we identified the conventional and electric bike related accident patients among the REDUCTION cohort, and the incidence and severity of the midfacial and mandibular fractures sustained by these patients.

Part II: Radiological advancements

The second part of this thesis focuses on radiological imaging, image quality optimization of CT datasets, and structural similarity analysis of midfacial fractures. Studying image quality optimization requires patients to be subjected to unnecessary radiation exposure. Hence, an experimental approach was used in which zygomaticomaxillary fractures were inflicted on human cadaver specimens artificially. Using this approach we were able to repeat data acquisition with varying scan parameters. **Chapter 6** compares low dose CT and conventional radiography for the diagnosis of zygomaticomaxillary fractures. Although low dose CT might combine the advantages of a CT and conventional radiography, it is unclear to what extent low dose CT images are better than conventional radiography. A study is described in which radiologist, radiographer and oral and maxillofacial surgeon preferences were assessed by means of a forced choice between low dose CT and conventional radiography images. **Chapter 7** focuses on the diagnostic reliability of reduced CT and CBCT radiation doses for the identification of individual fracture locations of the zygomaticomaxillary complex. Blinded randomized image assessments were organized in which the presence of fracture locations, as reported by radiologists and oral and maxillofacial surgeons, were compared to an open surgical approach used as a gold standard. In addition to studies focusing on radiation dose reduction, **Chapter 8** describes image quality optimization using iterative reconstructions and deep learning algorithms. We conducted noise related image quality measurements of bone and soft tissue datasets to assess the potential of these algorithms to maintain image quality after substantial radiation dose reduction. Finally, the feasibility of the structural similarity index measure is studied in **Chapter 9** as an alternative outcome of image quality for small non dislocated zygomaticomaxillary complex fractures. The aim was to study how radiation dose reduction, iterative reconstruction strength and a deep learning algorithm affect the structural image quality and the fracture characteristics of midfacial fractures.

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PART I

Clinical considerations

2

CHAPTER 2

Diagnostic accuracy of physical examination findings for midfacial fractures: a systematic review and meta-analysis

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Submitted
Adapted version of the manuscript

Abstract

Objective: To conduct a systematic review and meta-analysis to assess the diagnostic accuracy of physical examination findings and related clinical decision aids for midfacial fractures in comparison to Computed Tomography and Cone Beam Computed Tomography.

Methods: A systematic review was performed by searching the MEDLINE, Cochrane, EMBASE, and CINAHL databases. Risk of bias was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 tool. Pooled sensitivity, specificity, and diagnostic odds ratios with the corresponding 95% confidence intervals were calculated for each physical examination finding and reported clinical decision aids.

Results: After screening 2367 records, 12 studies were included. High risk of patient selection bias was detected in three studies (25%). Additionally, high concerns regarding applicability were found for the patient selection in five studies (41.7%), and for the reference standard in eleven studies (91.7%). Of the total 42 individual physical examination findings, only 31 were suitable for a meta-analysis. High specificity and low sensitivity was found for most findings. The pooled diagnostic odds ratio ranged from to 1.07 to 11.38. Clinical decision aids were reported by 8 studies, but none were constructed specifically for midfacial fractures.

Conclusion: Based on the current available evidence, the absence of physical examination findings can successfully identify patients who do not have a midfacial fracture, but the presence of individual findings does not necessarily mean that the patient has a midfacial fracture. Although various clinical decision aids were presented, none focused on exclusively midfacial fractures.

Introduction

Midfacial trauma is a frequent cause for presentation at the emergency department [1–3]. The epidemiology of midfacial fractures varies depending on the population studied and may be the result of cultural, social and environmental differences [4–6]. Leading causes include activities of daily living, sports, assault and traffic related accidents [4,6]. Knowledge of these epidemiological properties may help the emergency physician to deliver more accurate care to the patients [5]. The assessment of midfacial trauma can be particularly challenging in a coexisting multi-trauma setting [5,7–9]. Moreover, midfacial fractures present themselves with varying degrees of severity ranging from non-dislocated common nasal fractures to gross comminution in Le Fort type fractures in which patients require immediate airway control due to midface instability and oropharyngeal obstruction [10–12]. Upon entering the emergency department, each trauma patient is assessed by the principles of Advanced Trauma Life Support (ATLS) to resuscitate and identify all the potential injuries, including fractures in the midfacial region [11–13].

The anatomy of the midface is known for its complexity [14]. The midfacial skeleton is often conceptualized as a framework of buttresses that are responsible for the width and height of the facial profile and establishes functional support for the dental arch and globe [14–16]. As a consequence, the midface is particularly known for its specific physical examination findings. Zygomaticomaxillary complex fractures, for example, are associated with sensory disturbances due to compression of the infra-orbital nerve [17–19]. Also, orbital floor fractures are known to cause entrapment of the inferior rectus muscle leading to upward gaze limitations and diplopia [20]. In addition, the broad range of potential fracture patterns, including frontal sinus, maxillary sinus, nasal bone, nasoorbitoethmoid complex, Le Fort I, II, III type and maxillary dentoalveolar complex fractures can complicate the physical examination [6,21]. Understanding these fracture patterns is necessary as they are related to particular physical examination findings which are used to guide the need for radiological imaging.

Computed tomography (CT) and Cone Beam Computed Tomography (CBCT) are considered the gold-standard imaging modalities for the diagnosis of midfacial fractures [2,5,22–27]. The scanners produce volume datasets with submillimetre-sized voxels in all dimensions [22,28]. The image data can be used for orthogonal plane reconstruction and three-dimensional volume rendering [29–32]. Both scanning systems area associated with risks related to exposure to ionizing radiation [25,29,33–37], which is of concern because of the exponential increase in the use of these systems over the last few decades. The estimated effective radiation dose of scan protocols for midface trauma is considered to be 0.9 to 3.6 mSv [25,36,38]. The effective dose of a CBCT is known to be lower, ranging from 0.08 to 0.21 mSv on average, depending on the field of view that is used [34]. However, the effective dose of both a CT and CBCT can vary significantly based on a multitude of factors such as the system type, scan range, size of the patient and scan protocol parameters [25,34,36,39]. Hence, the interest in investigating whether physical examinations can be used to diagnose a fracture so as to reduce unnecessary imaging, health care costs and exposure to ionizing radiation [40,41].

Although oral and maxillofacial surgeons are specifically trained to assess maxillofacial trauma patients, the initial diagnostic management is mostly performed by emergency physicians and specialized trauma surgeons [1,5]. An awareness of how physical examination findings can predict midfacial fractures would enable adequate stratification of patients requiring radiological imaging. To date, no systematic review has been published on this topic. The aim of this systematic review and meta-analysis, thus, was to assess the diagnostic accuracy of physical examination findings and related clinical decision aids, in comparison to CT and CBCT, for the diagnosis of midfacial fractures.

Material and Methods

Protocol

This systematic review was conducted following the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions and reported according to the Preferred Reporting Items for a Systematic Review and Meta-Analysis of Diagnostic Test Accuracy Studies (PRISMA-DTA) [42,43]. The study protocol was registered in the international prospective register of systematic reviews (PROSPERO, registration number CRD210040).

Search strategy

An initial literature search was conducted on March 11, 2020 and updated on March 23, 2021 using the electronic databases of MEDLINE, EMBASE, CINAHL and Cochrane Controlled Trial Register. Relevant search terms regarding midfacial fractures, physical examination findings and their diagnostic accuracy were used and matched to relevant MeSH (MEDLINE, Cochrane) and EMTREE (EMBASE) terms, and to free text words according to the syntax rules of each database. The search strategy was conducted in collaboration with a medical information specialist. In addition, the references of the included studies were screened.

Study eligibility

The results of the literature search were imported into an EndNote X9.2 software environment (Clarivate Analytics, Philadelphia, Pennsylvania, USA) and duplicates were removed. The research question was defined using the PICOS format and, subsequently, the inclusion and exclusion criteria were determined (Table 1). The publications were assessed for eligibility in two rounds. In the first round, two reviewers (RR and MD) independently assessed the titles and abstracts according to the inclusion and exclusion criteria. The publications were allocated as 'included' or 'excluded' and in case of an indecisive verdict, publications were included for full text assessment. Publications selected for full text selection were independently assessed by the same two reviewers for final inclusion using the same selection criteria. After each selection round, discrepancies between the two reviewers were resolved in a consensus meeting. A third reviewer (BvM) was consulted to give a final judgement on any persisting disagreement. The interobserver agreement was calculated as the percentage of agreement, Cohen's κ coefficient and Gwet's AC1 statistic [44–46].

Risk of bias assessment

The risk of bias of all the included studies was independently assessed by the same two reviewers using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool [47]. This tool consists of four key domains covering patient selection, index test, reference standard, and flow and timing each including signaling questions focusing on the judgment of bias and concerns regarding applicability. Disagreements were resolved through discussion.

Data collection

Data were extracted using a pre-defined standardized form including the year of publication, study design, study set-up, single-center or multi-center study design, trauma center level according to the American College of Surgeons classification [48], the studies patient population, patient demographics, level of consciousness according the Glasgow Coma Scale (GCS), the reference test used, fracture prevalence, the type of fracture outcome, reported physical examination findings (i.e., any finding related to the visual appearance of the patient, outcomes of the nasal and ocular assessment, intra-oral examination, sensory disturbances, and to palpation of the midface) and any proposed clinical decision aids developed from a combination of the reported physical examination findings. Only those physical examination findings that were specifically related to the midfacial region were collected. Two by two tables were constructed. If insufficient data were reported to produce two-by-two tables, backward calculations were performed using the provided sensitivity, specificity, pre-test probability, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio with the corresponding 95% confidence intervals [49]. The authors of the included studies were contacted in case of missing data or inconsistencies in the calculations by means of a minimum of two email attempts.

Table 1: Inclusion and exclusion criteria

Inclusion criteria
Population
1. Patients with a midfacial trauma
2. Mean or median age of patients ≥ 16 years
3. Admission to emergency department or outpatient clinic
Index test
4. Physical examination findings dedicated to the midfacial region and diagnostic accuracy for midfacial fractures (e.g., any changes to the visual appearance, findings related to the nasal and ocular assessment, intra-oral related changes, dental and occlusal abnormalities, functional changes and findings related to palpation).
Type of outcome measures
5. Midfacial fractures (e.g., frontal sinus, maxillary sinus, nasal, nasoorbitoethmoid, zygomaticomaxillary, orbital, maxillary or Le Fort type fractures) diagnosed using: (a) Computed Tomography or (b) Cone Beam Computed Tomography (CBCT)
Data
6. Availability of sensitivity, specificity, pre-test probability, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio or a ROC/AUC curve or enough data should be available to construct two-by-two contingency tables to compute any of these statistics
7. Study design being either (a) Cohort, (b) Case control, (c) Case report (≥ 10 patents), (d) Diagnostic Randomized Controlled Trials
8. Full text availability
9. No language or time restrictions

Exclusion criteria
1. Case reports (< 10 patients), expert opinions, conference abstracts, reviews and systematic reviews

Statistical analysis

Interobserver agreement was calculated using the Statistical Package for the Social Sciences version 23 (SPSS, IBM Corp., Armonk, New York, USA). A meta-analysis, to calculate the pooled sensitivity, specificity and diagnostics odds ratio using R statistics package for Meta-Analysis of Diagnostic Accuracy (MADA version 0.5.10, R Foundation for Statistical Computing, Vienna, Austria) [50], was performed for all the physical examination findings that were reported more than once for the same fracture outcome. Physical examination findings were only combined if the reported phraseology was plausibly about the same finding (e.g., infra-orbital nerve hypoesthesia and reduced sensation in the maxillary division of the trigeminal nerve). Regarding the diagnostic odds ratio calculations, 0.5 was added to all the cells of the contingency table in case of a zero cell count [51]. Testing for publication bias was performed using Deek's funnel plots asymmetry test by a regression of the diagnostic log odds ratio against the inverse of the square root of the effective sample size [52,53]. The statistical significance of the slope coefficient was defined as a p-value < 0.05. A meta-regression analysis was undertaken if more than ten studies reported physical examination findings with the same outcome.

Results

Study identification and selection

The initial and updated literature search identified a total of 3171 publications (figure 1). After removing the duplicates, 2367 publications were screened by title and abstract. The percentage of agreement, kappa and Gwet's AC1 statistic were 98%, 0.55 and 0.98, respectively. A remaining total of 32 publications was eligible for full text screening. Twenty articles were excluded because they did not fulfil the inclusion or exclusion criteria. The percentage of agreement, kappa and Gwet's AC1 statistic of the full text selections were 97%, 0.93 and 0.94, respectively. After the second round, a total of 12 publications were finally included for both qualitative and quantitative syntheses. It was not necessary to consult the third reviewer for a consensus.

Methodological quality

Figure 2 presents the quality assessment of the included studies according to the QUADAS-2 tool. High risk of bias in patient selection was detected in three studies (25%). Unclear risk of bias was found for the 'index test' (75%), 'references test' (50%) and 'flow and timing' (75%) domains of the majority of the studies. Additionally, high concerns regarding applicability were found for 'patient selection' in five studies (41.7%) and 'reference standard' in eleven studies (91.7%), whereas the 'index test' was unclear for most of the studies (75%).

Table 2: Study characteristics

Author	Year	Study design	Study set-up	Setting	Center level*	Patient population	Patients (n)	Male/ female (n/n)	Age median or mean (yr.)	Age range (yr.)	GCS	Reference test	Fracture prev. (n (%))	Fracture outcomes
Holmgren et al. [61]	2005	Retro.	Single-center	ED	Level I	Head and orbital trauma patients	777	564/213	32.4 (mean)	-	-	CT	477 (61.4)	Midfacial and mandibular fractures
Exadaktylos et al. [62]	2005	Prosp.	Single-center	ED	Level I	Head and orbital trauma patients	600	440/160	45.3 (mean)	12-86	3-15	CT	118 (19.7)	Orbital fractures
Sitzman et al. [55]	2011	Retro.	Single-center	ED	Level I	Maxillofacial trauma patients	525	380/145	28 (median)	1-93	3-15	CT	332 (63.2)	Midfacial and mandibular fractures
Yadav et al. [59]	2012	Prosp.	Two-center	ED	Level I/II	Orbital trauma patients	2262	1544/718	38 (median)	-		CT	360 (15.9)	Orbital fractures
Smith et el. [54]	2013	Case-control	Single-center	ED	Level I	Midfacial trauma patients	166	105/61	47-50 (median)	18-?	9-15	CT	83 (50)	Midfacial fractures
Büttner et al. [64]	2014	Retro.	Single-center	ED	Level I	Minor head injury patients with a black eye	1676	1102/574	51 (mean)	16-99	13-15	CT	1144 (68.3)	Midfacial and mandibular fractures
Sitzman et al. [56]	2015	Retro.	Single-center	ED	Level I	Maxillofacial trauma patients	179	132/47	31 (median)	0-91	3-15	CT	116 (64.8)	Midfacial and mandibular fractures

Table 2 *(continued)*

Author	Year	Study design	Study set-up	Setting	Center level*	Patient population	Patients (n)	Male/ female (n/n)	Age median or mean (yr.)	Age range (yr.)	GCS	Reference test	Fracture prev. (n (%))	Fracture outcomes
Timashpolksy et al. [66]	2016	Prosp.	Single-center	ED	Level I	Maxillofacial trauma patients	57	44/13	40.04 (mean)	-	-	CT	52 (91.2)	Midfacial and mandibular fractures
Scolozzi et al. [60]	2017	Retro.	Single-center	ED	Level II	Orbital trauma patients	912	632/280	46.6 (mean)	-	-	CT	701 (76.9)	Orbital fractures
Huang et al. [65]	2017	Retro.	Single-center	ED	Level II	Traumatic brain injury patients with facial trauma	1649	918/713	53.1 (mean)	20-101	3-15	CT	200 (13.8)	Midfacial and mandibular fractures
Harrington et al. [58]	2018	Retro.	Single-center	ED	Level I	Maxillofacial trauma patients	167	105/62	50.5 (mean)	-	3-15	CT	99 (59.3)	Midfacial and mandibular fractures
Allison et al. [63]	2019	Retro.	Single-center	ED	Level III	Head and orbital trauma patients	47	41/6	40.6 (mean)	-	-	CT	35 (74.5)	Orbital fractures

Abbreviations: GCS Glasgow Coma Scale; Prev. Prevalence; Retro. Retrospective cohort study; Prosp. Prospective cohort study; ED Emergency Department; CT Computed Tomography

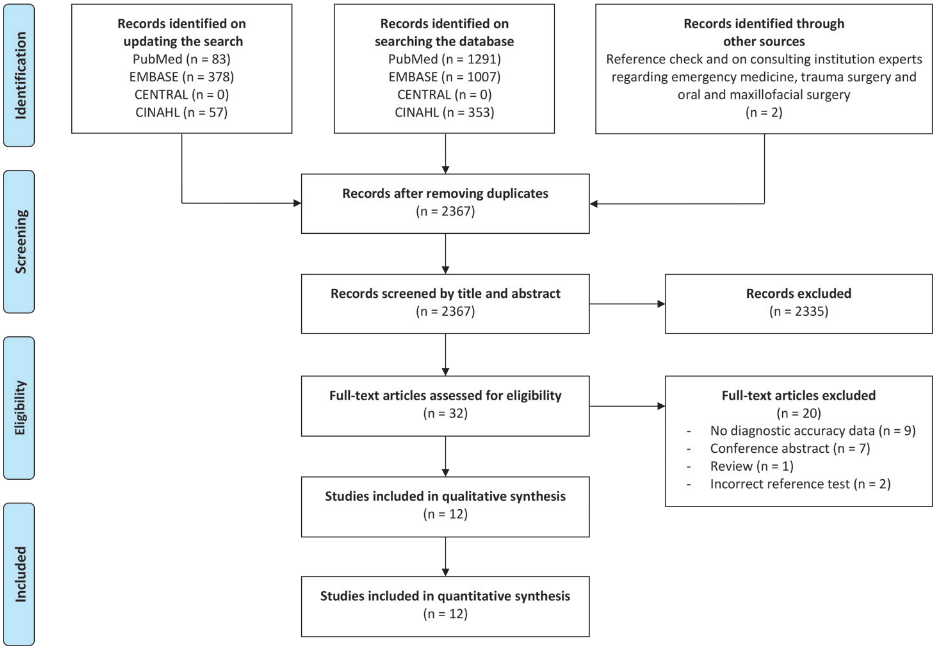

Figure 1: Flowchart of the study identification and selection process.

Study characteristics

The included publications consisted of eight retrospective studies, three prospective studies and one case control study. All 12 studies included emergency department patients; eleven studies investigated patients from a single center and one study had patients from two-centers. Among the single-center studies, eight studies included patients from level I trauma centers, two studies included patients from level II trauma centers and one study included patients from a level III center. The two-center study included patients from both a level I and II trauma center.

Patient characteristics

The number of patients in the studies ranged from 47 to 2262, resulting in a total of 9017 patients of whom 6007 were male and 3010 female. The reported mean age was 37.1 years, and the reported median age ranged from 28 to 50. The study population included midfacial trauma patients (n=1) [54], maxillofacial trauma patients (n=4) [55–58], orbital trauma patients (n=2) [59,60], head and orbital trauma patients (n=3) [61–63], minor head injury patients with a black eye (n=1) [64], and traumatic brain injury patients with facial trauma (n=1) [65]. All the studies had used CT as a reference test and thus no studies were included where CBCT was used as a reference test. Any midfacial fracture was used as an outcome by one study [54], whereas any midfacial or mandibular fracture was used as an outcome by seven studies [55–58,61,64,65], and orbital fracture was used as an outcome by four studies [59,60,62,63]. In one study, midfacial and mandibular fracture outcomes were stratified as frontal sinus, zygoma, orbital floor, naso-ethmoidal, nasal, maxilla and mandibular fractures [57]. The fracture prevalence ranged from 13.8% to 91.2%, resulting in an average of 41.2%.

Physical examination findings

A total of 42 distinct physical examination findings were identified and categorized into 5 distinct groups: visual appearance, nasal assessment, ocular assessment, intra-oral assessment, and findings related to functional and palpation assessment. The diagnostic accuracy of each individual physical examination finding is presented in Table 3. For 30 findings, the diagnostic accuracy was reported in more than one study. Meta-analysis was feasible for a total of 31 physical examination findings (Figure 3).

Findings related to visual appearance

A total of 24 distinct physical examination findings were identified as being related to the visual appearance of the patient and reported 52 times in the included studies [54,55,66,56,58–63,65]. The outcomes of the findings were any midfacial or mandibular fracture (n=40), any midfacial fracture (n=2), any orbital fracture (n=7), orbital floor fracture (n=1) and zygoma fracture (n=2). The identified findings included swelling, hematoma, laceration, asymmetry, globe position change and malar eminence flattening. Regarding swelling, hematoma and laceration, the diagnostic accuracy was also reported for specific regions of the midfacial skin. For swelling, this included that diagnostic accuracy was also reported for specifically the periorbital region [55,56,58,59]. The region specific findings for hematoma included the forehead [55,56], peri-orbital region [54–56,59–61,63], eyelid [61,62], nasal region [55,56], malar region [55,56], and the facial or scalp region [61]. For laceration, region specific findings included the forehead [54–56,65], peri-orbital region [55,56,59], eyebrow [61], eyelid [61], conjunctiva [61], nasal region [55,56,61], malar region [55,56], peri-oral region [55,56] and the lip [61]. Among the physical examination findings related to swelling, hematoma and laceration, high pooled specificity was found for eyelid hematoma, eyebrow laceration, conjunctival laceration, nasal laceration and malar laceration ranging from 0.19 to 0.98 (Table 3 & Figure 3a). The diagnostic odds ratio for these physical examination findings ranged from 1.10 to 3.48. Regarding asymmetry, globe position change and malar eminence flattening, the specificity, PPV and LR+ were found to be high.

Study	RISK OF BIAS				APPLICABILITY CONCERNS		
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Allison et al. (2019) [63]	-	?	?	?	+	?	+
Büttner et al. (2014) [64]	+	?	?	?	+	?	+
Exadaktylos et al. (2005) [62]	-	-	-	-	+	?	+
Harrington et al. (2018) [58]	-	?	?	?	-	?	+
Holmgren et al. (2005) [61]	?	?	?	?	+	?	+
Huang et al. (2017) [65]	-	?	-	?	+	?	+
Scolozzi et al. (2017) [60]	-	?	?	?	-	-	+
Sitzman et al. (2011) [55]	-	?	-	-	-	?	+
Sitzman et al. (2015) [56]	+	?	-	?	-	?	+
Smith et el. (2013) [54]	+	?	?	?	-	?	-
Timashpolksy et al. (2016) [66]	-	-	-	?	-	-	+
Yadav et al. (2012) [59]	-	-	-	-	-	-	+

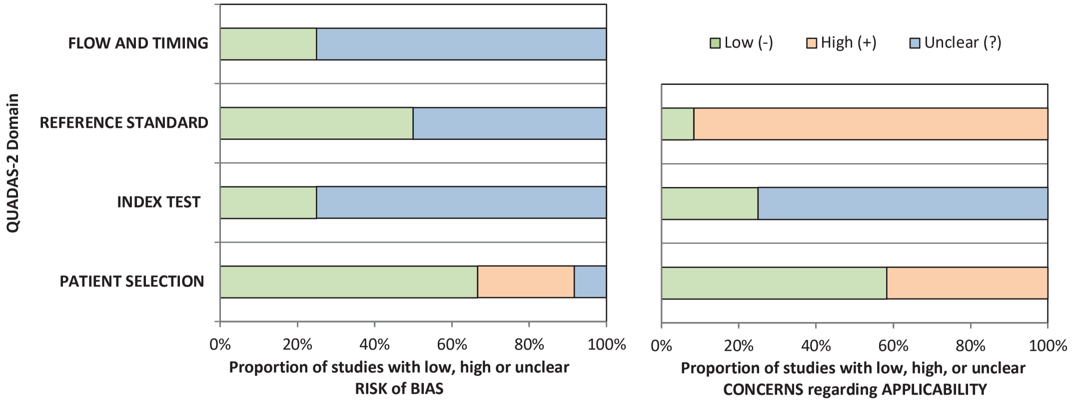

Figure 2: Risk of bias assessment.

Table 3: Diagnostic accuracy of individual physical examination findings

Physical examination finding	Authors and reference	Fracture outcome	Sens. (95% CI)	Spec. (95% CI)	Pre-test prob. (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+ (95% CI)	LR- (95% CI)
Visual appearance									
Swelling	Sitzman et al. [55]	Midfacial and mandibular fractures	81.0 (76.5-84.9)	47.2 (40.2-54.2)	63.2 (59.0-67.3)	72.5 (67.8-76.8)	59.1 (51.2-66.5)	1.5 (1.3-1.8)	0.4 (0.3-0.5)
	Sitzman et al. [56]	Midfacial and mandibular fractures	58.6 (49.5-67.2)	74.6 (62.7-83.7)	64.8 (57.6-71.4)	81.0 (71.3-87.9)	49.5 (39.6-59.4)	2.3 (1.5-3.6)	0.6 (0.4-0.7)
Swelling or hematoma	Timashpolsky et al. [57]	Orbital floor fractures	64.0 (44.5-79.8)	81.3 (64.7-91.1)	43.9 (31.8-56.7)	72.7 (51.8-86.8)	74.3 (57.9-85.8)	3.4 (1.6-7.4)	0.4 (0.3-0.8)
	Timashpolsky et al. [57]	Zygoma fractures	16.7 (5.8-39.2)	84.6 (70.3-92.8)	31.6 (21.0-44.5)	33.3 (12.1-64.6)	68.8 (54.7-80.1)	1.1 (0.3-3.9)	1.0 (0.8-1.3)
Swelling, peri-orbital	Yadav et al. [59]	Orbital fractures	78.3 (73.8-82.3)	43.7 (41.5-46.0)	15.9 (14.5-17.5)	20.9 (18.8-23.1)	91.4 (89.4-93.1)	1.4 (1.3-1.5)	0.5 (0.4-0.6)
Swelling or hematoma, peri-orbital	Harrington et al. [58]	Midfacial and mandibular fractures	47.5 (37.9-57.2)	63.2 (51.4-73.7)	59.3 (51.7-66.4)	65.3 (53.8-75.2)	45.3 (35.6-55.3)	1.3 (0.9-1.9)	0.8 (0.6-1.1)
	Sitzman et al. [55]	Midfacial and mandibular fractures	92.5 (88.7-95.1)	35.5 (29.9-41.5)	50.7 (46.4-54.9)	59.6 (54.8-64.2)	82.1 (74.0-88.1)	1.4 (1.3-1.6)	0.2 (0.1-0.3)
	Sitzman et al. [56]	Midfacial and mandibular fractures	82.8 (74.9-88.6)	34.9 (24.3-47.2)	64.8 (57.6-71.4)	70.1 (61.9-77.1)	52.4 (37.7-66.6)	1.3 (1.0-1.6)	0.5 (0.3-0.8)
Hematoma	Sitzman et al. [55]	Midfacial and mandibular fractures	87.3 (83.3-90.5)	17.1 (12.4-23.0)	63.2 (59.0-67.3)	64.4 (59.9-68.7)	44.0 (33.3-55.3)	1.1 (1.0-1.1)	0.7 (0.5-1.1)
	Sitzman et al. [56]	Midfacial and mandibular fractures	89.7 (82.8-94.0)	22.2 (13.7-33.9)	64.8 (57.6-71.4)	68.0 (60.2-74.8)	53.8 (35.5-71.2)	1.2 (1.0-1.3)	0.5 (0.2-0.9)
Hematoma, forehead	Sitzman et al. [55]	Midfacial and mandibular fractures	28.0 (23.5-33.1)	67.4 (60.5-73.6)	63.2 (59.0-67.3)	59.6 (51.8-67.0)	35.2 (30.5-40.2)	0.9 (0.7-1.1)	1.1 (0.9-1.2)
	Sitzman et al. [56]	Midfacial and mandibular fractures	28.4 (21.0-37.2)	82.5 (71.4-90.0)	64.8 (57.6-71.4)	75.0 (60.6-85.4)	38.5 (30.7-46.9)	1.6 (0.9-3.0)	0.9 (0.7-1.0)
Hematoma, peri-orbital	Allison et al. [63]	Orbital fractures	74.3 (57.9-85.8)	41.7 (19.3-68.0)	74.5 (60.5-84.7)	78.8 (62.2-89.3)	35.7 (16.3-61.2)	1.3 (0.8-2.1)	0.6 (0.3-1.5)
	Holmgren et al. [61]	Midfacial and mandibular fractures	29.4 (25.4-33.6)	85.3 (80.9-88.9)	61.4 (57.9-64.7)	76.1 (69.4-81.7)	43.2 (39.2-47.2)	2.0 (1.5-2.7)	0.8 (0.8-0.9)

Table 3 *(continued)*

Physical examination finding	Authors and reference	Fracture outcome	Sens. (95% CI)	Spec. (95% CI)	Pre-test prob. (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+ (95% CI)	LR- (95% CI)
	Scolozzi et al. [60]	Orbital fractures	95.9 (94.1-97.1)	5.2 (2.9-9.1)	76.9 (74.0-79.5)	77.1 (74.2-79.7)	27.5 (16.1-42.8)	1.0 (1.0-1.0)	0.8 (0.4-1.6)
	Sitzman et al. [55]	Midfacial and mandibular fractures	74.1 (69.1-78.5)	43.0 (36.2-50.1)	63.2 (59.0-67.3)	69.1 (64.1-73.7)	49.1 (41.7-56.6)	1.3 (1.1-1.5)	0.6 (0.5-0.8)
	Sitzman et al. [56]	Midfacial and mandibular fractures	77.6 (69.2-84.2)	41.3 (30.0-53.6)	64.8 (57.6-71.4)	70.9 (62.4-78.1)	50.0 (36.9-63.1)	1.3 (1.1-1.7)	0.5 (0.3-0.9)
	Smith et al. [54]	Midfacial fractures	38.6 (28.8-49.3)	95.2 (88.3-98.1)	50.0 (42.5-57.5)	88.9 (74.7-95.6)	60.8 (52.2-68.7)	8.0 (3.0-21.6)	0.6 (0.5-0.8)
	Yadav et al. [59]	Orbital fractures	75.3 (70.6-79.5)	47.5 (45.2-49.7)	15.9 (14.5-17.5)	21.3 (19.2-23.7)	91.0 (89.1-92.7)	1.4 (1.3-1.5)	0.5 (0.4-0.6)
Hematoma, eyelid	Holmgren et al. [61]	Midfacial and mandibular fractures	2.7 (1.6-4.6)	98.7 (96.6-99.5)	61.4 (57.9-64.7)	76.5 (52.7-90.4)	38.9 (35.5-42.5)	2.0 (0.7-6.2)	1.0 (1.0-1.0)
	Exadaktylos et al. [62]	Orbital fractures	68.6 (59.8-76.3)	94.8 (92.5-96.5)	19.7 (16.7-23.0)	76.4 (67.5-83.5)	92.5 (89.8-94.5)	13.2 (8.9-19.8)	0.3 (0.3-0.4)
Hematoma, nasal	Sitzman et al. [55]	Midfacial and mandibular fractures	24.1 (19.8-29.0)	78.2 (71.9-83.5)	63.2 (59.0-67.3)	65.6 (56.8-73.4)	37.5 (32.9-42.3)	1.1 (0.8-1.5)	1.0 (0.9-1.1)
	Sitzman et al. [56]	Midfacial and mandibular fractures	20.7 (14.3-28.9)	79.4 (67.8-87.5)	64.8 (57.6-71.4)	64.9 (48.8-78.2)	35.2 (27.8-43.4)	1.0 (0.5-1.8)	1.0 (0.9-1.2)
Hematoma, malar	Sitzman et al. [55]	Midfacial and mandibular fractures	34.0 (29.1-39.3)	69.4 (62.6-75.5)	63.2 (59.0-67.3)	65.7 (58.3-72.4)	38.0 (33.1-43.1)	1.1 (0.9-1.4)	1.0 (0.8-1.1)
	Sitzman et al. [56]	Midfacial and mandibular fractures	21.6 (15.0-29.9)	85.7 (75.0-92.3)	64.8 (57.6-71.4)	73.5 (56.9-85.4)	37.2 (29.8-45.3)	1.5 (0.8-3.0)	0.9 (0.8-1.1)
Hematoma, facial or scalp	Holmgren et al. [61]	Midfacial and mandibular fractures	24.9 (21.3-29.0)	47.3 (41.8-53.0)	61.4 (57.9-64.7)	43.0 (37.3-48.8)	28.4 (24.6-32.5)	0.5 (0.4-0.6)	1.6 (1.4-1.8)
Laceration	Harrington et al. [58]	Midfacial and mandibular fractures	42.4 (33.2-52.3)	57.4 (45.5-68.4)	59.3 (51.7-66.4)	59.2 (47.5-69.8)	40.6 (31.3-50.6)	1.0 (0.7-1.4)	1.0 (0.8-1.3)
	Huang et al. [65]	Midfacial and mandibular fractures	98.0 (95.0-99.2)	70.0 (67.6-72.3)	12.1 (10.6-13.8)	31.1 (27.6-34.8)	99.6 (99.0-99.8)	3.3 (3.0-3.5)	0.0 (0.0-0.1)

Table 3 *(continued)*

Physical examination finding	Authors and reference	Fracture outcome	Sens. (95% CI)	Spec. (95% CI)	Pre-test prob. (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+ (95% CI)	LR- (95% CI)
	Sitzman et al. [55]	Midfacial and mandibular fractures	69.3 (64.1-74.0)	40.9 (34.2-48.0)	63.2 (59.0-67.3)	66.9 (61.7-71.6)	43.6 (36.6-50.9)	1.2 (1.0-1.3)	0.8 (0.6-0.9)
	Sitzman et al. [56]	Midfacial and mandibular fractures	70.7 (61.8-78.2)	30.2 (20.2-42.4)	64.8 (57.6-71.4)	65.1 (56.4-72.8)	35.8 (24.3-49.3)	1.0 (0.8-1.2)	1.0 (0.6-1.6)
Laceration, forehead	Huang et al. [65]	Midfacial and mandibular fractures	28.0 (22.2-34.6)	85.5 (83.6-87.2)	12.1 (10.6-13.8)	21.1 (16.6-26.3)	89.6 (87.9-91.1)	1.9 (1.5-2.5)	0.8 (0.8-0.9)
	Sitzman et al. [55]	Midfacial and mandibular fractures	25.6 (21.2-30.6)	71.5 (64.8-77.4)	63.2 (59.0-67.3)	60.7 (52.4-68.4)	35.8 (31.2-40.8)	0.9 (0.7-1.2)	1.0 (0.9-1.2)
	Sitzman et al. [56]	Midfacial and mandibular fractures	20.7 (14.3-28.9)	69.8 (57.6-79.8)	64.8 (57.6-71.4)	55.8 (41.1-69.6)	32.4 (25.1-40.6)	0.7 (0.4-1.2)	1.1 (0.9-1.4)
	Smith et al. [54]	Midfacial fractures	22.9 (15.2-33.0)	90.4 (82.1-95.0)	50.0 (42.5-57.5)	70.4 (51.5-84.1)	54.0 (45.7-62.0)	2.4 (1.1-5.1)	0.9 (0.7-1.0)
Laceration, peri-orbital	Sitzman et al. [55]	Midfacial and mandibular fractures	23.8 (19.5-28.7)	79.8 (73.6-84.9)	63.2 (59.0-67.3)	66.9 (58.0-74.8)	37.8 (33.3-42.6)	1.2 (0.8-1.7)	1.0 (0.9-1.0)
	Sitzman et al. [56]	Midfacial and mandibular fractures	28.4 (21.0-37.2)	71.4 (59.3-81.1)	64.8 (57.6-71.4)	64.7 (51.0-76.4)	35.2 (27.4-43.8)	1.0 (0.6-1.6)	1.0 (0.8-1.2)
	Yadav et al. [59]	Orbital fractures	32.8 (28.1-37.8)	77.4 (75.5-79.3)	15.9 (14.5-17.5)	21.6 (18.3-25.2)	85.9 (84.2-87.5)	1.5 (1.2-1.7)	0.9 (0.8-0.9)
Laceration, eyebrow	Holmgren et al. [61]	Midfacial and mandibular fractures	9.9 (7.5-12.9)	90.0 (86.1-92.9)	61.4 (57.9-64.7)	61.0 (49.9-71.2)	38.6 (35.0-42.2)	1.0 (0.6-1.5)	1.0 (1.0-1.1)
Laceration, eyelid	Holmgren et al. [61]	Midfacial and mandibular fractures	13.2 (10.5-16.5)	87.0 (82.7-90.3)	61.4 (57.9-64.7)	61.8 (52.1-70.6)	38.7 (35.1-42.4)	1.0 (0.7-1.5)	1.0 (0.9-1.1)
Laceration, conjunctival	Holmgren et al. [61]	Midfacial and mandibular fractures	0.6 (0.2-1.8)	99.0 (97.1-99.7)	61.4 (57.9-64.7)	50.0 (18.8-81.2)	38.5 (35.2-42.0)	0.6 (0.1-3.1)	1.0 (1.0-1.0)
Laceration, nasal	Sitzman et al. [55]	Midfacial and mandibular fractures	7.2 (4.9-10.5)	89.1 (83.9-92.8)	63.2 (59.0-67.3)	53.3 (39.1-67.1)	35.8 (31.7-40.2)	0.7 (0.4-1.2)	1.0 (1.0-1.1)
	Sitzman et al. [56]	Midfacial and mandibular fractures	11.2 (6.7-18.2)	87.3 (76.9-93.4)	64.8 (57.6-71.4)	61.9 (40.9-79.2)	34.8 (27.8-42.5)	0.9 (0.4-2.0)	1.0 (0.9-1.1)

Table 3 *(continued)*

Physical examination finding	Authors and reference	Fracture outcome	Sens. (95% CI)	Spec. (95% CI)	Pre-test prob. (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+ (95% CI)	LR- (95% CI)
	Holmgren et al. [61]	Midfacial and mandibular fractures	21.0 (17.6-24.8)	91.3 (87.6-94.0)	61.4 (57.9-64.7)	79.4 (71.5-85.5)	42.1 (38.4-45.9)	2.4 (1.6-3.6)	0.9 (0.8-0.9)
Laceration, malar	Sitzman et al. [55]	Midfacial and mandibular fractures	13.3 (10.0-17.3)	88.6 (83.3-92.4)	63.2 (59.0-67.3)	66.7 (54.7-76.8)	37.3 (33.0-41.8)	1.2 (0.7-1.9)	1.0 (0.9-1.0)
	Sitzman et al. [56]	Midfacial and mandibular fractures	5.2 (2.4-10.8)	92.1 (82.7-96.6)	64.8 (57.6-71.4)	54.5 (28.0-78.7)	34.5 (27.8-42.0)	0.7 (0.2-2.1)	1.0 (0.9-1.1)
Laceration, peri-oral	Sitzman et al. [55]	Midfacial and mandibular fractures	18.1 (14.3-22.6)	88.1 (82.8-91.9)	63.2 (59.0-67.3)	72.3 (61.8-80.8)	38.5 (34.0-43.1)	1.5 (1.0-2.4)	0.9 (0.9-1.0)
	Sitzman et al. [56]	Midfacial and mandibular fractures	12.9 (8.0-20.2)	87.3 (76.9-93.4)	64.8 (57.6-71.4)	65.2 (44.9-81.2)	35.3 (28.2-43.0)	1.0 (0.5-2.3)	1.0 (0.9-1.1)
Laceration, lip	Holmgren et al. [61]	Midfacial and mandibular fractures	26.2 (22.5-30.3)	85.3 (80.9-88.9)	61.4 (57.9-64.7)	74.0 (66.9-80.0)	42.1 (38.2-46.1)	1.8 (1.3-2.4)	0.9 (0.8-0.9)
Asymmetry	Sitzman et al. [55]	Midfacial and mandibular fractures	6.9 (4.7-10.2)	99.0 (96.3-99.7)	63.2 (59.0-67.3)	92.0 (75.0-97.8)	38.2 (34.0-42.5)	6.7 (1.6-28.0)	0.9 (0.9-1.0)
	Sitzman et al. [56]	Midfacial and mandibular fractures	6.0 (3.0-11.9)	95.2 (86.9-98.4)	64.8 (57.6-71.4)	70.0 (39.7-89.2)	35.5 (28.7-43.0)	1.3 (0.3-4.7)	1.0 (0.9-1.1)
Globe position change	Allison et al. [63]	Orbital fractures	17.1 (8.1-32.7)	100.0 (75.7-100.0)	74.5 (60.5-84.7)	100.0 (61.0-100.0)	29.3 (17.6-44.5)	∞	0.8 (0.7-1.0)
Malar eminence flattening	Timashpolsky et al. [57]	Zygoma fractures	72.2 (49.1-87.5)	94.9 (83.1-98.6)	31.6 (21.0-44.5)	86.7 (62.1-96.3)	88.1 (75.0-94.8)	14.1 (3.5-56.0)	0.3 (0.1-0.6)
Nasal assessment									
Epistaxis	Büttner et al. [64]	Midfacial and mandibular fractures	15.6 (13.6-17.8)	95.5 (93.4-96.9)	68.3 (66.0-70.4)	88.1 (82.9-91.9)	34.5 (32.1-36.9)	3.4 (2.3-5.2)	0.9 (0.9-0.9)
	Huang et al.[65]	Midfacial and mandibular fractures	25.0 (19.5-31.4)	99.3 (98.7-99.6)	12.1 (10.6-13.8)	83.3 (72.0-90.7)	90.6 (89.0-91.9)	36.2 (18.7-70.3)	0.8 (0.7-0.8)
	Sitzman et al. [55]	Midfacial and mandibular fractures	31.9 (27.1-37.1)	87.6 (82.2-91.5)	63.2 (59.0-67.3)	81.5 (74.0-87.3)	42.8 (38.0-47.7)	2.6 (1.7-3.9)	0.8 (0.7-0.9)

Table 3 *(continued)*

Physical examination finding	Authors and reference	Fracture outcome	Sens. (95% CI)	Spec. (95% CI)	Pre-test prob. (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+ (95% CI)	LR- (95% CI)
	Sitzman et al. [56]	Midfacial and mandibular fractures	29.3 (21.8-38.2)	77.8 (66.1-86.3)	64.8 (57.6-71.4)	70.8 (56.8-81.8)	37.4 (29.6-45.9)	1.3 (0.8-2.3)	0.9 (0.8-1.1)
	Smith et al. [54]	Midfacial fractures	22.9 (15.2-33.0)	96.4 (89.9-98.8)	50.0 (42.5-57.5)	86.4 (66.7-95.3)	55.6 (47.4-63.4)	6.3 (1.9-20.6)	0.8 (0.7-0.9)
	Yadav et al. [59]	Orbital fractures	22.5 (18.5-27.1)	86.5 (84.9-88.0)	15.9 (14.5-17.5)	24.0 (19.7-28.8)	85.5 (83.9-87.0)	1.7 (1.3-2.1)	0.9 (0.8-0.9)
Ocular assessment									
Subconjunctival hemorrhage	Allison et al. [63]	Orbital fractures	45.7 (30.5-61.8)	91.7 (64.6-98.5)	74.5 (60.5-84.7)	94.1 (73.0-99.0)	36.7 (21.9-54.5)	5.5 (0.8-37.1)	0.6 (0.4-0.8)
	Büttner et al. [64]	Midfacial and mandibular fractures	16.3 (14.3-18.6)	90.4 (87.6-92.6)	68.3 (66.0-70.4)	78.6 (72.9-83.3)	33.4 (31.1-35.9)	1.7 (1.3-2.3)	0.9 (0.9-1.0)
	Holmgren et al. [61]	Midfacial and mandibular fractures	8.8 (6.6-11.7)	96.0 (93.1-97.7)	61.4 (57.9-64.7)	77.8 (65.1-86.8)	39.8 (36.3-43.4)	2.2 (1.2-4.1)	0.9 (0.9-1.0)
	Sitzman et al. [55]	Midfacial and mandibular fractures	31.3 (26.6-36.5)	86.5 (81.0-90.6)	63.2 (59.0-67.3)	80.0 (72.3-86.0)	42.3 (37.5-47.2)	2.3 (1.6-3.4)	0.8 (0.7-0.9)
	Sitzman et al. [56]	Midfacial and mandibular fractures	33.6 (25.7-42.6)	88.9 (78.8-94.5)	64.8 (57.6-71.4)	84.8 (71.8-92.4)	42.1 (34.1-50.6)	3.0 (1.4-6.4)	0.7 (0.6-0.9)
	Timashpolsky et al. [57]	Orbital floor fractures	76.0 (56.6-88.5)	90.6 (75.8-96.8)	43.9 (31.8-56.7)	86.4 (66.7-95.3)	82.9 (67.3-91.9)	8.1 (2.7-24.3)	0.3 (0.1-0.5)
	Timashpolsky et al. [57]	Zygoma fractures	55.6 (33.7-75.4)	69.2 (53.6-81.4)	31.6 (21.0-44.5)	45.5 (26.9-65.3)	77.1 (61.0-87.9)	1.8 (1.0-3.4)	0.6 (0.4-1.1)
	Yadav et al. [59]	Orbital fractures	31.4 (26.8-36.4)	87.3 (85.8-88.7)	15.9 (14.5-17.5)	31.9 (27.3-36.9)	87.1 (85.5-88.5)	2.5 (2.0-3.0)	0.8 (0.7-0.8)
Hyphema	Yadav et al. [59]	Orbital fractures	4.7 (3.0-7.4)	97.6 (96.8-98.2)	15.9 (14.5-17.5)	27.0 (17.6-39.0)	84.4 (82.8-85.9)	2.0 (1.1-3.4)	1.0 (1.0-1.0)
Diplopia	Allison et al. [63]	Orbital fractures	42.9 (28.0-59.1)	83.3 (55.2-95.3)	74.5 (60.5-84.7)	88.2 (65.7-96.7)	33.3 (19.2-51.2)	2.6 (0.7-9.6)	0.7 (0.5-1.0)

Table 3 *(continued)*

Physical examination finding	**Authors and reference**	**Fracture outcome**	**Sens. (95% CI)**	**Spec. (95% CI)**	**Pre-test prob. (95% CI)**	**PPV (95% CI)**	**NPV (95% CI)**	**LR+ (95% CI)**	**LR- (95% CI)**
	Büttner et al. [64]	Midfacial and mandibular fractures	15.0 (13.1-17.2)	98.3 (96.8-99.1)	68.3 (66.0-70.4)	95.0 (90.8-97.4)	35.0 (32.6-37.4)	8.9 (4.6-17.2)	0.9 (0.8-0.9)
	Scolozzi et al. [60]	Orbital fractures	39.9 (36.4-43.6)	84.8 (79.4-89.0)	76.9 (74.0-79.5)	89.7 (85.9-92.6)	29.8 (26.3-33.6)	2.6 (1.9-3.7)	0.7 (0.7-0.8)
	Sitzman et al. [55]	Midfacial and mandibular fractures	7.2 (4.9-10.5)	95.9 (92.0-97.9)	63.2 (59.0-67.3)	75.0 (57.9-86.7)	37.5 (33.4-41.9)	1.7 (0.8-3.8)	1.0 (0.9-1.0)
	Sitzman et al. [56]	Midfacial and mandibular fractures	4.3 (1.9-9.7)	100.0 (94.3-100.0)	64.8 (57.6-71.4)	100.0 (56.6-100.0)	36.2 (29.4-43.6)	∞	1.0 (0.9-1.0)
	Yadav et al. [59]	Orbital fractures	3.3 (1.9-5.7)	98.5 (97.8-98.9)	15.9 (14.5-17.5)	29.3 (17.6-44.5)	84.3 (82.8-85.8)	2.2 (1.1-4.2)	1.0 (1.0-1.0)
Extra-ocular movement limitation	Allison et al. [63]	Orbital fractures	25.7 (14.2-42.1)	83.3 (55.2-95.3)	74.5 (60.5-84.7)	81.8 (52.3-94.9)	27.8 (15.8-44.0)	1.5 (0.4-6.2)	0.9 (0.6-1.2)
	Sitzman et al. [55]	Midfacial and mandibular fractures	14.2 (10.8-18.3)	96.4 (92.7-98.2)	63.2 (59.0-67.3)	87.0 (75.6-93.6)	39.5 (35.2-44.0)	3.9 (1.8-8.5)	0.9 (0.8-0.9)
	Sitzman et al. [56]	Midfacial and mandibular fractures	12.1 (7.3-19.2)	98.4 (91.5-99.7)	64.8 (57.6-71.4)	93.3 (70.2-98.8)	37.8 (30.7-45.4)	7.6 (1.0-56.5)	0.9 (0.8-1.0)
	Yadav et al. [59]	Orbital fractures	11.7 (8.7-15.4)	95.9 (94.9-96.7)	15.9 (14.5-17.5)	35.0 (27.1-43.9)	85.2 (83.6-86.6)	2.8 (2.0-4.1)	0.9 (0.9-1.0)
Extra-ocular movement pain	Yadav et al. [59]	Orbital fractures	21.4 (17.5-25.9)	92.1 (90.8-93.2)	15.9 (14.5-17.5)	33.9 (28.1-40.3)	86.1 (84.5-87.5)	2.7 (2.1-3.5)	0.9 (0.8-0.9)
Visual acuity change	Allison et al. [63]	Orbital fractures	20.0 (10.0-35.9)	100.0 (75.7-100.0)	74.5 (60.5-84.7)	100.0 (64.6-100.0)	30.0 (18.1-45.4)	∞	0.8 (0.7-0.9)
	Sitzman et al. [55]	Midfacial and mandibular fractures	9.9 (7.2-13.6)	93.8 (89.4-96.4)	63.2 (59.0-67.3)	73.3 (59.0-84.0)	37.7 (33.5-42.1)	1.6 (0.8-3.0)	1.0 (0.9-1.0)
	Sitzman et al. [56]	Midfacial and mandibular fractures	7.8 (4.1-14.1)	96.8 (89.1-99.1)	64.8 (57.6-71.4)	81.8 (52.3-94.9)	36.3 (29.4-43.8)	2.4 (0.5-11.0)	1.0 (0.9-1.0)

Table 3 *(continued)*

Physical examination finding	Authors and reference	Fracture outcome	Sens. (95% CI)	Spec. (95% CI)	Pre-test prob. (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+ (95% CI)	LR- (95% CI)
Intra-oral assessment									
Laceration, intra-oral	Holmgren et al. [61]	Midfacial and mandibular fractures	28.5 (24.6-32.7)	90.3 (86.5-93.2)	61.4 (57.9-64.7)	82.4 (75.9-87.5)	44.3 (40.4-48.2)	2.9 (2.0-4.3)	0.8 (0.7-0.8)
	Sitzman et al. [55]	Midfacial and mandibular fractures	17.2 (13.5-21.6)	92.7 (88.2-95.6)	63.2 (59.0-67.3)	80.3 (69.6-87.9)	39.4 (35.0-44.0)	2.4 (1.4-4.1)	0.9 (0.8-1.0)
	Sitzman et al. [56]	Midfacial and mandibular fractures	19.0 (12.9-27.0)	95.2 (86.9-98.4)	64.8 (57.6-71.4)	88.0 (70.0-95.8)	39.0 (31.6-46.8)	4.0 (1.2-12.8)	0.9 (0.8-0.9)
Tooth avulsion	Harrington et al. [58]	Midfacial and mandibular fractures	11.1 (6.3-18.8)	100.0 (94.7-100.0)	59.3 (51.7-66.4)	100.0 (74.1-100.0)	43.6 (36.1-51.4)	∞	0.9 (0.8-1.0)
	Huang et al.[65]	Midfacial and mandibular fractures	4.5 (2.4-8.3)	99.2 (98.6-99.5)	12.1 (10.6-13.8)	42.9 (24.5-63.5)	88.3 (86.6-89.7)	5.4 (2.3-12.7)	1.0 (0.9-1.0)
	Sitzman et al. [55]	Midfacial and mandibular fractures	16.6 (13.0-20.9)	97.9 (94.8-99.2)	63.2 (59.0-67.3)	93.2 (83.8-97.3)	40.6 (36.2-45.1)	8.0 (2.9-21.7)	0.9 (0.8-0.9)
	Sitzman et al. [56]	Midfacial and mandibular fractures	11.2 (6.7-18.2)	96.8 (89.1-99.1)	64.8 (57.6-71.4)	86.7 (62.1-96.3)	37.2 (30.2-44.8)	3.5 (0.8-15.2)	0.9 (0.8-1.0)
Malocclusion	Harrington et al. [58]	Midfacial and mandibular fractures	8.1 (4.2-15.1)	100.0 (94.7-100.0)	59.3 (51.7-66.4)	100.0 (67.6-100.0)	42.8 (35.3-50.5)	∞	0.9 (0.9-1.0)
	Sitzman et al. [55]	Midfacial and mandibular fractures	26.2 (21.8-31.2)	92.7 (88.2-95.6)	63.2 (59.0-67.3)	86.1 (78.1-91.6)	42.2 (37.6-47.0)	3.6 (2.1-6.2)	0.8 (0.7-0.9)
	Sitzman et al. [56]	Midfacial and mandibular fractures	19.0 (12.9-27.0)	95.2 (86.9-98.4)	64.8 (57.6-71.4)	88.0 (70.0-95.8)	39.0 (31.6-46.8)	4.0 (1.2-12.8)	0.9 (0.8-0.9)
Functional and palpation assessment									
Facial pain	Sitzman et al. [55]	Midfacial and mandibular fractures	35.2 (30.3-40.5)	68.9 (62.1-75.0)	63.2 (59.0-67.3)	66.1 (58.9-72.7)	38.2 (33.3-43.4)	1.1 (0.9-1.5)	0.9 (0.8-1.1)
	Sitzman et al. [56]	Midfacial and mandibular fractures	44.8 (36.1-53.9)	69.8 (57.6-79.8)	64.8 (57.6-71.4)	73.2 (61.9-82.1)	40.7 (31.9-50.2)	1.5 (1.0-2.3)	0.8 (0.6-1.0)
Infra-orbital nerve paresthesia	Allison et al. [63]	Orbital fractures	25.7 (14.2-42.1)	91.7 (64.6-98.5)	74.5 (60.5-84.7)	90.0 (59.6-98.2)	29.7 (17.5-45.8)	3.1 (0.4-21.9)	0.8 (0.6-1.1)

Table 3 *(continued)*

Physical examination finding	Authors and reference	Fracture outcome	Sens. (95% CI)	Spec. (95% CI)	Pre-test prob. (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+ (95% CI)	LR- (95% CI)
	Büttner et al. [64]	Midfacial and mandibular fractures	22.2 (19.9-24.7)	96.4 (94.5-97.7)	68.3 (66.0-70.4)	93.0 (89.4-95.5)	36.6 (34.1-39.1)	6.2 (3.9-9.8)	0.8 (0.8-0.8)
	Scolozzi et al. [60]	Orbital fractures	31.1 (27.8-34.6)	91.0 (86.4-94.2)	76.9 (74.0-79.5)	92.0 (87.8-94.8)	28.4 (25.2-32.0)	3.5 (2.2-5.4)	0.8 (0.7-0.8)
	Sitzman et al. [55]	Midfacial and mandibular fractures	0.3 (0.1-1.7)	100.0 (98.0-100.0)	63.2 (59.0-67.3)	100.0 (20.7-100.0)	36.8 (32.8-41.0)	∞	1.0 (1.0-1.0)
	Sitzman et al. [56]	Midfacial and mandibular fractures	5.2 (2.4-10.8)	98.4 (91.5-99.7)	64.8 (57.6-71.4)	85.7 (48.7-97.4)	36.0 (29.2-43.5)	3.3 (0.4-26.5)	1.0 (0.9-1.0)
	Timashpolsky et al. [577]	Orbital floor fractures	36.0 (20.2-55.5)	90.6 (75.8-96.8)	43.9 (31.8-56.7)	75.0 (46.8-91.1)	64.4 (49.8-76.8)	3.8 (1.2-12.7)	0.7 (0.5-1.0)
	Timashpolsky et al. [57]	Zygoma fractures	38.9 (20.3-61.4)	87.2 (73.3-94.4)	31.6 (21.0-44.5)	58.3 (32.0-80.7)	75.6 (61.3-85.8)	3.0 (1.1-8.3)	0.7 (0.5-1.0)
	Yadav et al. [59]	Orbital fractures	5.6 (3.6-8.4)	97.5 (96.7-98.1)	15.9 (14.5-17.5)	29.9 (20.2-41.7)	84.5 (82.9-86.0)	2.2 (1.3-3.7)	1.0 (0.9-1.0)
Subcutaneous emphysema	Büttner et al. [64]	Midfacial and mandibular fractures	10.7 (9.0-12.6)	99.6 (98.6-99.9)	68.3 (66.0-70.4)	98.4 (94.3-99.6)	34.1 (31.8-36.5)	28.4 (7.0-114.3)	0.9 (0.9-0.9)
	Scolozzi et al. [60]	Orbital fractures	25.4 (22.3-28.7)	94.8 (90.9-97.1)	76.9 (74.0-79.5)	94.2 (89.9-96.7)	27.7 (24.5-31.0)	4.9 (2.7-8.8)	0.8 (0.7-0.8)
Tenderness on palpation	Timashpolsky et al. [57]	Nasal bone fracture	87.5 (52.9-97.8)	89.8 (78.2-95.6)	14.0 (7.3-25.3)	58.3 (32.0-80.7)	97.8 (88.4-99.6)	8.6 (3.6-20.5)	0.1 (0.0-0.9)
	Yadav et al. [59]	Orbital fractures	72.8 (68.0-77.1)	48.7 (46.5-51.0)	15.9 (14.5-17.5)	21.2 (19.0-23.5)	90.4 (88.5-92.1)	1.4 (1.3-1.5)	0.6 (0.5-0.7)
Palpable step-off	Büttner et al. [64]	Midfacial and mandibular fractures	18.5 (16.4-20.9)	99.8 (98.9-100.0)	68.3 (66.0-70.4)	99.5 (97.4-99.9)	36.3 (33.9-38.8)	98.6 (13.9-701.3)	0.8 (0.8-0.8)
	Harrington et al. [58]	Midfacial and mandibular fractures	5.1 (2.2-11.3)	100.0 (94.7-100.0)	59.3 (51.7-66.4)	100.0 (56.6-100.0)	42.0 (34.6-49.7)	∞	0.9 (0.9-1.0)
	Sitzman et al. [55]	Midfacial and mandibular fractures	41.9 (36.7-47.2)	89.6 (84.5-93.2)	63.2 (59.0-67.3)	87.4 (81.4-91.7)	47.3 (42.2-52.4)	4.0 (2.6-6.2)	0.6 (0.6-0.7)

Table 3 *(continued)*

Physical examination finding	Authors and reference	Fracture outcome	Sens. (95% CI)	Spec. (95% CI)	Pre-test prob. (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+ (95% CI)	LR- (95% CI)
	Sitzman et al. [56]	Midfacial and mandibular fractures	32.8 (24.9-41.7)	93.7 (84.8-97.5)	64.8 (57.6-71.4)	90.5 (77.9-96.2)	43.1 (35.1-51.4)	5.2 (1.9-13.8)	0.7 (0.6-0.8)
	Yadav et al. [59]	Orbital fractures	7.8 (5.4-11.0)	94.7 (93.6-95.7)	15.9 (14.5-17.5)	21.9 (15.6-29.8)	84.4 (82.8-85.9)	1.5 (1.0-2.2)	1.0 (0.9-1.0)
Trismus	Timashpolsky et al. [57]	Zygoma fractures	38.9 (20.3-61.4)	94.9 (83.1-98.6)	31.6 (21.0-44.5)	77.8 (45.3-93.7)	77.1 (63.5-86.7)	7.6 (1.7-32.9)	0.6 (0.4-0.9)
	Yadav et al. [59]	Orbital fractures	3.6 (2.1-6.1)	95.5 (94.5-96.4)	15.9 (14.5-17.5)	13.3 (7.9-21.4)	84.0 (82.4-85.5)	0.8 (0.5-1.4)	1.0 (1.0-1.0)
Mandible locked open	Yadav et al. [59]	Orbital fractures	0.8 (0.3-2.4)	98.6 (97.9-99.0)	15.9 (14.5-17.5)	10.0 (3.5-25.6)	84.0 (82.4-85.5)	0.6 (0.2-1.9)	1.0 (1.0-1.0)
Open fracture	Sitzman et al. [55]	Midfacial and mandibular fractures	6.3 (4.2-9.5)	98.4 (95.5-99.5)	63.2 (59.0-67.3)	87.5 (69.0-95.7)	37.9 (33.8-42.2)	4.1 (1.2-13.5)	1.0 (0.9-1.0)
	Sitzman et al. [56]	Midfacial and mandibular fractures	6.9 (3.5-13.0)	100.0 (94.3-100.0)	64.8 (57.6-71.4)	100.0 (67.6-100.0)	36.8 (30.0-44.3)	∞	0.9 (0.9-1.0)

Abbreviations: Sens. Sensitivity; Spec. Specificity; Pre-test prob. Pre-test probability; PPV Positive Predictive Value; NPV Negative Predictive Value; LR+ Positive Likelihood Ratio; LR- Negative Likelihood Ratio; CI Confidence Interval; ∞ Infinite.

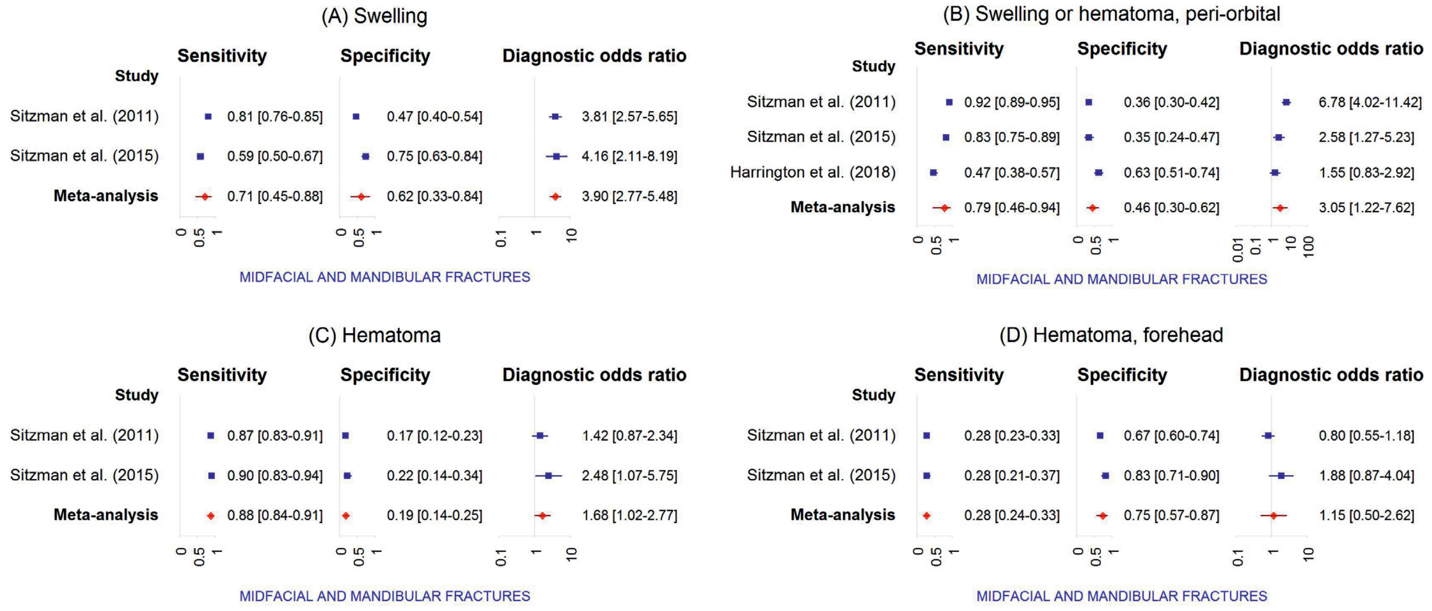

Figure 3a: Forest plots showing study-specific and pooled specificity, sensitivity and diagnostic odds ratio of the physical examination findings related to visual appearance for (a) swelling, (b) peri-orbital swelling or hematoma, (c) hematoma, (d) forehead hematoma, (e) peri-orbital hematoma, (f) nasal hematoma, (g) malar hematoma, (h) laceration, (i) forehead laceration, (j) peri-orbital laceration, (k) nasal laceration, (l) malar laceration, (m) peri-oral laceration, (n) asymmetry in diagnosing midfacial fractures.

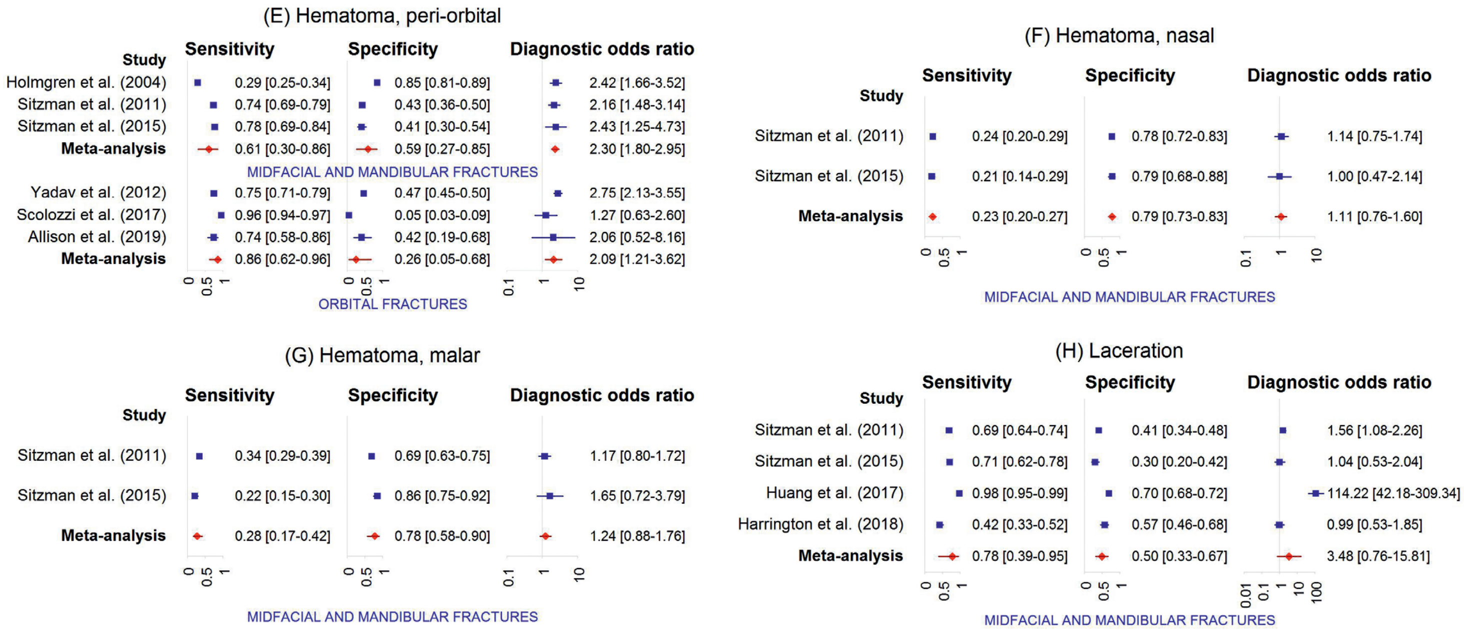

Figure 3a: *(continued)*

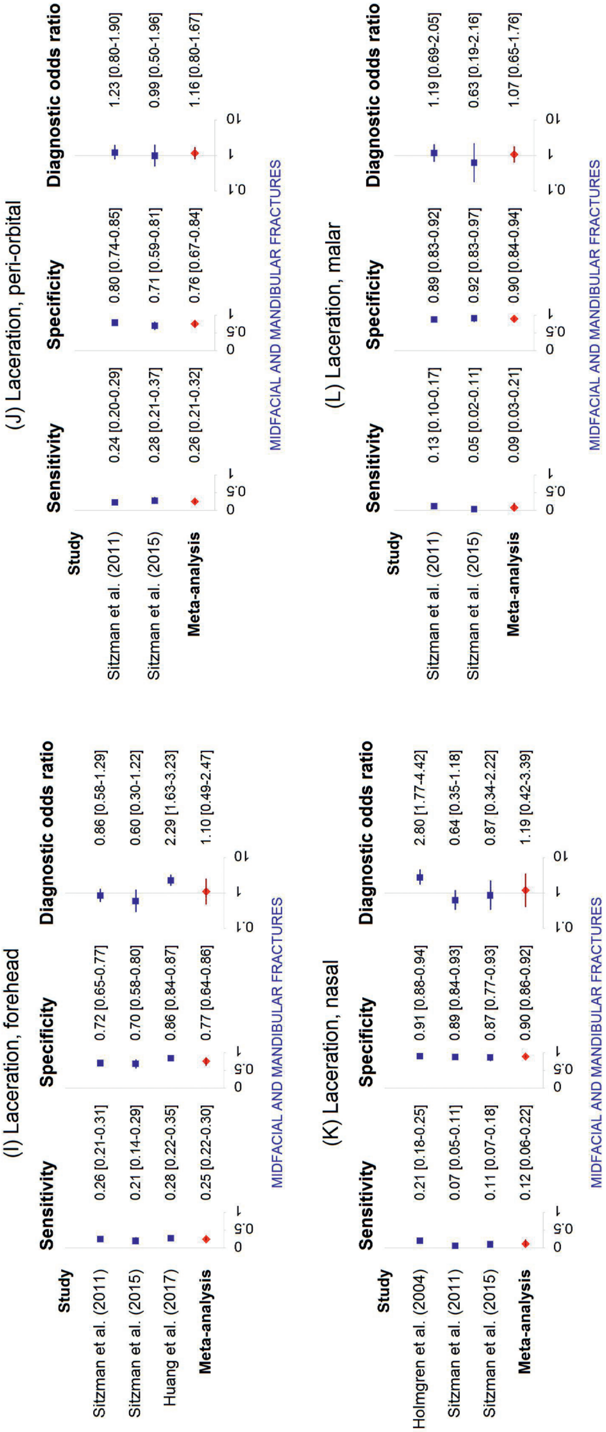

Figure 3a: *(continued)*

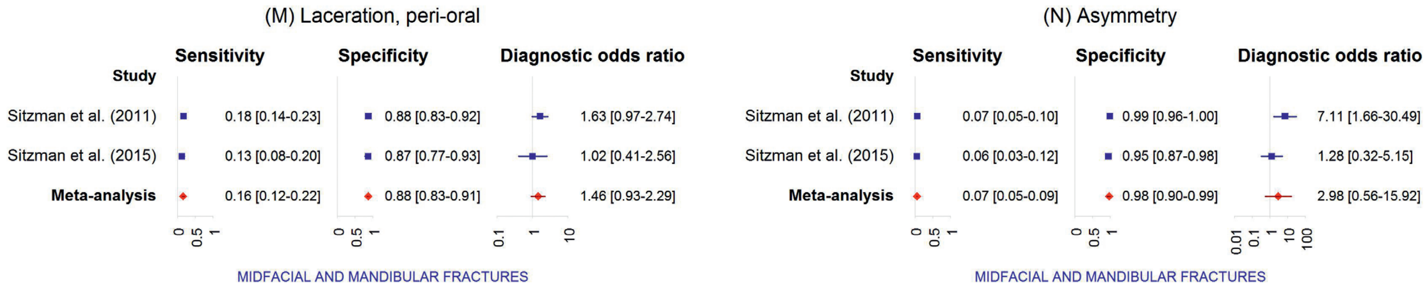

Figure 3a: *(continued)*

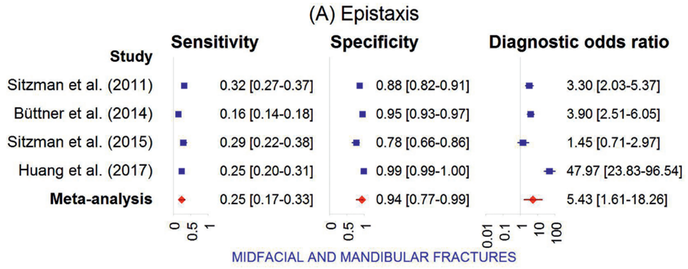

Figure 3b: Forest plots showing study-specific and pooled specificity, sensitivity and diagnostic odds ratio of the physical examination findings related to nasal assessment for (a) epistaxis in diagnosing midfacial fractures.

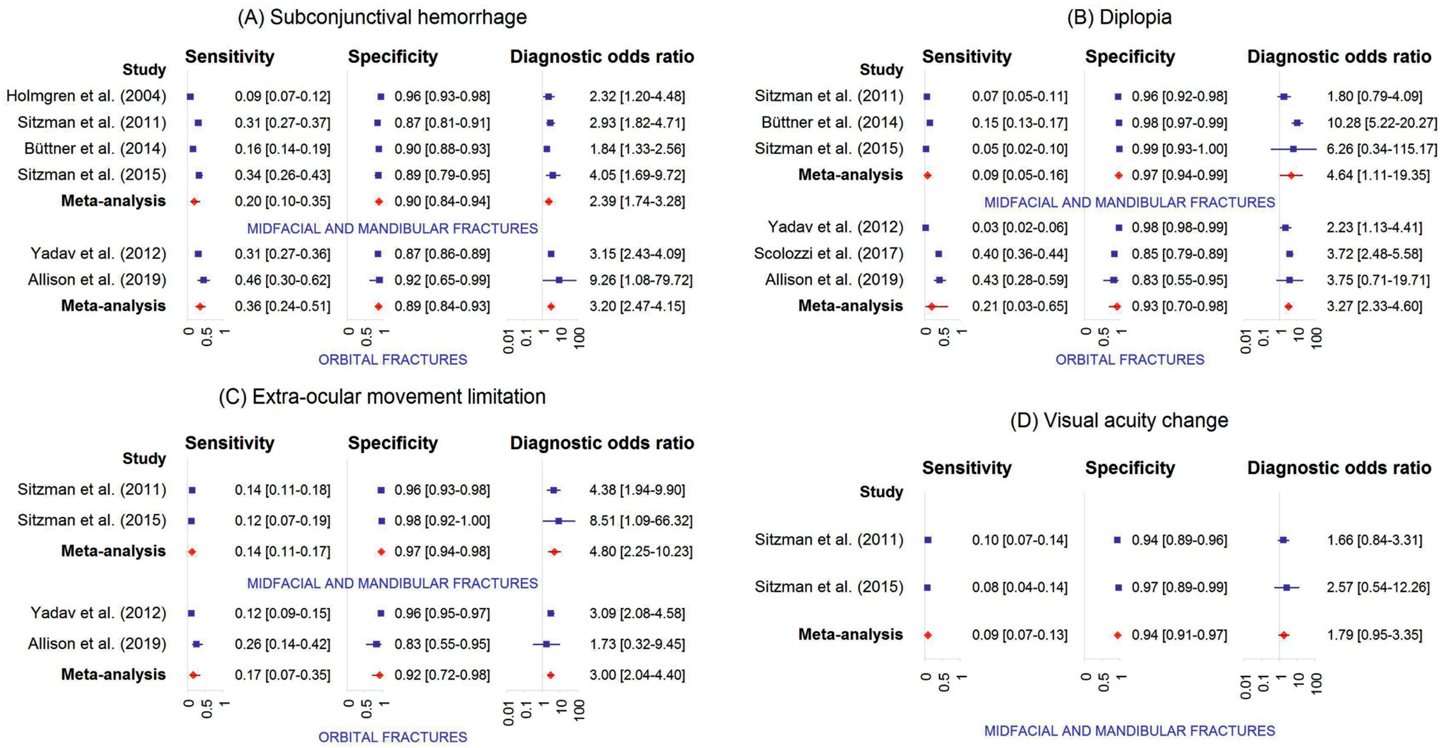

Figure 3c: Forest plots showing study-specific and pooled specificity, sensitivity and diagnostic odds ratio of the physical examination findings related to ocular assessment for (a) subconjuctival hemorrhage, (b) diplopia, (c) extra-ocular movement limitation, and (d) visual acuity change in diagnosing midfacial fractures.

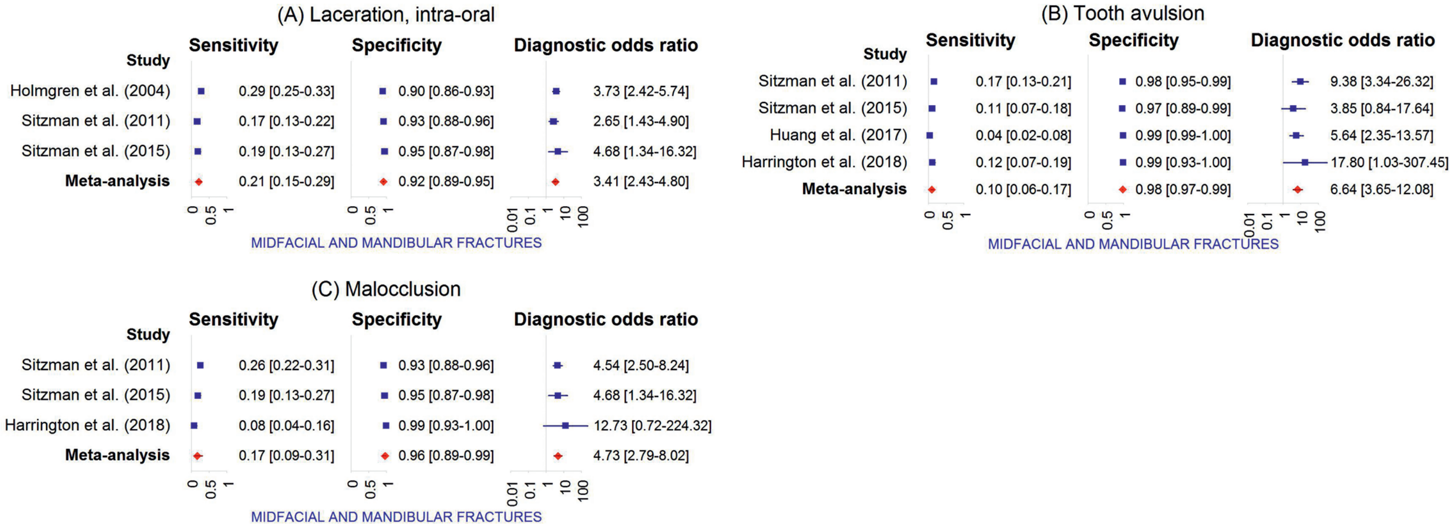

Figure 3d: Forest plots showing study-specific and pooled specificity, sensitivity and diagnostic odds ratio of the physical examination findings related to intra-oral assessment for (a) intra-oral laceration, (b) tooth avulsion and (c) malocclusion in diagnosing midfacial fractures.

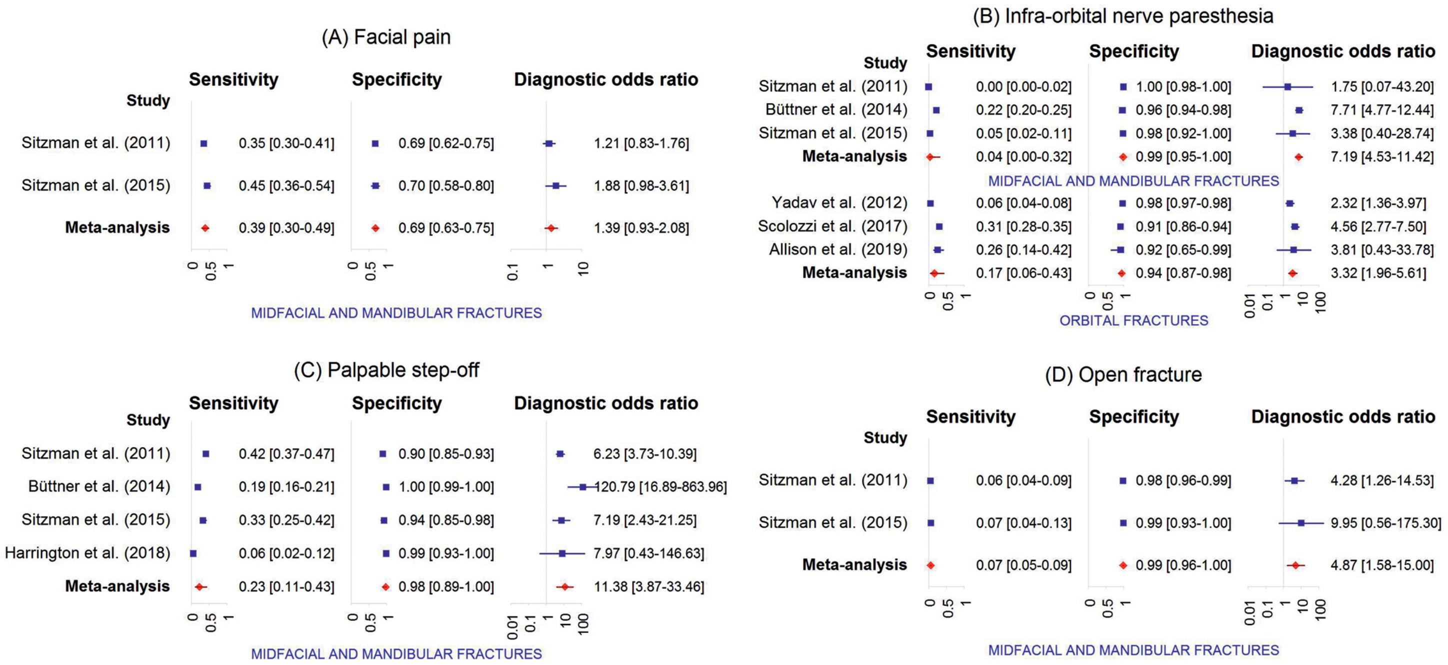

Figure 3e: Forest plots showing study-specific and pooled specificity, sensitivity and diagnostic odds ratio of the physical examination findings related to functional and palpation assessment for (a) facial pain, (b) infra-orbital nerve paresthesia, (c) palpable step-off and (d) open fracture in diagnosing midfacial fractures.

Findings related to nasal assessment

Epistaxis was the only reported physical examination finding related to the nasal assessment and was reported in 6 studies [54–56,59,64,65]. The outcomes included any midfacial or mandibular fracture (n=4), any midfacial fracture (n=1), and any orbital fracture (n=1). The pooled specificity was found to be high (0.94) and the pooled sensitivity remained low (0.25). The diagnostic odds ratio was 5.43 (Table 3 & Figure 3b).

Findings related to ocular assessment

A total of 6 distinct physical examination findings were identified in relation to the ocular assessment and reported 23 times in the included studies [55,56,59–61,63,64,66]. The outcomes were any midfacial or mandibular fracture (n=11), any orbital fracture (n=10), orbital floor fracture (n=1) and zygoma fracture (n=1). The identified findings included subconjunctival hemorrhage [55,56,59,61,63,64,66], hyphema [59], diplopia [55,56,59,60,63,64], extra-ocular movement limitation [55,56,59,63], extra-ocular movement pain [59], and visual acuity change [55,56,63]. The pooled specificity of all the physical examination findings was high, ranging from 0.89 to 0.94, and the pooled sensitivity was low, ranging from 0.09 to 0.36 (Table 3 & Figure 3c). The diagnostic odds ratio ranged from 1.79 to 3.27. Although the outcomes varied, most of the studies reported a high PPV and LR+ for the findings related to the ocular assessment, with two individual studies reporting a PPV of 100 and infinite LR+ for diplopia and visual acuity change [56,63].

Findings related to the intra-oral assessment

A total of 3 distinct physical examination findings were identified to be related to the intra-oral assessment and reported in 10 times of the included studies [55,56,58,61,65]. All of these reported physical examination findings were studied using any midfacial or mandibular fracture as outcome (n=10). Identified findings included malocclusion [55,56,58], intra-oral laceration [55,56,61], and tooth avulsion [55,56,58,65]. The pooled specificity was high, ranging from 0.92 to 0.98, and the sensitivity was low for all findings, ranging from 0.10 to 0.21 (Table 3 & Figure 3d). The diagnostic odds ratio ranged from 3.41 to 6.64. The PPV found higher than 80.0 in almost all of the studies, with one study reporting a PPV of 100 and an infinite LR+ for malocclusion and tooth avulsion [58]. The NPV was low in all studies.

Findings related to functional assessment and palpation of the midface

Regarding findings related to the functional assessment and palpation of the midface, a total of 8 distinct physical examination were identified that were reported 24 times in the included studies [55,56,58–60,63,64,66]. The outcomes were any midfacial or mandibular fracture (n=12), any orbital fracture (n=8), orbital floor fracture (n=1), nasal bone fracture (n=1) and zygoma fracture (n=2). The identified findings included facial pain [55,56], infra-orbital nerve paresthesia [55,56,59,60,63,64,66], subcutaneous emphysema [60,64], tenderness on palpation [59,66], palpable step-off [55,56,58,59,64], trismus [59,66], mandible locked open [59], and open fracture [55,56]. The pooled specificity was high for infra-orbital nerve paresthesia, subcutaneous emphysema, palpable step-off, trismus, mandible locked open and open fracture, ranging from 0.69 to 0.99. The pooled sensitivity remained low for the findings, ranging from 0.04 to 0.39 (Table 3 & Figure 3e). The diagnostic odds ratio ranged from 1.39 to 11.38. A high PPV and LR+ was found for infra-orbital nerve paresthesia, subcutaneous emphysema, palpable step-off and open fracture. Individual studies reported a PPV of 100 and a corresponding infinite LR+ for infra-orbital nerve paraesthesia, palpable step-off and open fracture [55,56,58]. A high NPV was found for tenderness on palpation. The NPV of the other physical examination findings was low.

Publication bias

The Deek's funnel plot tests showed that publication bias was significant for subconjunctival hemorrhage with midfacial and mandibular fractures. The statistical significance of the publication bias could not be assessed for 15 physical examination findings because only two studies provided data.

Clinical decision aids

Clinical decision aids were reported in 8 studies (Table 4). Four studies assessed the Wisconsin criteria [55–58]. The criteria were defined as any presence of a bony step-off or instability, malocclusion, tooth absence, peri-orbital swelling or contusion, and a Glasgow coma score of less than 14, using any midfacial or mandibular fracture as an outcome [55]. The sensitivity of these criteria ranged from 80.2 to 98.2%, and the specificity ranged from 22.3% to 41.2%. Clinical decision aids specifically for orbital fractures were presented in 2 studies [62,63]. One study focused on the need for a facial CT for head injury patients [62], and constructed a clinical decision aid that produced a sensitivity of 55.1% and a specificity of 100.0% in the presence of either blepharohematoma in one or two orbits, palpable fracture line, infra-orbital nerve hypesthesia, ocular motility disturbance, skin emphysema, enophthalmos or exophthalmos, impaired pupil reaction, and decrease in vision. Another study focused on the identification of head injury patients who had benefitted from including the orbits in the head CT [63]. Another clinical decision aid was constructed based on unbounded subconjunctival hemorrhage, reduced sensation in the

Table 4: Reported clinical decision aids

Author	Year	Clinical decision aid	**Sens. (95% CI)**	**Spec. (95% CI)**	**PPV (95% CI)**	**NPV (95% CI)**	**LR+ (95% CI)**	**LR- (95% CI)**
Exadaktylos et al. [62]	2005	Orbital fracture decision tool for no symptoms	15.3 (9.9-22.8)	5.2 (3.5-7.5)	3.8 (2.4-5.9)	20.0 (13.9-27.9)	0.2 (0.1-0.2)	16.3 (11.1-24.1)
Exadaktylos et al. [62]	2005	Orbital fracture decision tool for blepharohematoma only	29.7 (22.2-38.4)	94.8 (92.5-96.5)	58.3 (45.7-69.9)	84.6 (81.3-87.4)	5.7 (3.6-9.2)	0.7 (0.7-0.8)
Exadaktylos et al. [62]	2005	Orbital fracture decision tool for any symptoms	55.1 (46.1-63.8)	100.0 (99.2-100.0)	100.0 (94.4-100.0)	90.1 (87.3-92.3)	∞	0.4 (0.4-0.5)
Sitzman et al. [55]	2011	Wisconsin criteria	98.2 (96.1-99.2)	22.3 (17.0-28.7)	68.5 (64.2-72.5)	87.8 (75.8-94.3)	1.3 (1.2-1.4)	0.1 (0.0-0.2)
Sitzman et al. [56]	2015	Wisconsin criteria	97.4 (92.7-99.1)	20.6 (12.5-32.2)	69.3 (61.9-75.9)	81.3 (57.0-93.4)	1.2 (1.1-1.4)	0.1 (0.0-0.4)
Timashpolksy et al. [66]	2016	Wisconsin criteria	89.8 (78.2-95.6)	40.0 (11.8-76.9)	93.6 (82.8-97.8)	28.6 (8.2-64.1)	1.5 (0.7-3.1)	0.3 (0.1-1.0)
Harrington et al. [58]	2018	Wisconsin criteria	80.8 (72.0-87.4)	41.2 (30.3-53.0)	66.7 (57.8-74.5)	59.6 (45.3-72.4)	1.4 (1.1-1.7)	0.5 (0.3-0.8)
Yadav et al. [59]	2012	Orbital fracture risk score 0	88.5 (85.0-92.0)	32.5 (30.3-34.7)	-	93.7 (91.8-95.7)	-	0.4 (0.3-0.5)
		Orbital fracture risk score 1	55.3 (49.7-61.0)	77.1 (75.0-79.1)	-	90.1 (88.6-91.6)	-	0.6 (0.5-0.7)
		Orbital fracture risk score 2	25.8 (21.0-30.7)	93.8 (92.6-94.9)	-	87.0 (85.5-88.5)	-	0.8 (0.7-0.8)
		Orbital fracture risk score 3	8.2 (5.3-11.2)	98.9 (98.4-99.4)	-	85.1 (83.6-86.5)	-	0.9 (0.9-1.0)
		Orbital fracture risk score 4	1.9 (0.2-3.5)	99.7 (99.5-100.0)	-	84.3 (82.8-85.8)	-	1.0 (1.0-1.0)
		Orbital fracture risk score 5-6	0.2 (0.0-0.7)	99.9 (99.7-100.0)	-	84.1 (82.6-85.6)	-	1.0 (1.0-1.0)
Scolozzi et al. [60]	2017	Orbital fracture score >1	97.3 (95.8-98.3)	6.2 (3.6-10.3)	77.5 (74.6-80.1)	40.6 (25.5-57.7)	1.0 (1.0-1.1)	0.4 (0.2-0.9)
		Orbital fracture score >2	76.7 (73.5-79.7)	60.2 (53.5-66.6)	86.5 (83.6-89.0)	43.8 (38.2-49.5)	1.9 (1.6-2.3)	0.4 (0.3-0.5)

Table 4 *(continued)*

Author	Year	Clinical decision aid	**Sens. (95% CI)**	**Spec. (95% CI)**	**PPV (95% CI)**	**NPV (95% CI)**	**LR+ (95% CI)**	**LR- (95% CI)**
		Orbital fracture score >3	40.1 (36.5-43.8)	90.5 (85.8-93.8)	93.4 (90.0-95.7)	31.3 (27.7-35.0)	4.2 (2.8-6.5)	0.7 (0.6-0.7)
		Orbital fracture score >4	14.7 (12.3-17.5)	97.2 (93.9-98.7)	94.5 (88.5-97.5)	25.5 (22.6-28.7)	5.2 (2.3-11.6)	0.9 (0.8-0.9)
Allison et al. [63]	2019	Orbital fracture decision tool	80.0 (64.1-90.0)	75.0 (46.8-91.1)	90.3 (75.1-96.7)	56.3 (33.2-76.9)	3.2 (1.2-8.6)	0.3 (0.1-0.6)
Timashpolksy et al. [66]	2016	SBUH nose	87.5 (52.9-97.8)	87.8 (75.8-94.3)	53.8 (29.1-76.8)	97.7 (88.2-99.6)	7.1 (3.2-15.8)	0.1 (0.0-0.9)
		SBUH orbital floor	92.0 (75.0-97.8)	75.0 (57.9-86.7)	74.2 (56.8-86.3)	92.3 (75.9-97.9)	3.7 (2.0-6.8)	0.1 (0.0-0.4)
		SBUH zygoma	88.9 (67.2-96.9)	51.3 (36.2-66.1)	45.7 (30.5-61.8)	90.9 (72.2-97.5)	1.8 (1.3-2.6)	0.2 (0.1-0.8)

Abbreviations: Sens. Sensitivity; Spec. Specificity; PPV Positive Predictive Value; NPV Negative Predictive Value; LR+ Positive Likelihood Ratio; LR- Negative Likelihood Ratio; CI Confidence Interval; SBUH Stony Brook University Hospital

- *Orbital fracture decision tool*- divided into: 'no symptoms', 'blepharohaematoma only' or 'any symptoms' thereof; blepharohaematoma of one or two orbits, palpable fracture line, infra-orbital nerve hypesthesia, ocular motility disturbance, skin emphysema, enophthalmos or exophthalmos, impaired pupil reaction and decrease in vision.
- *Wisconsin criteria*- the presence of any of the following findings: bony step-off or instability, malocclusion, tooth absence, peri-orbital swelling or contusion, and a Glasgow coma score of less than 14.
- *Orbital fracture risk score (0-6)*- a risk score assigning a point for: orbital rim tenderness, peri-orbital emphysema, subconjunctival hemorrhage, impaired extra-ocular movement, painful extra-ocular movement and epistaxis.
- *Orbital fracture score (0-4+)*- a risk score assigning a point for: male sex, etiology other than assault, peri-orbital ecchymosis, peri-orbital emphysema, infra-orbital nerve hypoesthesia and diplopia.
- *Orbital fracture decision tool*- the presence of any of the following findings: unbounded subconjunctival hemorrhage, reduced sensation in the distribution of the infra-orbital nerve, change in position of the globe, reduced visual acuity or any two from peri-orbital bruising, diplopia and limited eye movement.
- *SBUH nose*- presence of the any of the following findings: bony or septal deviation, septal hematoma, tenderness, depression/angulation, ecchymosis or swelling.
- *SBUH orbital floor*- the presence of the any of the following findings: subjective diplopia, upgaze limitation, enophthalmos /depression, infra-orbital nerve paresthesia or anaesthesia, subconjunctival hemorrhage, ecchymosis or swelling.
- *SBUH zygoma*- presence of the any of the following findings: cheek flatness, subconjuctival haemorrhage, trismus, antimongoloid slant, infra-orbital nerve paraesthesia/anaesthesia, ecchymosis or swelling and palpable step.

distribution of the infra-orbital nerve, change in the position of the globe, reduced visual acuity or any two of the following, peri-orbital bruising, diplopia and limited eye movement. The presence of any of these findings produced a sensitivity of 80.0% and specificity of 75.0%. Two studies produced a clinical decision aid for orbital fractures using a risk score [59,60]. In one study, the risk score consisted of assigning a point for orbital rim tenderness, peri-orbital emphysema, subconjunctival hemorrhage, impaired extra-ocular movement, painful extra-ocular movement and epistaxis [59]. The other study assigned one point for male sex, etiology other than assault, peri-orbital ecchymosis, peri-orbital emphysema, infra-orbital nerve hypoesthesia and diplopia. One study introduced clinical decision aids, which were referred to as the Stony Brook University Hospital (SBUH) criteria, for orbital floor fractures, zygoma fractures and nasal fractures[66]. The respective sensitivities and specificities were 92.0% and 75.0% for orbital floor fractures, 88.9% and 51.3% for zygoma fractures, and 87.5% and 87.8% for nasal fractures.

Discussion

The assessment of midfacial and mandibular injury is characterized by particular physical examination findings. Understanding the predictive value of each finding may help emergency physicians to deliver a more optimal diagnostic management. In this systematic review and meta-analysis, we synthesized the best available evidence regarding the diagnostic accuracy of the physical examination findings and the accompanying clinical decision aids. The meta-analysis provided evidence of high specificity and low sensitivity for most of the individual physical examination findings related to the visual appearance of the patient, nasal, ocular and intra-oral assessments, and findings related to the functional assessment and palpation of the midface. This indicates that the absence of any physical examination findings can be used to successfully identify patients who do not have a midfacial fracture, whereas the presence of individual findings does not necessarily mean that patients have a midfacial fracture. Among these physical examination findings, we observed a high diagnostic odds ratio for epistaxis, tooth avulsion, malocclusion, infra-orbital nerve paraesthesia and palpable step-off, indicating that the likelihood of diagnosing a midfacial fracture is high when these findings are present during the physical examination. Also, particular findings had a high PPV and corresponding LR+. From a clinical perspective, emergency department physicians are blinded for the potential presence of a fracture during the physical examination and so these individual findings are especially useful for identifying patients at risk of the presence of a midfacial fracture and radiological imaging should be strongly considered for these patients. The NPV and LR- remained low for almost all the physical examination findings. Hence, the individual findings were unable to identify patients with a low risk of midfacial fractures and who did not require radiological imaging. However, this should be interpreted with caution due the low number of included studies and the high degree of risk of bias and concerns regarding the applicability of most of the studies.

It is of particular interest how a combination of physical examination findings performs as a clinical decision aid. Accordingly, the studies included in this systematic review proposed a variety of clinical decision aids using any midfacial or mandibular fracture, orbital fracture, orbital floor fracture, nasal fracture, and zygoma fractures as an outcome. The University of Wisconsin produced a clinical decision aid with sufficient diagnostic accuracy for patients suspected of midfacial or mandibular fractures [55]. However, validation of these criteria was unsuccessful in three other studies due to lower diagnostic accuracy outcomes [56–58]. The other studies focused on clinical decision aids for the identification of specific midfacial fractures, five of which were for orbital fractures [59,60,62,63,66]. The relevance of specifically studying the latter is emphasized for two reasons. First, orbital fractures are commonly found in patients presenting with a head injury and, therefore, it is often discussed whether the orbits should be included when performing a head CT [7,62,65]. Second, orbital fractures are associated with complications, such as entrapment of the extraocular muscles or retrobulbar hemorrhage, that require immediate surgical intervention and should therefore not be missed [15,67–70]. Three of the five studies successfully produced a clinical decision aid with this focus, whereas the two other produced a score to stratify patients into risk categories for the presence of orbital fractures [59,60]. One study based the risk score on physical examination findings only [59] whereas the other study also included sex and the mechanism of injury [60]. Although these scores identified the high risk fracture patients, the authors emphasized that further research is needed to determine a weighted cut-off. Nevertheless, patients with a high score were strongly suspected of having orbital fractures. None of these clinical decision aids were validated.

Most importantly, this systematic review did not identify a clinical decision aid that used any midfacial anatomy as an outcome. Yet, both the midface and mandible are known for their characteristic and complex anatomy, consequently each producing region-specific physical examination findings. Hence, we believe that both the midfacial and mandibular region should have a dedicated clinical decision aid, and we suspect that false positive findings might be more likely in studies where any midfacial or mandibular fracture is used as an outcome. For instance, the Wisconsin criteria score was positive for patients suffering peri-orbital hematoma while being diagnosed with a mandibular fracture. Conversely, malocclusion is considered to be a more common finding in mandibular trauma patients due to changes to the temporomandibular joints and the more prominent position of the alveolar process. Dedicating a clinical decision aid to midfacial fractures would allow it to be focused on physical examination findings related to the midfacial region, making it more easily reproducible. This is especially appreciated because a majority of midfacial trauma patients are initially assessed by emergency physicians and trauma surgeons who are not specifically trained to assess these patients.

Our systematic review did not find any studies that used CBCT as a reference test. CBCT scanners are dedicated to the oral and maxillofacial region and datasets are acquired while the system rotates around the patient [22,33,71]. A probable explanation is that the system can only be used on patients with isolated midfacial trauma, or patients for whom the initial management did not provide evidence of additional injuries [72]. For that reason, the availability of CBCT scanners in the emergency department is usually limited, and the systems are mostly used in outpatient clinics. A CT, on the other hand, is able to scan multiple body parts resulting in single data acquisition by transporting the patient through the gantry in synchrony with continuous data acquisition [73]. This is especially appreciated for midfacial trauma patients with concomitant cervical spine and head injuries which force the patients into a supine position [7,74–77]. Nevertheless, both CT and CBCT have the major advantage that they overcome superimposition of structures that inevitably occurs with conventional radiography [22,30,32].

In most of the included studies, there was an unclear risk of bias for the domains of the index test, reference standard, and flow and timing. Information regarding either the blinded interpretation of physical examination findings, or the blinded interpretation of CT data, was not reported in these studies. Not blinding the interpretation introduces important biases such as, for example, recording physical examination findings as present more likely if the emergency department workers are aware a priori of fractures being diagnosed on a CT. This type of bias cannot be controlled and therefore was judged as unclear in the studies. High unclear risk of bias was found for the flow and timing domain because no information was provided regarding the interval between the assessment of the physical examination findings and the CT. The accuracy of the interpretation decreases as the interval increases and should therefore be as short as possible. However, it is likely that in an emergency department setting the majority of patients are assessed within hours after the trauma, and a CT is conducted within the same time frame. High applicability concerns were found for the patient selection and reference standard domains. Regarding the selection of patients, a variety of studies focused on head injury patients only who, one would expect, were injured more severely, therefore introducing selection bias and affecting the interpretation of the physical examination findings. Concerns regarding the applicability of the reference standard were due to the use of an outcome other than ‘any midfacial fracture’. Concerns regarding the applicability of the index test were unclear in many studies (i.e., the standardization, handling or interpretation of the physical examination findings). It was especially unclear how the scoring of the chart review was handled by the retrospective studies, and if the data were reported systematically. Not reporting data as an absent physical examination finding could result in bias due to false negative outcomes. Also, the included studies did not report how ‘not assessable’ physical examination findings were handled, for instance the inability to score ocular related findings in patients with severe peri-orbital swelling.

The strength of this review is the detailed literature search, eligibility assessment of studies by two independent reviewers, good inter-observer agreement, structured risk of bias assessment using the QUADAS-2 tool, and conducting and reporting analyses according to the Cochrane handbook and PRISMA statement. A major limitation is the interpretation of the pooled outcomes due to the low or unclear quality of the studies, as well as the high concerns regarding applicability. The likely source of this bias was due to the patient selections and the fracture outcomes. Also, most of the studies were single-center trials thereby possibly introducing geographic and demographic biases. Another limitation is that we were unable to perform a meta-regression analysis of the midfacial fracture subgroups due the limited number of studies and data.

Future research should focus on the diagnostic accuracy of the physical examination findings using 'any midfacial fractures' as an outcome. Particular interest should be paid to the QUADAS-2 domains where high and unclear risk of bias was observed. Studies should include a consecutive population of midfacial trauma patients and inappropriate exclusion, such as multi-trauma patients, should be avoided. A standardized set of physical examination findings should be reproducible and should be assessed before knowing the CT outcome. The interpretation of the CT datasets should be interpreted by either a board certified radiologist or oral and maxillofacial surgeon. Ideally, the study should be conducted as a prospective multi-center trial to avoid geographical bias. Data from a large population of midfacial fracture patients should allow for a regression analysis to study how physical examination findings can predict fracture subtypes, such as orbital or zygomaticomaxillary complex fractures. Above all, the aim of identifying relevant individual findings would be to produce a clinical decision aid to reduce exposure of patients to unnecessary radiological imaging.

Based on all the currently available evidence, the present systematic review and meta-analysis identified the diagnostic accuracy of individual physical examination findings related to visual appearance, nasal and ocular assessment, intra-oral assessment and functional and palpation assessment of midfacial fractures compared to CT. The high specificity reveals that the absence of physical examination findings can aid in identifying patients who do not have a midfacial fracture, whereas the low sensitivity is evidence that the presence of individual findings cannot be used to accurately identify patients with midfacial fractures. Although, various clinical decision aids and risk scores were presented in the reviewed studies, none focused on the identification of any midfacial fracture. The results herein should be interpreted with caution due the limited number of studies as well as the high risk of bias and concerns regarding the applicability.

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3

CHAPTER 3

Diagnostic accuracy of physical examination findings for midfacial and mandibular fractures: a retrospective cohort study

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Published in Injury: International Journal of the Care of the Injured
Volume 52, Issue 9, September 2021, Pages 2616-2624
Adapted version of the manuscript

Abstract

Objective: To assess the diagnostic accuracy of physical examination findings used to identify patients at risk for midfacial or mandibular fractures.

Methods: A five-year retrospective cohort was constructed from all emergency department patients with a midfacial or mandibular trauma. The sensitivity, specificity, pre-test probability, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio data was calculated for 19 and 14 physical examination findings for midfacial and mandibular fractures respectively. Computed Tomography and panoramic radiography were used as index tests.

Results: A total of 1484 patients were identified among whom 40.4% midfacial and 33.4% mandibular fractures were diagnosed. Overall, specificity was found to be higher than sensitivity. Regarding midfacial fractures, high specificity was found for raccoon eyes, malar eminence flattening and all the findings that are related to palpation, the nasal, ocular and intra-oral assessment. Malar eminence flattening, external nasal deformity, nasal septum hematoma, change of globe position and palpable step-off had ad high positive predictive value and positive likelihood ratio. Regarding mandibular fractures high specificity was found for mouth opening restriction, auditory canal bleeding, intra-oral assessment related findings, palpable step-off, inferior alveolar nerve paresthesia, the angular compression test and chin axial pressure test.

Conclusion: The diagnostic accuracy of relevant physical examination findings were identified for the prediction of midfacial and mandibular fractures.

Introduction

Maxillofacial injuries comprise a substantial part of head and neck trauma's in today's emergency department. The primary and secondary assessments are used to evaluate all injuries and to identify critically injured patients. For the maxillofacial region, patients are assessed clinically to determine which patients are at risk for midfacial and mandibular fractures and require radiological imaging.

The physical examination of the midface and mandible is characterized by the complex anatomy and broad range of potential fracture type outcomes. Hence, the physical examination should cover all aspects such as the visual appearance, palpable abnormalities, sensory disturbances and ocular related findings. Previous studies assessed how a selection of these physical examination findings can be used to predict midfacial and mandibular fractures [1–3]. However, those studies only investigated a selection of physical examination findings, and data from other findings regarding predictability is lacking.

Thus, evidence is required regarding the diagnostic accuracy of all a potential midfacial and mandibular physical examination findings and understanding them could be used for a better diagnostic work-up and a potential reduction in unnecessary radiological investigations. Therefore, we gathered a large retrospective cohort of emergency department patients with either a midfacial or mandibular trauma to assess the diagnostic accuracy of related physical examination findings.

Material and Methods

Study design

A retrospective cohort study was conducted of maxillofacial trauma patients admitted to the emergency department. Chart review was conducted to calculate the diagnostic accuracy of physical examination findings for midfacial and mandibular fractures. The local Medical Ethical Review Board reviewed the study design and waived further need for approval (ref.nr. M17.212837). The study was reported using the STARD guidelines (Standards for Reporting of Diagnostic Accuracy Studies) [4].

Study cohort

The cohort consisted of patients with midfacial or mandibular trauma that were admitted consecutively to the emergency department of the level I trauma center of the University Medical Center Groningen, the Netherlands between 2013-2017. The patients who had undergone Computed Tomography (CT) or panoramic radiography of the head and neck region were identified from all the emergency department records. Patient selection was based on age (≥16yr.), trauma related visits, radiological imaging protocols and full availability of medical records. Subsequently, each medical record was individually consulted to assess whether the patients had sustained trauma of the midfacial and/or mandibular regions.

Index test

CTs of the maxillofacial region and panoramic radiography of the mandible were used as an index test. The outcome was the diagnosis of any midfacial or mandibular fracture. A midfacial fracture was defined as any fracture of the frontal sinus, orbital rim and walls, maxillary sinus, zygomaticomaxillary complex, nasoorbitoethmoid complex, nasal bone, Le Fort I, II, III complex and maxillary dentoalveolar complex fractures. A mandibular fracture was defined as any fracture of the median, paramedian, corpus, angular, coronoid and condylar process, and fractures of the mandibular dentoalveolar complex. The CT and panoramic radiography data was examined by a board-certified radiologist or oral and maxillofacial surgeon. The interpretation of the index test could not be blinded due the retrospective study design.

Reference standard

Physical examination findings related to midfacial and mandibular traumas were used as the reference standard. A pre-defined selection of 19 parameters for midfacial and 14 parameters for mandibular trauma patients was extracted from the data collected from the medical records of the emergency department's primary and secondary assessments of the patients. The data was categorized as absent, present, not assessable, or not reported. The following parameters were considered as not assessable for patients who had been sedated and intubated during the clinical examination: ocular movements, diplopia, visual acuity, occlusal changes, infraorbital nerve paresthesia, inferior alveolar nerve paresthesia, compression pain, and axial chin pressure pain. The following parameters were considered as not assessable for fully removable denture or edentulous patients: occlusal changes, tooth mobility, luxation or avulsion. Blinding of the reference test could not be controlled due the retrospective study design.

Data extraction

The data was extracted using a chart review template. Additional data on gender, age distribution, treatment urgency, time of admission and mechanism of injury, was collected and categorized according to the Manchester Triage System (MTS) [5].

Statistical analysis

The Statistical Package for the Social Sciences was used for the data analysis (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0). Continuous variables were reported as median and interquartile range and categorical variables were presented as frequency distributions and percentages. Contingency tables were constructed for the individual physical examination findings to calculate their sensitivity, specificity, pre-test probability, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+) and negative likelihood ratio (LR-), with corresponding standard error and 95% confidence interval [6]. The calculations were performed according to whether the physical examination reported "present" and "absent" findings or "did not report absent" findings. Additional calculations were performed on only "present" and "absent" reported physical examination findings.

Results

Patient characteristics

A total of 1484 maxillofacial trauma patients were identified (figure 1). From this population, 1375 had sustained a midfacial trauma and 556 (40.4%) of these patients were diagnosed with a midfacial fracture. Of the 347 patients with a mandibular trauma, 116 (33.4%) were diagnosed with a mandibular fracture. A total of 236 (15.9%) patients were diagnosed with both a midfacial and mandibular trauma. The patient characteristics are summarized in table 1 and figure 2.

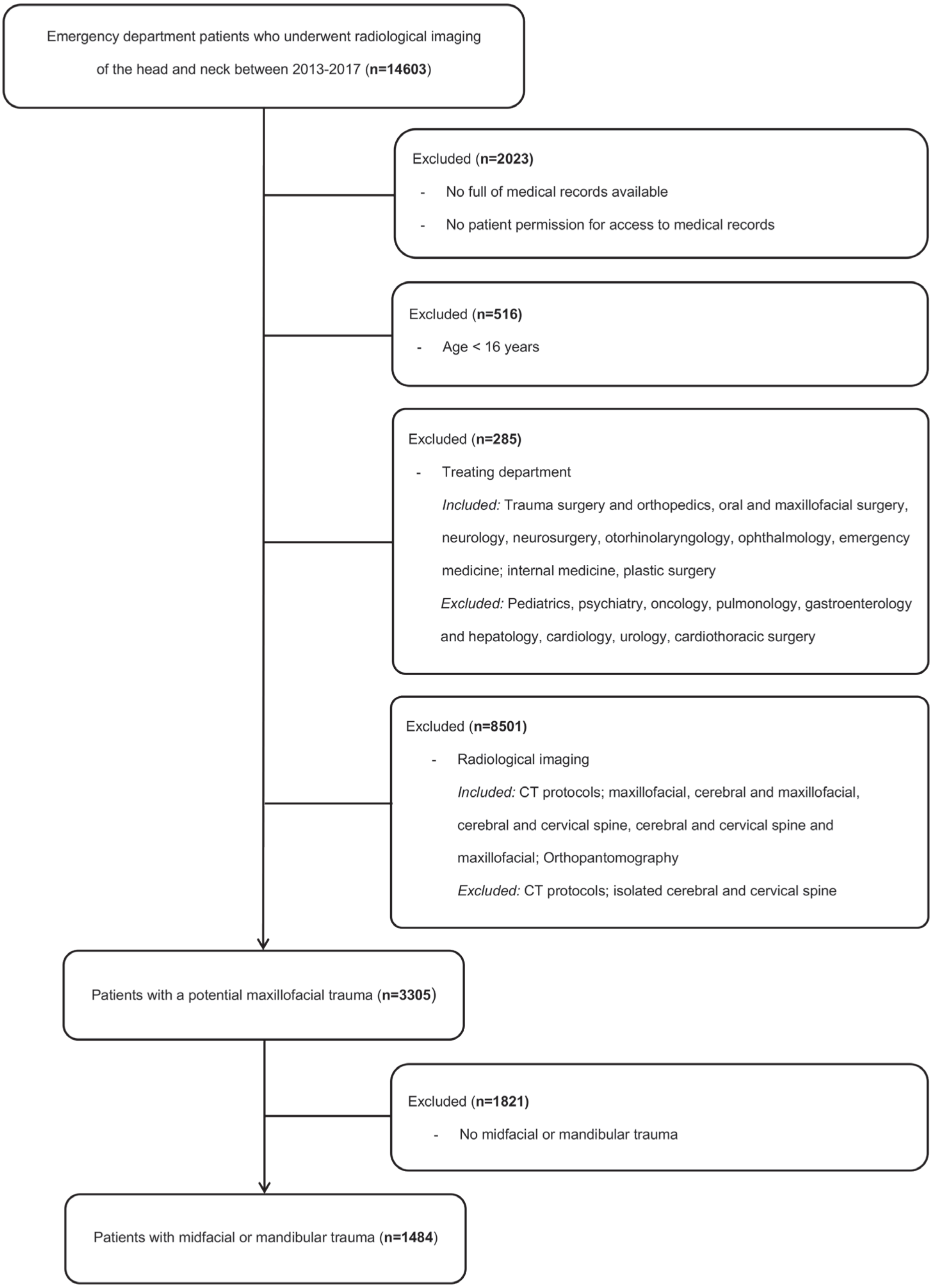

Figure 1: Flowchart of midfacial and mandibular trauma patient identification.

Table 1: Patient characteristics

Total patients (n)	1484
Gender distribution (n(%))	
Male	1021 (68.8)
Female	463 (31.2)
Age	
Median and interquartile range (years)	40 (34.75)
Range (years)	16-96
Age distribution (n(%))	
16-19 years	119 (8)
20-29 years	424 (28.6)
30-39 years	184 (12.3)
40-49 years	214 (14.4)
50-59 years	189 (12.6)
60-69 years	152 (10.1)
70-79 years	107 (7.4)
80-89 years	73 (5.0)
90-99 years	22 (1.4)
Mechanism of injury (n(%))	
At home and private	357 (24.1)
Work related	62 (4.2)
Traffic	674 (45.4)
Sports	73 (4.9)
Violence	234 (15.8)
Other	66 (4.4)
Not reported or verifiable	18 (1.2)
MTS urgency triage code (n(%))	
Blue – Non urgent	4 (0.3)
Green – Standard	320 (21.6)
Yellow - Urgent	444 (29.9)
Orange – Very Urgent	467 (31.5)
Red – Immediate	249 (16.8)
Time of admission (n(%))	
Night (00:00-05:59)	403 (27.2)
Morning (06:00-11:59)	263 (17.7)
Afternoon (12:00-17:59)	460 (31.0)
Evening (18:00-23:59)	358 (24.1)

Abbreviations: MTS Manchester Triage System

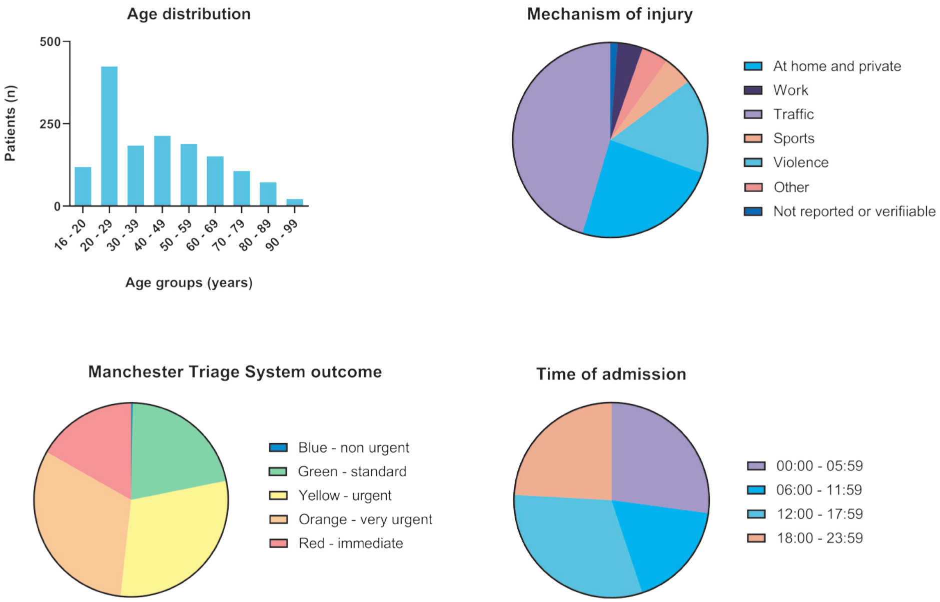

Figure 2: Patient characteristics.

Reported physical examination findings

The data form the reported physical examination findings are summarized in table 2. Among the midfacial traumas, swelling (44.1%), lacerations (52.2%) and peri-orbital hematoma (50.1%) were the most commonly reported physical examination findings. Swelling (14.2%), mouth opening restriction (15.7%), mandibular movement pain (16.2%) and malocclusion (21.1%/ 15.0%) were the most commonly reported physical examination findings for mandibular trauma's. The highest rates physical examination findings considered not assessable were found for ocular movement limitations, diplopia, visual acuity changes, malocclusion, dental injury, angular compression test, chin axial pressure test and assessment of infra-orbital- and inferior alveolar nerve paresthesia.

Diagnostic accuracy for midfacial and mandibular fractures

Table 3 shows the diagnostic accuracy of the physical examination findings for midfacial fractures. Overall, specificity was found to be higher than sensitivity. High rates of specificity were found for raccoon eyes (98.2%), malar eminence flattening (99.6%), external nasal deformity (99.4%), epistaxis (93.8%), nasal septum hematoma (100%), subconjunctival hemorrhage (97.6%), ocular movement limitations (97.6%), diplopia (98.5%), visual acuity changes (97.5%), change of globe position (100%), malocclusion (99.1/98.2%), tooth mobility or luxation (97.2%), tooth avulsion (98.1%), palpable step-off (99.6%), bony crepitus (99.4%) and infraorbital nerve paresthesia (98.1%). High PPV and LR+ rates were found for malar eminence flattening, external nasal deformity, nasal septum hematoma, change of globe position and palpable step-off.

Table 2: Reported physical examination findings characteristics

		Reported data (n(%))				
		No fracture	Fracture	Total		
	Prevalence (%)	Present	Present	Absent	Not assessable	Not reported
Midface						
Swelling	44.1	297 (21.6)	310 (22.5)	70 (5.1)	0 (0)	698 (50.8)
Laceration	52.2	431 (31.3)	287 (20.9)	108 (7.9)	0 (0)	549 (39.9)
Peri-orbital hematoma	50.1	400 (29.1)	289 (21.0)	48 (3.5)	0 (0)	638 (46.4)
Raccoon eyes	3.4	15 (1.1)	32 (2.3)	21 (1.5)	0 (0)	1307 (95.1)
External nasal deformity	3.3	5 (0.4)	40 (2.9)	65 (4.7)	1 (0.1)	1264 (91.9)
Malar eminence flattening	4.1	3 (0.2)	53 (3.9)	83 (6.0)	5 (0.3)	1231 (89.5)
Epistaxis	12.1	51 (3.7)	115 (8.4)	57 (4.1)	0 (0)	1152 (83.8)
Nasal septal hematoma	0.2	0 (0.0)	3 (0.2)	145 (10.5)	2 (0.1)	1225 (89.1)
Subconjunctival hemorrhage	5.6	20 (1.5)	56 (4.1)	124 (9.0)	7 (0.5)	1168 (84.9)
Ocular movement limitations	1.8	5 (0.4)	19 (1.4)	557 (40.5)	137 (10.0)	657 (47.8)
Diplopia	2.5	12 (0.9)	22 (1.6)	321 (23.3)	129 (9.4)	891 (64.8)
Visual acuity changes	2.4	20 (1.5)	12 (0.9)	245 (17.8)	122 (8.9)	976 (71.0)
Change of globe position	0.3	0 (0.0)	4 (0.3)	26 (1.9)	4 (0.3)	1341 (97.5)
Malocclusion (solitary midfacial traumas)	0.9	6 (0.5)	5 (0.4)	213 (18.7)	118 (10.4)	797 (70.0)
Malocclusion (all midfacial traumas) [a]	2.5	14 (1.0)	20 (1.5)	295 (21.5)	165 (12.0)	881 (64.1)
Tooth mobility or luxation	4.5	23 (1.7)	38 (2.8)	249 (18.1)	41 (3.0)	1024 (74.5)
Tooth avulsion	2.5	15 (1.1)	19 (1.4)	261 (19.0)	41 (3.0)	1039 (77.3)
Palpable step-off	5.4	3 (0.2)	71 (5.2)	314 (22.8)	23 (1.7)	964 (70.1)
Bony crepitus	2.4	5 (0.4)	27 (2.0)	84 (6.1)	1 (0.1)	1258 (91.5)
Infraorbital nerve paresthesia	5.3	15 (1.1)	58 (4.2)	359 (26.1)	92 (6.7)	851 (61.9)
Mandible						
Swelling	14.2	26 (7.5)	23 (6.7)	16 (4.6)	0 (0)	280 (81.2)
Extra-oral lacerations	34.8	70 (20.3)	50 (14.5)	18 (5.2)	0 (0)	207 (60.0)
Mouth opening restriction	15.7	22 (6.4)	32 (9.3)	60 (17.4)	11 (3.2)	220 (63.8)
Mandibular movement pain	16.2	28 (8.1)	28 (8.1)	25 (7.2)	11 (3.2)	253 (73.3)
Auditory canal bleeding	4.9	9 (2.6)	8 (2.3)	14 (4.1)	0 (0)	314 (91.0)
Malocclusion (solitary mandibular traumas)	21.1	6 (5.5)	17 (15.6)	45 (41.3)	3 (2.8)	38 (34.9)
Malocclusion (all mandibular traumas) [a]	15.0	15 (4.3)	37 (10.7)	128 (37.1)	50 (14.5)	115 (33.3)
Tooth mobility or luxation	9.0	12 (3.5)	19 (5.5)	121 (35.1)	13 (3.8)	180 (52.2)
Tooth avulsion	2.6	2 (0.6)	7 (2.0)	127 (36.8)	13 (3.8)	196 (56.8)
Intra-oral hematoma	11.5	15 (4.3)	25 (7.2)	102 (29.6)	2 (0.6)	201 (58.3)
Intra-oral lacerations	13.1	24 (7.0)	21 (6.1)	66 (19.1)	1 (0.3)	233 (67.5)
Angular compression test pain	6.7	3 (0.9)	20 (5.8)	59 (4.6)	25 (7.2)	238 (69.0)
Chin axial pressure test pain	4.1	2 (0.6)	12 (3.5)	42 (12.2)	25 (7.2)	264 (76.5)
Palpable step-off	2.9	3 (0.9)	7 (2.0)	41 (11.9)	5 (1.4)	290 (84.1)
Inferior alveolar nerve paresthesia	3.2	1 (0.3)	10 (2.9)	49 (14.2)	25 (7.2)	260 (75.4)

[a] Including patients with both a midfacial and mandibular trauma

Table 3: Diagnostic accuracy of physical examination findings for midfacial fractures [*]

	Sens. (CI)	Spec. (CI)	Pr (CI)	PPV (CI)	NPV (CI)	LR+ (CI)	LR- (CI)
Extra-oral assessment							
Swelling	55.8 (51.6-59.8)	63.7 (60.4-67.0)	40.4 (37.9-43.1)	51.1 (47.1-55.0)	68.0 (64.6-71.2)	1.5 (1.4-1.7)	0.7 (0.6-0.8)
Laceration	51.6 (47.5-55.7)	47.4 (44.0-50.8)	40.4 (37.9-43.1)	40.0 (36.5-43.6)	59.1 (55.3-62.8)	1.0 (0.9-1.1)	1.0 (0.9-1.1)
Periorbital hematoma	52.0 (47.8-56.1)	51.2 (47.7-54.6)	40.4 (37.9-43.1)	41.9 (38.3-45.7)	61.1 (57.4-64.7)	1.1 (1.0-1.2)	0.9 (0.8-1.0)
Raccoon eyes	5.8 (4.1-8.0)	98.2 (97.0-98.9)	40.4 (37.9-43.1)	68.1 (53.8-79.6)	60.5 (57.9-63.1)	3.1 (1.7-5.7)	1.0 (0.9-1.0)
Malar eminence flattening	9.6 (7.4-12.4)	99.6 (98.9-99.9)	40.2 (37.7-42.8)	94.6 (85.4-98.2)	62.1 (59.4-64.7)	26.3 (8.2-83.6)	0.9 (0.9-0.9)
Nasal assessment							
External nasal deformity	7.2 (5.3-9.6)	99.4 (98.6-99.7)	40.5 (37.9-43.1)	88.9 (76.5-95.2)	61.2 (58.5-63.8)	11.8 (4.7-29.6)	0.9 (0.9-1.0)
Epistaxis	20.7 (17.5-24.2)	93.8 (91.9-95.2)	40.4 (37.9-43.1)	69.3 (61.9-75.8)	63.5 (60.8-66.2)	3.3 (2.4-4.5)	0.8 (0.8-0.9)
Nasal septum hematoma	0.5 (0.2-1.6)	100.0 (99.5-100.0)	40.3 (37.8-43.0)	100.0 (43.8-100.0)	59.8 (57.2-62.3)	∞	1.0 (1.0-1.0)
Ocular assessment							
Subconjunctival hemorrhage	10.2 (7.9-13.0)	97.6 (96.3-98.4)	40.2 (37.6-42.8)	73.7 (62.8-82.3)	61.8 (59.1-64.4)	4.2 (2.5-6.9)	0.9 (0.9-0.9)
Ocular movement limitations	4.2 (2.7-6.5)	99.4 (98.5-99.7)	36.6 (34.0-39.3)	79.2 (59.5-90.8)	64.3 (61.5-66.9)	6.6 (2.5-17.5)	1.0 (0.9-1.0)
Diplopia	4.8 (3.2-7.2)	98.5 (97.4-99.1)	36.8 (34.2-39.6)	64.7 (47.9-78.5)	63.9 (61.2-66.6)	3.1 (1.6-6.3)	1.0 (0.9-1.0)
Visual acuity changes	2.6 (1.5-4.5)	97.5 (96.1-98.4)	37.0 (34.4-39.7)	37.5 (22.9-54.7)	63.0 (60.2-65.6)	1.0 (0.5-2.1)	1.0 (1.0-1.0)
Change of globe position	0.7 (0.3-1.8)	100.0 (99.5-100.0)	40.3 (37.8-43.0)	100.0 (51.0-100.0)	59.8 (57.2-62.4)	∞	1.0 (1.0-1.0)
Intra-oral assessment							
Malocclusion (solitary midfacial traumas)	1.5 (0.6-3.5)	99.1 (98.1-99.6)	32.7 (29.9-35.7)	45.5 (21.3-72.0)	67.4 (64.5-70.2)	1.7 (0.5-5.6)	1.0 (1.0-1.0)
Malocclusion (all midfacial traumas)	4.6 (3.0-7.0)	98.2 (97.0-98.9)	36.1 (33.5-38.9)	58.8 (42.2-73.6)	64.5 (61.8-67.2)	2.5 (1.3-5.0)	1.0 (1.0-1.0)
Tooth mobility or luxation	7.2 (5.3-9.8)	97.2 (95.8-98.1)	39.4 (36.8-42.0)	62.3 (49.7-73.4)	61.7 (59.0-64.4)	2.5 (1.5-4.2)	1.0 (0.9-1.0)
Tooth avulsion	3.6 (2.3-5.6)	98.1 (97.0-98.9)	39.4 (36.8-42.0)	55.9 (39.5-71.1)	61.1 (58.4-63.7)	2.0 (1.0-3.8)	1.0 (1.0-1.0)
Palpation							
Palpable step-off	13.2 (10.6-16.3)	99.6 (98.9-99.9)	39.9 (37.3-42.5)	95.9 (88.7-98.6)	63.4 (60.7-66.0)	35.7 (11.3-112.8)	0.9 (0.8-0.9)
Bony crepitus	4.9 (3.4-7.0)	99.4 (98.6-99.7)	40.4 (37.8-43.0)	84.4 (68.2-93.1)	60.7 (58.0-63.2)	8.0 (3.1-20.6)	1.0 (0.9-1.0)
Infraorbital nerve paresthesia	11.9 (9.3-15.0)	98.1 (96.9-98.9)	38.1 (35.5-40.8)	79.5 (68.8-87.1)	64.4 (61.6-67.0)	6.3 (3.6-11.0)	0.9 (0.9-0.9)

[*] Calculations were performed by considering the reported physical examination findings as "present" or as "absent", or "not reported as absent"

Abbreviations: Sens. sensitivity, spec. specificity, Pr Pre-test probability, PPV positive predictive value, NPV negative predictive value, LR+ positive likelihood ratio, LR- negative likelihood ratio

Table 4: Diagnostic accuracy of physical examination findings for mandibular fractures [*]

	Sens.	Spec.	Pr	PPV	NPV	LR+	LR-
Extra-oral assessment							
Swelling	19.8 (13.6-28.0)	88.6 (83.9-92.1)	33.6 (28.8-38.8)	46.9 (33.7-60.6)	68.6 (63.1-73.6)	1.7 (1.0-2.9)	0.9 (0.8-1.0)
Laceration	43.1 (34.5-52.2)	69.4 (63.2-75.0)	33.6 (28.8-38.8)	41.7 (33.2-50.6)	70.7 (64.4-76.2)	1.4 (1.1-1.9)	0.8 (0.7-1.0)
Mouth opening restriction	29.4 (21.6-38.5)	90.2 (85.6-93.5)	32.6 (27.8-37.8)	59.3 (46.0-71.3)	72.5 (67.0-77.4)	3.0 (1.8-4.9)	0.8 (0.7-0.9)
Mandibular movement pain	25.7 (18.4-34.6)	87.6 (82.6-91.2)	32.6 (27.8-37.8)	50.0 (37.3-62.7)	70.9 (65.3-75.9)	2.1 (1.3-3.3)	0.8 (0.8-1.0)
Auditory canal bleeding	6.9 (3.5-13.0)	96.1 (92.7-97.9)	33.6 (28.8-38.8)	47.1 (26.2-69.0)	67.1 (61.8-71.9)	1.8 (0.7-4.4)	1.0 (0.9-1.0)
Intra-oral assessment							
Malocclusion (solitary mandibular trauma)	41.5 (27.8-56.6)	90.8 (81.3-95.7)	38.7 (30.0-48.2)	73.9 (53.5-87.5)	71.1 (60.6-79.7)	4.5 (1.9-10.5)	0.6 (0.5-0.8)
Malocclusion (all patients)	42.5 (32.7-53.0)	92.8 (88.4-95.6)	29.5 (24.6-34.9)	71.2 (57.7-81.7)	79.4 (73.9-84.0)	5.9 (3.4-10.2)	0.6 (0.5-0.7)
Tooth mobility or luxation	16.8 (11.0-24.8)	94.5 (90.7-96.8)	34.0 (29.1-39.3)	61.3 (43.8-76.3)	68.8 (63.3-73.7)	3.1 (1.5-6.1)	0.9 (0.8-1.0)
Tooth avulsion	6.2 (3.0-12.2)	99.1 (96.7-99.7)	34.0 (29.1-39.3)	77.8 (45.3-93.7)	67.2 (61.9-72.1)	6.8 (1.4-32.1)	0.9 (0.9-1.0)
Hematoma	21.9 (15.3-30.4)	93.4 (89.5-96.0)	33.2 (28.5-38.4)	62.5 (47.0-75.8)	70.6 (65.3-75.5)	3.3 (1.8-6.1)	0.8 (0.8-0.9)
Laceration	18.3 (12.3-26.3)	89.5 (84.9-92.9)	33.4 (28.7-38.6)	46.7 (32.9-60.9)	68.6 (63.1-73.6)	1.7 (1.0-3.0)	0.9 (0.8-1.0)
Palpation							
Angular compression test pain	19.8 (13.2-28.6)	98.6 (96.1-99.5)	31.6 (26.7-36.8)	87.0 (67.9-95.5)	72.7 (67.4-77.5)	14.5 (4.4-47.5)	0.8 (0.7-0.9)
Chin axial pressure test pain	11.9 (6.9-19.6)	99.1 (96.7-99.7)	31.6 (26.7-36.8)	85.7 (60.1-96.0)	70.9 (65.6-75.7)	13.0 (3.0-57.1)	0.9 (0.8-1.0)
Palpable step-off	6.1 (3.0-12.1)	99.1 (96.8-99.8)	33.5 (28.7-38.7)	77.8 (45.3-93.7)	67.7 (62.5-72.5)	6.9 (1.5-32.9)	0.9 (0.9-1.0)
Inferior alveolar nerve paresthesia	9.9 (5.5-17.3)	99.5 (97.5-99.9)	31.6 (26.7-36.8)	90.9 (62.3-98.4)	70.6 (65.2-75.4)	21.7 (2.8-167.1)	0.9 (0.8-1.0)

[*] Calculations were performed by considering the reported physical examination findings as "present" or as "absent", or "not reported as absent"

Abbreviations: Sens. sensitivity, spec. specificity, Pr Pre-test probability, PPV positive predictive value, NPV negative predictive value, LR+ positive likelihood ratio, LR- negative likelihood ratio

For mandibular fractures, the diagnostic accuracy of physical examination findings are presented in table 4. High specificity was found for mouth opening restriction (90.2%), auditory canal bleeding (96.1%), malocclusion (90.8%/92.8%), tooth mobility or luxation (94.5%), tooth avulsion (99.1%), intra-oral hematoma (93.8%), angular compression test pain (98.6%), chin axial pressure test pain (99.1%), palpable step-off (99.1%) and inferior alveolar nerve paresthesia (99.5%). A high PPV was found for inferior alveolar nerve paresthesia and a high LR+ was found for angular compression test pain, chin axial pressure test pain and inferior alveolar nerve paresthesia.

Discussion

Emergency department patients with head and neck trauma require a systematic assessment of the maxillofacial region. Abnormal physical examination findings are used to assess the injury severity and guide the need for radiological imaging. Emergency department workers need an insight into the diagnostic properties of these findings to identify any patients at risk for midfacial and mandibular fractures. This large retrospective cohort study of 1484 patients calculated the diagnostic accuracy of individual physical examination findings for both midfacial and mandibular fractures. The presented data for a total of 19 and 14 physical examination findings for midfacial and mandibular trauma patients respectively, has not been studied before.

For midfacial fractures, a variety of studies focused on the diagnostic accuracy of physical examination findings. A retrospective study of 525 maxillofacial trauma patients assessed the diagnostic accuracy of eight physical examination findings [1]. They found high sensitivity for swelling (81.0%), lacerations (69.3%), any contusion (87.4%) and peri-orbital contusion (74.1%) and high specificity for sensory loss (95.9%), bony step-off or instability (89.6%), malocclusion (92.7%) and tooth absence (97.9%). Within their analysis, no differentiation was made between midfacial and mandibular fractures. Another blinded prospective study of 57 patients found high sensitivity for tenderness (88%) in nasal bone fractures, subconjunctival hemorrhage (76%) associated with orbital floor fractures, and cheek flatness (72%) related to zygomaticomaxillary fractures [2]. Our study's physical examination findings did not demonstrate high sensitivity. However, we did find a high specificity for raccoon eyes, malar eminence flattening, external nasal deformity, epistaxis, nasal septum hematoma, subconjunctival hemorrhage, ocular movement limitations, diplopia, visual acuity changes, change of globe position, malocclusion, tooth mobility or luxation, tooth avulsion, palpable step-off, bony crepitus and infra-orbital nerve paresthesia. Any findings that do not appear abnormal seem particularly useful for excluding midfacial fractures. Malar eminence flattening, external nasal deformity, nasal septum hematoma, change of globe position and palpable step-off resulted in a high PPV and LR+. The LR+ for nasal septum hematoma and change of globe position was infinite and thus pathognomonic. As these physical examination findings strongly suggest the presence of a midfacial fracture, radiological imaging should be strongly considered.

Publications of the diagnostic accuracy of mandibular fracture related physical examination findings are limited. A prospective study of 119 patients found a high specificity for malocclusion (96%), facial asymmetry (96%), crepitus (96%) and sublingual hematoma (96%) [3]. Furthermore, they noted a high PPV and NPV for malocclusion (92%/87%) and facial asymmetry (88%/76%). The authors also assessed the so called tongue blade test, resulting in a sensitivity of 95% and a NPV of 96%. They stated this test is useful for excluding mandibular fractures. Other studies corroborated this statement [7,8]. However, in their study, the authors used conventional radiography as an index test. As far as we know, our present study provides the diagnostic accuracy of mandibular fractures related to physical examination findings that have not been published before. We find high specificity for mouth opening restriction, auditory canal bleeding, malocclusion, tooth mobility or luxation, tooth avulsion, intra-oral hematoma, angular compression test pain, chin axial pressure test pain, palpable step-off and inferior alveolar nerve paresthesia. Furthermore, a high PPV and LR+ was found for angular compression test pain, chin axial pressure test pain and inferior alveolar nerve paresthesia. These results emphasize that both extra and intra-oral assessments should be part of the standardized assessment of mandibular trauma patients. The intra-oral assessment should include evaluation of occlusal changes, dental injury, gingival or mucosal lacerations and musical or sublingual hematoma.

Although oral and maxillofacial surgeons are trained to specifically assess midfacial and mandibular trauma patients, one should realize that the primary assessment is mostly performed by either emergency physician and specialized trauma surgeons. Furthermore, primary care physicians, such as general practitioners and dentists, are also faced with these patients and requested to provide adequate diagnostic management in the absence of immediate availability of radiological imaging. For that reason, the diagnostic accuracy of physical examination findings found in this study can be used for the initial management for these patients. Especially findings that produced a PPV and LR+ may aid in identifying patients who have a high risk of a fracture and, subsequently, should be referred for radiological imaging or additional assessment by an oral and maxillofacial surgeon. Above all, our data emphasizes the need to standardize the physical examination for each maxillofacial trauma patient. Other authors suggested the use of a structured record keeping tool to improve documentation [9]. In our study, we chose a stratification between extra- and intraoral assessment, nasal, ocular, and palpation related parameters, which is a feasible structure for the routine assessment of midfacial and mandibular trauma patients. Despite the findings found during the physical examination, interpretation should always be conducted in relation to the patient's history, mechanism of injury and trauma severity.

In our study, diagnostic accuracy calculations were performed for individual physical examination findings. However, decision making in the emergency department is the result of a multitude of abnormal physical examination findings. Although our study was conducted to assess individual physical examination findings, other studies proposed a combination of findings as a decisional instrument. Authors from the university of Wisconsin provided the eponymous criteria by manually assembling five findings including bony step-off or instability, malocclusion, tooth absence, periorbital swelling or contusion and a Glasgow Coma Scale score of less than 14 resulting in a sensitivity of 98.2% [1]. Although internal validation resulted in a sensitivity of 97.4%, the attempt to validate the instrument externally, with a sensitivity of 81%, was unsuccessful [10,11]. These Wisconsin criteria were compared to the results of a blinded prospective study of 57 patients using grouped physical examination findings for area specific fractures. Sensitivities of 89%, 92%, 88% and 100% were found for zygomaticomaxillary, orbital floor, nose and mandible fractures respectively. Another study proposed a decisional instrument for displaced zygomaticomaxillary fractures, combing palpable step-off, subconjunctival hemorrhage, infraorbital nerve paresthesia and palpable emphysema, resulting in a sensitivity of 100% and a specificity of 72.6% [12]. In contrast to our study, they chose a specific fracture type as an outcome. However, from a clinical perspective, emergency department workers are blinded to a broad spectrum of potential midfacial and mandibular fractures as outcomes. Therefore, we believe that the physical examination of the midfacial and mandibular regions should be done separately since specific physical examination findings are associated with fractures in these regions. All things considered, there is need for a well validated and reproducible decision instrument that is generalizable for different institutions. Data from the current study and previous studies should be used for the conceptualization of a prospective multicenter study to produce a clinical decision aid consisting of standardized physical examination parameters.

The above was the main limitation of the present study, due the inability to standardize the physical examination. A common phenomenon of retrospectively designed studies is that the data is exposed to bias due to uncontrolled variables, inconsistency of data accumulation and missing data. We noted that the outcomes of physical examination findings are not systematically reported, resulting in high rates of missing data. Although, multiple imputation with chained equations is suggested for such situations, these statistical models are not usable with a high degree of missing data [13]. Consequently, the diagnostic accuracy was also calculated for only “absent” and “present” reported physical examination findings, resulting in higher sensitivity and lower specificity outcomes. Using this approach, we provide an appropriate representation of the range of diagnostic accuracy for each physical examination finding. Another limitation of our study was that only patients were included which received CT or panoramic radiography. In these patients, physical examination findings are more likely to be present. Therefore, future research should include a reference standard for each patient, regardless the likelihood of a maxillofacial fracture.

In conclusion, the diagnostic accuracy of individual physical examination findings was calculated for both midfacial and mandibular fractures. The identified relevant findings are suitable as ‘a priori’ knowledge for emergency department physicians for the assessment of midfacial and mandibular trauma. Prospective multicenter data is needed to contribute towards the standardization of the physical examination and the consecutive construction of a validated clinical decision aid.

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4a

CHAPTER 4a

A clinical decision aid for patients with suspected midfacial and mandibular fractures (the REDUCTION-I study): a prospective multicentre cohort study

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Submitted
Adapted version of the manuscript

Abstract

Objective: To assess physical examination findings related to maxillofacial trauma to identify patients at risk of midfacial and mandibular fractures and then to construct a clinical decision aid to rule out the presence of midfacial and mandibular fractures in emergency department patients.

Methods: We performed a prospective multicentre cohort study in four hospitals in the Netherlands, including consecutive patients with maxillofacial trauma. Each patient received a standardized physical examination consisting of fifteen and fourteen findings for midfacial and mandibular trauma, respectively. Consequently, clinical decision aids were constructed with the focus being on ruling out the presence of midfacial and mandibular fractures, and diagnostic accuracy was calculated.

Results: A total of 993 consecutive patients were identified of whom 766 and 280 patients were suspected of midfacial and mandibular fractures, respectively. Midfacial fractures were diagnosed in 339 patients (44.3%), whereas mandibular fractures were observed in 66 patients (23.6%). The decision aid for midfacial trauma consisting of peri-orbital hematoma, epistaxis, ocular movement limitation, infra-orbital nerve paresthesia, palpable step-off and tooth mobility or avulsion, produced a sensitivity of 89.7 (86.0-92.5), a specificity of 42.6 (38.0-47.4), and a negative predictive value of 83.9% (78.4-88.2). The decision aid for mandibular trauma consisting of the angular compression test, axial chin pressure test, objective malocclusion, tooth mobility or avulsion and the tongue blade bite test, resulted in a sensitivity of 98.5 (91.9-99.7) a specificity of 34.6 (28.5-41.2), and a negative predictive value of 98.7% (92.8-99.8).

Conclusion: The constructed clinical decision aids for maxillofacial trauma may aid in stratifying patients suspected for midfacial and mandibular fractures to reduce unnecessary diagnostic imaging.

Introduction

Maxillofacial injuries comprise a substantial part of today's emergency department visits. Computed Tomography (CT) has been widely accepted as the routine imaging modality of choice for the diagnosis of these injuries. In the past decades, the increased use of CT has raised concerns regarding radiation dose associated risks, such as the carcinogenic potential [1]. Thus, clinical decisions aids were proposed to reduce unnecessary diagnostic imaging and associated health care costs.

The Wisconsin criteria were suggested as a clinical decision aid for midfacial and mandibular fractures [2]. Attempts to validate these criteria was unsuccessful in other studies [3–5]. A variety of studies published risk scores and clinical decision aids specifically for orbital fractures [6–9]. Separate clinical decision aids were also proposed for zygoma, orbital floor, nasal and mandibular fractures [4,10,11]. However, these decision aids have important limitations. First, a decision aid for specific fracture types is only useful for a selection of the maxillofacial trauma population. Second, combining midfacial and mandibular fractures as outcome does not allow for separate decision making for patients with isolated midfacial or mandibular trauma. Third, most studies collected data in single-centers resulting in geographic and demographic biases.

To our belief, a clinical decision aid for maxillofacial trauma should be straightforward and reproducible for all emergency department workers, including emergency physicians and specialized trauma surgeons. Moreover, a clinical decision aid should be applicable to both isolated and multitrauma patients. In today's emergency care, diagnostic imaging is routinely considered in case of signs related to maxillofacial trauma. Therefore, it would be especially useful for identifying patients with a low risk of maxillofacial fractures thus reducing unnecessary imaging and, subsequently, in lowering radiation exposure and associated health care costs. Also, we believe it would optimize the workflow of emergency department visits for these specific patients. We therefore initiated a prospective multicenter so called REDUCTION-I study (*RED*ucing *U*nnecessary *C*omputed *T*omography *I*n *M*axill*O*facial I*N*jury). The aim of this study was twofold. First, to assess the diagnostic accuracy of physical examination findings for patients with clinically suspected midfacial or mandibular trauma. Second, to construct a clinical decision aid with the focus being on ruling out the presence of midfacial and mandibular fractures in emergency department patients.

Material and Methods

Study design and ethical approval

A prospective multicenter observational cohort study was conducted of all patients admitted with a midfacial or mandibular trauma. The Medical Ethical Committee of the University Medical Center Groningen confirmed that the Medical Research Involving Human Subjects Act does not apply (METc code 2017/249) and local feasibility was approved for the Isala hospitals (METC171208) and Nij Smellinghe hospital (MEC6383/JS/AB). The study was performed in compliance with the Declaration of Helsinki and the FEDERA (Foundation Federation of Dutch Medical Scientific Societies) code of conduct. The study was registered at ClinicalTrials.gov (NCT03314480) and reported according to the STARD guidelines (Standards for Reporting of Diagnostic Accuracy Studies) and Methodologic Standards for Interpreting Clinical Decision Rules in Emergency Medicine [12,13].

Inclusion and exclusion criteria

All consecutive patients presenting with a midfacial or mandibular trauma at the emergency department of the University Medical Center Groningen (level I), Isala hospital Zwolle (Level I), Isala Diaconessenhuis hospital Meppel (level III) and Nij Smellinghe hospital Drachten (level III) between the period of May 2018 and October 2019 were included. Patients younger than 18 years and patients admitted a second time for maxillofacial trauma within the inclusion period were excluded. Patients were also excluded if the initial assessment was performed in another hospital or access to medical records was declined.

Standardized assessment

All the eligible patients underwent a full physical examination consisting of fifteen and fourteen physical examination findings dedicated to the midfacial and mandibular region respectively. The physical examination was conducted by emergency physicians, surgeons or resident physicians of these professions. The process to standardize the physical examination was established using a tripartite strategy. First, each physician received an individual hands-on instruction on how to standardize each physical examination parameter. Second, we provided instructional videos on an open accessible online educational tool. Third, a pocket card was provided for bedside use, containing eligibility criteria and visualized physical examination findings. The findings were assessed during the primary or secondary assessment, and scored as absent, present or not assessable (supplementary table S1). The findings were assessed without knowledge of the radiological imaging outcome, unless the emergent medical need of the patient required otherwise.

Outcome and radiological imaging

The primary outcome was the presence of either a midfacial or mandibular fracture diagnosed with Computed Tomography (CT), Cone Beam Computed Tomography (CBCT) or panoramic orthopantomography (OPT). Midfacial fractures were defined as any fracture of the frontal sinus, orbital rim and walls, maxillary sinus, zygomaticomaxillary complex, nasoorbitoethmoid (NOE) complex, nasal bone, Le Fort I, II, III complex, and maxillary dentoalveolar complex. A mandibular fracture was defined as any fracture of the symphyseal, parasymhyseal, corpus, angular, ramus, coronoid and condylar process, and fractures of the mandibular dentoalveolar complex. CT datasets were assessed by radiologists, and CBCT and OPT were assessed by oral and maxillofacial surgeons. Radiological interpretations were performed blinded from the physical examination findings. Fracture classification was performed by a board certified oral and maxillofacial surgeon (BvM). Secondary outcomes were source of referral, mechanism of injury, age, reported alcohol use, state of consciousness in accordance with the Glasgow Coma Score, and status of intubation and sedation.

Statistical analysis

The Statistical Package for the Social Sciences was used for the data analysis (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). Categorical variables were reported as frequencies and percentages. Normally distributed variables were reported as means and standard deviations, and variables with a skewed distribution were reported as median and inter quartile range. Normality was examined using Q-Q plots and tested using the Kolmogorov-Smirnov test. The diagnostic accuracy with corresponding 95 percent confidence intervals was calculated for the individual physical examination findings considering absent and present findings.

Principle component analysis (PCA) was used to construct a clinical decision aid for midfacial and mandibular trauma separately, with the focus being on identifying patients with a low fracture risk. The PCA analysis was performed with subsequent promax rotation and Kaiser normalization, and used to identify the underlying structure among physical examination findings. The Barlett's test of sphericity and the Kaiser-Meyer-Olkin measure of sampling adequacy were conducted to test whether the variables were uncorrelated in the correlation matrix. Factors with Eigenvalues greater than one were initially retained. The factor loadings and clinical considerations of two board certified oral and maxillofacial surgeons (MD and BvM) were perused to identify the best combination of clinical physical examination findings to predict the presence of midfacial or mandibular fractures. Contingency tables were constructed with the absent findings being listed as 'negative' whereas the present, not testable and missing findings were listed as a 'positive' findings. The diagnostic accuracy outcomes included: prevalence, pre-test probability, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+) and negative likelihood ratio (LR-).

Results

Patient identification

A total of 1128 consecutive patients with clinically suspected maxillofacial fracture(s) were screened in the four participating hospitals of whom 135 (12.0%) were excluded (figure 1). Among the remaining 993 patients, 766 were suspected of midfacial fractures, 280 of mandibular fractures. Of the total population, 208 patients were suspected for both midfacial and mandibular fractures. Patient characteristics are summarized in Table 1.

Radiological imaging

CT was obtained in 752 (98.2%) and CBCT in 14 (1.8%) midfacial trauma patients of whom fractures were diagnosed in 339 patients (44.3%). For mandibular trauma patients, CT was obtained in 238 (85.0%) patients, CBCT in 10 (3.6%) patients, and OPT in 32 (11.4%) patients. Mandibular fractures were diagnosed in 66 (23.6%) patients. Among the 208 patients with both midfacial and mandibular trauma, 106 (51.0%) of the patients only had midfacial fractures and 28 (13.5%) only had mandibular fractures. The remaining 11 (5.3%) patients had both a midfacial and mandibular fracture.

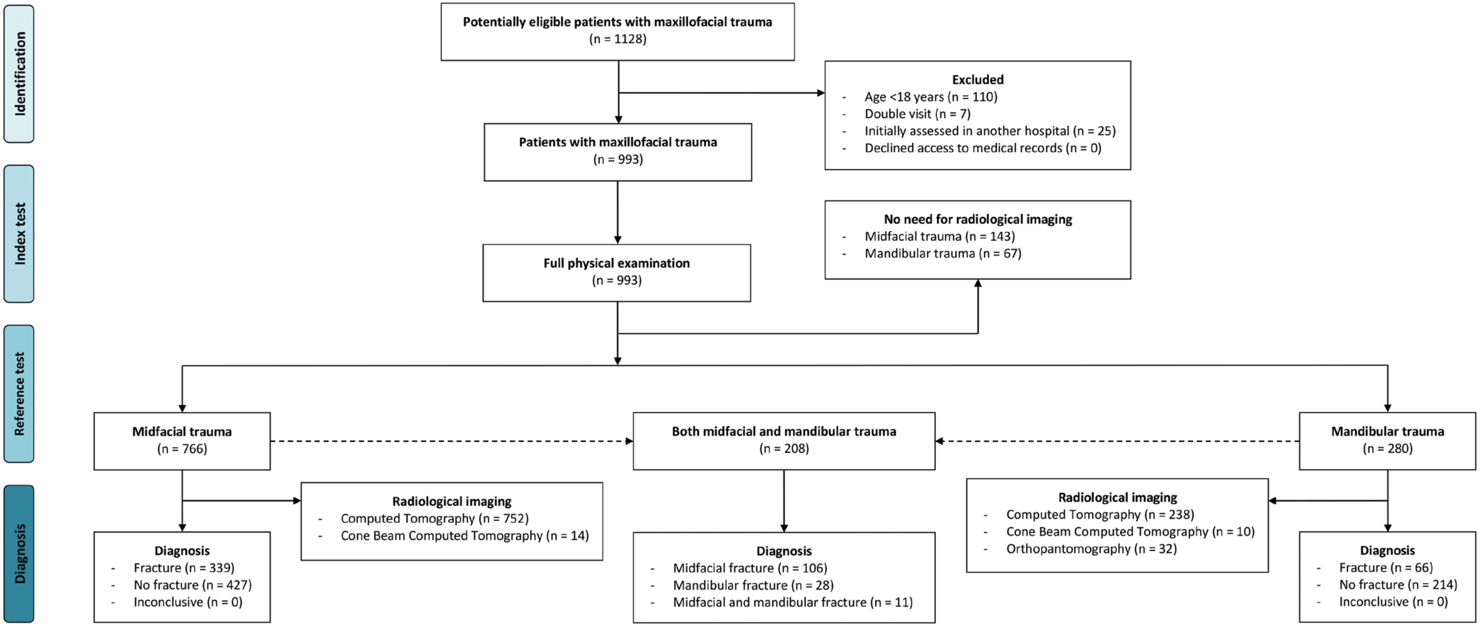

Figure 1: Flowchart of study patients

Table 1: Patient characteristics

Total patients (n)	993
Hospital (n(%))	
University Medical Center Groningen	331 (33.3)
Isala hospital Zwolle	449 (45.2)
Isala Diaconessenhuis hospital Meppel	71 (7.2)
Nij Smellinghe hospital Drachten	142 (14.3)
Gender distribution (n(%))	
Male	522 (52.6)
Female	471 (47.4)
Age (years)	
Median	56
Interquartile range	41
Range	18-102
Source of referral (n(%))	
Ambulance	591 (59.5)
Air ambulance services	25 (2.5%)
General practitioner	254 (25.6%)
Dentist	8 (0.8%)
Self-referral	88 (8.9)
Other	27 (2.7%)
Mechanism of injury (n(%))	
Activities of daily living, home or private	312 (31.4)
Work	34 (3.4)
Traffic	443 (44.6)
Motor vehicles	10 (1.0)
Scooters and mopeds	37 (3.7)
Bicycles	334 (33.6)
Pedestrians	15 (1.5)
Sports	33 (3.3)
Violence	121 (12.2)
Fall from same level	4 (0.4)
Fall from high level	0 (0)
Suspected suicide attempt	3 (0.3)
Other	33 (3.3)
Not verifiable	10 (1.0)
Reported alcohol use (n(%))	226 (22.8)
GCS categories (n(%))	
Minor (14-15)	941 (94.8)
Moderate (9-13)	9 (0.9)
Severe (3-8)	33 (3.3)
Not reported	10 (1.0)
Status of intubation and/or sedation (n(%))	25 (2.5)

Abbreviations: GCS Glasgow Coma Scale

Physical examination findings for midfacial trauma patients

The diagnostic accuracy outcomes of the individual physical examination findings are summarized in Table 2. Swelling (81.1%), laceration (56.1%), peri-orbital hematoma (46.3%) and epistaxis (37.7%) were the most common physical examination findings for the midfacial trauma populations. Physical examination findings that were least common included ocular movement limitations (1.9%), diplopia (2.9%), and subjective (3.7%) and objective malocclusion (1.4%). High sensitivity was found for swelling (86.7%) and high specificity was found for facial depression (99.3), raccoon eyes (95.3), subconjunctival haemorrhage (95.9), ocular movement limitations (99.8), diplopia (98.3), infra-orbital nerve paresthesia (97.0), subjective (98.2) and objective malocclusion (98.6), tooth mobility or avulsion (96.5), palpable step-off (98.6) and maxillary mobility (96.1). A high PPV and corresponding LR+ was found for facial depression (93.9/20.0), ocular movement limitations (92.3/16.3) and palpable step-off (91.2/13.6). For NPV of the individual physical findings was low, ranging from 57.5 to 70.6.

Physical examination findings for mandibular trauma patients

For mandibular trauma patients, jaw movement pain (47.6%) and subjective malocclusion (55.0%) were the most common physical examination findings, whereas inferior alveolar nerve paresthesia (3.1%), palpable step-off (6.3%) and tooth mobility or avulsion (6.6%) were less common. High sensitivity was found for jaw movement pain (95.2) and high specificity was found for inferior alveolar nerve paresthesia (98.0), intra-oral hematoma (92.3), palpable step-off (99.5), tooth mobility or avulsion (96.7), objective malocclusion (96.2) and the tongue blade bite test (95.0). A high PPV and LR+ was found for palpable step-off (94.1/55.7) and objective malocclusion (95.5/16.5) whereas high NPV and low LR- was found for swelling (90.9/0.3), jaw movement pain (97.9/0.1), mouth opening limitations (95.7/0.2), the angular compression test (94.7/0.2), the axial chin pressure test (94.9/0.2) and the tongue blade bite test (90.5/0.5).

Table 2: Diagnostic accuracy of individual physical examination findings

	Outcome				Statistics						
Midface	Present (n)	Absent (n)	Not testable (n)	Missing data (n)	Prev. (CI)	Sens. (CI)	Spec. (CI)	PPV (CI)	NPV (CI)	LR+ (CI)	LR- (CI)
Swelling	621	145	0	0	81.1 (78.1-83.7)	86.7 (82.7-89.9)	23.4 (19.7-27.7)	47.3 (43.4-51.3)	69.0 (61.0-75.9)	1.1 (1.1-1.2)	0.6 (0.4-0.8)
Laceration	430	336	0	0	56.1 (52.6-59.6)	59.0 (53.7-64.1)	46.1 (41.5-50.9)	46.5 (41.8-51.2)	58.6 (53.3-63.8)	1.1 (1.0-1.2)	0.9 (0.8-1.0)
Facial depression	49	693	21	3	6.6 (5.0-8.6)	14.3 (10.9-18.5)	99.3 (97.9-99.8)	93.9 (83.5-97.9)	60.2 (56.5-63.8)	20.0 (6.3-63.7)	0.9 (0.8-0.9)
Peri-orbital hematoma	355	411	0	0	46.3 (42.8-49.9)	58.7 (53.4-63.8)	63.5 (58.8-67.9)	56.1 (50.9-61.1)	65.9 (61.2-70.4)	1.6 (1.4-1.9)	0.7 (0.6-0.8)
Raccoon eyes	55	708	0	3	7.2 (5.6-9.3)	10.4 (7.6-14.1)	95.3 (92.9-96.9)	63.6 (50.4-75.1)	57.5 (53.8-61.1)	2.2 (1.3-3.8)	0.9 (0.9-1.0)
Epistaxis	285	470	9	2	37.7 (34.4-41.3)	58.4 (53.1-63.6)	78.5 (74.3-82.1)	68.1 (62.4-73.2)	70.6 (66.4-74.6)	2.7 (2.2-3.3)	0.5 (0.5-0.6)
Subconjunctival hemorrhage	69	656	36	5	9.5 (7.6-11.9)	16.6 (12.9-21.1)	95.9 (93.5-97.4)	75.4 (64.0-84.0)	60.1 (56.3-63.7)	4.0 (2.4-6.8)	0.9 (0.8-0.9)
Ocular movement limitation	13	686	65	2	1.9 (1.1-3.2)	4.1 (2.3-7.0)	99.8 (98.6-100.0)	92.3 (66.7-98.6)	58.6 (54.9-62.2)	16.3 (2.1-125.0)	1.0 (0.9-1.0)
Diplopia	20	676	68	2	2.9 (1.9-4.4)	4.4 (2.6-7.4)	98.3 (96.5-99.2)	65.0 (43.3-81.9)	58.6 (54.8-62.2)	2.6 (1.0-6.3)	1.0 (0.9-1.0)
Infra-orbital nerve paresthesia	62	635	66	3	8.9 (7.0-11.2)	17.1 (13.2-21.8)	97.0 (94.9-98.3)	80.6 (69.1-88.6)	61.7 (57.9-65.4)	5.7 (3.1-10.6)	0.9 (0.8-0.9)
Subjective malocclusion [a]	13	342	183	1	3.7 (2.2-6.2)	6.3 (3.3-11.5)	98.1 (95.2-99.3)	69.2 (42.4-87.3)	60.5 (55.3-65.6)	3.3 (1.0-10.5)	1.0 (0.9-1.0)
Objective malocclusion [a]	5	353	179	2	1.4 (0.6-3.2)	1.4 (0.4-5.1)	98.6 (96.1-99.5)	40.0 (11.8-76.9)	61.5 (56.4-66.4)	1.1 (0.2-6.3)	1.0 (1.0-1.0)
Tooth mobility or avulsion	48	707	8	3	6.4 (4.8-8.3)	10.0 (7.2-13.7)	96.5 (94.2-97.8)	68.8 (54.7-80.1)	57.9 (54.2-61.4)	2.8 (1.6-5.1)	0.9 (0.9-1.0)

Table 2 *(continued)*

	Outcome				Statistics						
Midface	Present (n)	Absent (n)	Not testable (n)	Missing data (n)	Prev. (CI)	Sens. (CI)	Spec. (CI)	PPV (CI)	NPV (CI)	LR+ (CI)	LR- (CI)
Palpable step-off	68	663	29	6	9.3 (7.4-11.6)	19.6 (15.6-24.4)	98.6 (96.9-99.3)	91.2 (82.1-95.9)	61.7 (57.9-65.3)	13.6 (5.9-31.0)	0.8 (0.8-0.9)
Maxillary mobility	36	680	38	12	5.0 (3.7-6.9)	6.5 (4.3-9.8)	96.1 (93.7-97.6)	55.6 (39.6-70.5)	57.8 (54.0-61.5)	1.7 (0.9-3.2)	1.0 (0.9-1.0)
Mandible											
Swelling	105	175	0	0	37.5 (32.0-43.3)	75.8 (64.2-84.5)	74.3 (68.1-79.7)	47.6 (38.3-57.1)	90.9 (85.7-94.3)	2.9 (2.3-3.8)	0.3 (0.2-0.5)
Extra-oral laceration	101	179	0	0	36.1 (30.7-41.8)	54.5 (42.6-66.0)	69.6 (63.2-75.4)	35.6 (27.0-45.4)	83.2 (77.1-88.0)	1.8 (1.3-2.4)	0.7 (0.5-0.9)
Jaw movement pain	129	142	9	0	47.6 (41.7-53.5)	95.2 (86.7-98.3)	66.5 (59.9-72.6)	45.7 (37.4-54.3)	97.9 (94.0-99.3)	2.8 (2.3-3.5)	0.1 (0.0-0.2)
Mouth opening limitation	88	185	7	0	32.2 (27.0-38.0)	87.1 (76.6-93.3)	83.9 (78.3-88.2)	61.4 (50.9-70.9)	95.7 (91.7-97.8)	5.4 (3.9-7.5)	0.2 (0.1-0.3)
Inferior alveolar nerve paresthesia	8	253	17	2	3.1 (1.6-5.9)	6.7 (2.6-15.9)	98.0 (95.0-99.2)	50.0 (21.5-78.5)	77.9 (72.4-82.5)	3.4 (0.9-13.0)	1.0 (0.9-1.0)
Intra-oral hematoma	35	229	13	3	13.3 (9.7-17.9)	33.3 (22.5-46.3)	92.3 (87.8-95.2)	54.3 (38.2-69.5)	83.4 (78.0-87.7)	4.3 (2.4-7.8)	0.7 (0.6-0.9)
Intra-oral laceration	62	206	10	2	23.1 (18.5-28.5)	40.7 (29.1-53.4)	81.8 (76.0-86.5)	38.7 (27.6-51.2)	83.0 (77.3-87.5)	2.2 (1.5-3.4)	0.7 (0.6-0.9)
Palpable step-off	17	252	9	2	6.3 (4.0-9.9)	26.7 (17.1-39.0)	99.5 (97.3-99.9)	94.1 (73.0-99.0)	82.5 (77.4-86.7)	55.7 (7.5-411.7)	0.7 (0.6-0.9)
Tooth mobility or avulsion	18	256	5	1	6.6 (4.2-10.1)	17.5 (10.0-28.6)	96.7 (93.3-98.4)	61.1 (38.6-79.7)	79.7 (74.3-84.2)	5.3 (2.1-13.0)	0.9 (0.8-1.0)
Subjective malocclusion [a]	31	27	7	0	55.0 (42.5-66.9)	81.8 (65.6-91.4)	77.8 (59.2-89.4)	81.8 (65.6-91.4)	77.8 (59.2-89.4)	3.7 (1.8-7.6)	0.2 (0.1-0.5)

Table 2 *(continued)*

	Outcome				Statistics						
Midface	Present (n)	Absent (n)	Not testable (n)	Missing data (n)	Prev. (CI)	Sens. (CI)	Spec. (CI)	PPV (CI)	NPV (CI)	LR+ (CI)	LR- (CI)
Objective malocclusion [a]	22	37	6	0	37.3 (26.1-50.0)	63.6 (46.6-77.8)	96.2 (81.1-99.3)	95.5 (78.2-99.2)	67.6 (51.5-80.4)	16.5 (2.4-115.0)	0.4 (0.2-0.6)
Angular compression test pain	96	171	12	1	36.0 (30.4-41.9)	85.0 (73.9-91.9)	78.3 (72.2-83.3)	53.1 (43.2-62.8)	94.7 (90.3-97.2)	3.9 (3.0-5.2)	0.2 (0.1-0.4)
Axial chin pressure pain	82	178	17	3	31.5 (26.2-37.4)	84.7 (73.5-91.8)	84.1 (78.4-88.5)	61.0 (50.2-70.8)	94.9 (90.7-97.3)	5.3 (3.8-7.4)	0.2 (0.1-0.3)
Tongue blade bite test	22	148	86	24	12.9 (8.7-18.8)	51.7 (34.4-68.6)	95.0 (90.1-97.6)	68.2 (47.3-83.6)	90.5 (84.7-94.3)	10.4 (4.7-23.3)	0.5 (0.3-0.7)

Abbreviations: Prev. prevalence; Sens. sensitivity; Spec. specificity; PPV positive predictive value; NPV negative predictive value; LR+ positive likelihood ratio; LR- negative likelihood ratio

[a] Excluding patients with both a midfacial and mandibular trauma

Table 3: Clinical decision aid for ruling out patients with midfacial and mandibular fractures.

			Contingency table outcome		Cumulative diagnostic accuracy					
Clinical decision aid	Physical examination finding	Definition	TN (%)	FN (%)	Sens. (CI)	Spec. (CI)	PPV (CI)	NPV (CI)	LR+ (CI)	LR- (CI)
Midfacial trauma	Peri-orbital hematoma	Any hematoma of the orbital or zygomaticomaxillary area that is not defined as swelling or raccoon eyes.	271 (35.4)	140 (18.3)	58.7 (53.4-63.8)	63.5 (58.8-67.9)	56.1 (50.9-61.1)	65.9 (61.2-70.4)	1.6 (1.4-1.9)	0.7 (0.6-0.8)
	Epistaxis	A unilateral or bilateral active or past nosebleed.	211 (27.5)	63 (8.2)	81.4 (76.9-85.2)	49.4 (44.7-54.1)	56.1 (51.7-60.4)	77.0 (71.7-81.6)	1.6 (1.4-1.8)	0.4 (0.3-0.5)
	Ocular movement limitation	Unilateral restricted gazing or limited eye movements in any direction.	205 (26.8)	56 (7.3)	83.5 (79.2-87.1)	48.0 (43.3-52.7)	56.0 (51.7-60.3)	78.5 (73.2-83.1)	1.6 (1.4-1.8)	0.3 (0.3-0.4)

Table 3 *(continued)*

Clinical decision aid	Physical examination finding	Definition	Contingency table outcome		Cumulative diagnostic accuracy					
			TN (%)	FN (%)	Sens. (CI)	Spec. (CI)	PPV (CI)	NPV (CI)	LR+ (CI)	LR- (CI)
	Infra-orbital nerve paresthesia	Any numbness, change or loss of sensation of the infra-orbital nerve area of innervation.	195 (25.5)	52 (6.8)	84.7 (80.4-88.1)	45.7 (41.0-50.4)	55.3 (51.0-59.5)	78.9 (73.4-83.6)	1.6 (1.4-1.7)	0.3 (0.3-0.4)
	Palpable step-off	The presence of a bony step-off found during palpation of the zygomatic arch, infra-orbital rim, supra and lateral orbital rim, nasal bridge and zygomaticoalveolar crest intra-orally.	189 (24.7)	43 (5.6)	87.3 (83.3-90.4)	44.3 (39.6-49.0)	55.4 (51.2-59.6)	81.5 (76.0-85.9)	1.6 (1.4-1.7)	0.3 (0.2-0.4)
	Tooth mobility or avulsion	Mobility or avulsion of any maxillary tooth element.	182 (23.8)	35 (4.6)	89.7 (86.0-92.5)	42.6 (38.0-47.4)	55.4 (51.2-59.5)	83.9 (78.4-88.2)	1.6 (1.4-1.7)	0.2 (0.2-0.3)
Mandible trauma	Angular compression test pain	Noteworthy presence of pain of the symphyseal or parasymphyseal region induced by simultaneous bilateral pressure of the mandibular angle.	162 (57.9)	9 (3.2)	86.2 (75.7-92.5)	75.7 (69.5-81.0)	51.9 (42.5-61.0)	94.7 (90.3-97.2)	3.5 (2.7-4.6)	0.2 (0.1-0.3)
	Axial chin pressure test pain	Noteworthy unilateral or bilateral pain of the condylar or temporomandibular region induced by axial pressure on the chin.	152 (54.3)	3 (1.1)	95.5 (87.5-98.4)	71.0 (64.6-76.7)	50.4 (41.8-59.0)	98.1 (94.5-99.3)	3.3 (2.7-4.1)	0.1 (0.0-0.2)
	Objective malocclusion	Objectively identified traumatic misalignment of the maxillary and mandibular dental arches.	102 (36.4)	2 (0.7)	97.0 (89.6-99.2)	47.7 (41.1-54.3)	36.4 (29.6-43.7)	98.1 (93.3-99.5)	1.9 (1.6-2.1)	0.1 (0.0-0.3)
	Tooth mobility or avulsion	Mobility or avulsion of any mandibular tooth element.	96 (34.3)	2 (0.7)	97.0 (89.6-99.2)	40.7 (34.3-47.3)	33.5 (27.2-40.5)	97.8 (92.2-99.4)	1.6 (1.5-1.8)	0.1 (0.0-0.3)
	Tongue blade bite test	The patient's ability to maintain bilateral inter-maxillary fixation of a tongue depressor (1.6 mm) while it gets broken by rotation.	74 (26.4)	1 (0.4)	98.5 (91.9-99.7)	34.6 (28.5-41.2)	31.7 (25.7-38.4)	98.7 (92.8-99.8)	1.5 (1.4-1.7)	0.0 (0.0-0.3)

Abbreviations: TN true negatives; FN false negatives; NPV negative predictive value; LR- negative likelihood ratio; Sens. sensitivity

Clinical decision aids

A clinical decision aid was constructed for midfacial and mandibular trauma based on the positive factor loadings and the findings that were considered to be clinically relevant. The decision aid for midfacial trauma consisted of: peri-orbital haematoma, epistaxis, ocular movement limitation, infra-orbital nerve paraesthesia, palpable step-off and tooth mobility or avulsion resulting in sensitivity of 89.7 (86.0-92.5), NPV of 83.9 (78.4-88.2) and a LR- of 0.2 (0.2-0.3). Thereby, a total of 182 (23.8%) truly negative patients were identified when all the physical examination findings were absent. The fracture types that were ruled out by the clinical decision aid included orbital fractures (n=9), zygomaticomaxillary complex fractures (n=15) and nasal bone fractures (n=12) (table 4). Regarding mandibular trauma patients, the decision aid consisted of the angular compression test, axial chin pressure test, objective malocclusion, tooth mobility or avulsion and the tongue blade bite test, resulting in a sensitivity of 98.5 (91.9-99.7), NPV of 98.7 (92.8-99.8) and a LR- of 0.0 (0.0-0.3). A total of 74 (26.4%) truly negative patients were identified when all these physical examination findings were absent. The clinical decision aid did not rule out a symphyseal/parasymhyseal fracture (n=1).

Table 4: Fracture outcomes

Clinical decision aid	False negatives (n)	True positives (n)	Total (n)
Midface	35	304	339
Frontal sinus	1	24	25
Orbital rim and walls	9	87	96
Maxillary sinus	4	26	30
Zygomaticomaxillary complex	15	119	134
Nasoorbitoethmoid complex	0	17	17
Nasal bone	12	114	126
Le Fort I	1	8	9
Le Fort II	1	7	8
Le Fort III	0	6	6
Dentoalveolar complex	1	14	15
Mandible	1	65	66
Symphyseal or parasymphyseal	1	23	24
Corpus	0	17	17
Angular	0	8	8
Ramus	0	7	7
Coronoid	0	4	4
Condylar process	0	44	44
Dentoalveolar complex	0	1	1

Discussion

Emergency department workers are frequently faced with patients suspected of fractures of the maxillofacial region. Both the midfacial and mandibular region are characterized by a set of distinctive physical examination findings that can be used to predict the likelihood of a fracture and, consequently, justify the need for radiological imaging. Clinical decision aids were constructed for this large prospective multicentre cohort study of emergency department patients with the aim to diagnose or rule out the presence of midfacial and mandibular fractures. We found that the clinical decision aid for midfacial trauma patients produced a sensitivity of 89.7 and NPV of 83.9, correctly identifying 23.8% of the patients who did not have a fracture. The aid for mandibular trauma patients gave a sensitivity of 98.5 and NPV of 98.7 thus identifying that 26.4% of the population did not have a fracture. Hence, the clinical decision aid can be used to reduce unnecessary use of radiological imaging, consequently reducing radiation exposure and associated health care costs for this population of patients.

Physical examination findings related to midfacial trauma are based on the distinctive and complex anatomy of the midface. Since facial depression, ocular movement limitations, infra-orbital nerve paraesthesia and palpable step-off individually had a high PPV (>90) and LR+ (>10) means a midfacial fracture is very likely when one or more of these findings is present. Our clinical decision aid, consisting of peri-orbital haematoma, epistaxis, ocular movement limitation, infra-orbital nerve paraesthesia, palpable step-off and tooth mobility or avulsion, was unable to identify over 90% of the patients without fractures. Although 182 patients were correctly identified as not having a fracture, 35 patients were missed among whom orbital, zygomaticomaxillary complex and nasal fractures were most common. Clinical decision aids for midfacial trauma were also proposed by other authors. For example, the Wisconsin criteria uses a combination of bony step-off or instability, peri-orbital swelling or contusion, a Glasgow Coma Scale score of less than 14, malocclusion and tooth absence 2. The authors combined midfacial and mandibular fractures as an outcome. The presence of any of these findings resulted in a NPV of 87.8 and a sensitivity of 98.2, whereas the validation of these criteria by three studies resulted in a NPV of 81.3, 28.6 and 60, and a sensitivity of 97.4, 90.0 and 81.0, respectively. Other authors presented clinical decision aids for specific midfacial fracture types 8,14. A decision tool for orbital fractures was defined as any presence of subconjunctival haemorrhage, infra-orbital nerve paraesthesia, a change in position of the globe, reduced visual acuity or any two from peri-orbital haemorrhage, diplopia or limited eye movement, resulting in a NPV of 56.3 and a sensitivity of 80.0 8. Another study provided a decision tool for orbital floor fractures in the presence of any of the following: subconjunctival haemorrhage, infra-orbital nerve paraesthesia and ecchymosis or swelling, and resulted in a NPV and PPV of 92.3 and 74.2, respectively 14. They also provided a decision aid for nasal and zygomaticomaxillary fractures, showing a NPV of 97.8 and 90.9. The clinical decision aids presented in their study were specifically constructed to rule out particular fracture types. However, from a clinical perspective, emergency department workers are blinded for the outcome of interest and, therefore, need to consider the full range of potential fracture types. In this present study, any midfacial fracture was chosen as an outcome to reflect the emergency department setting. Post-hoc analysis can provide evidence of how the physical examination findings are related to these fracture types.

The distinctive mandibular trauma physical examination findings are related to the bilateral temporomandibular joint articulation that allows dental occlusion and articulation by mandibular motion. As individual findings, palpable step-off and objective malocclusion were found to have a particularly high PPV and LR+ and so therefore strongly suggest the presence of a mandibular fracture. On the other hand, swelling, jaw movement pain, mouth opening limitation, the angular compression test, the axial chin pressure test and the tongue blade bite test gave a high NPV and LR-, indicating that these individual findings seems particularly useful for excluding the presence of mandibular fractures. This is in line with previous research which also found a high NPV for the tongue blade bite test [14–16]. We have successfully constructed a clinical decision aid for mandibular trauma patients resulting in a NPV of 98.7 and so identifying, retrospectively, that 26.4% of the patients had redundantly received radiological imaging. The clinical decision aid only missed one patient with a symphyseal fracture. Moreover, the cumulative diagnostic accuracy revealed that the clinical decision aid without the tongue blade bite test resulted in a NPV of 98.0 and so identified 34.3% of the patients correctly. There is no data available from previous research on the angular compression test and the axial chin pressure test. The utility of these tests seems particularly useful because of their generalizability and reproducibility for all emergency department workers.

The methodological strengths of the study include the prospective multicenter study design, the large number of consecutive patients and the standardized physical examinations strategy for each patient. Furthermore, we included patients whose physical examination findings were stated as 'not testable'. On using this approach we were able to include patients who could not be assessed because of, for example, severe swelling with respect to ocular related findings, or the state of consciousness since interaction with the patients is necessary. The results of our study show that the physical examinations of both midfacial and mandibular trauma patients can lead to "not testable" findings, emphasizing the need to score this as an outcome. Previous studies did not report these specific outcomes. Most importantly, our approach to constructing the clinical decision aids makes them applicable to a full range of midfacial and mandibular trauma patients, regardless of age, mechanism of injury or trauma severity.

Limitations of our study include that the physical examination were performed by various professions, each with different years of experience. However, from a clinical perspective, the diagnostic management of these patients is also conducted by a multidisciplinary team. Another limitation is that no validation was performed. Therefore, future research should focus on how these clinical decision aids safely can reduce unnecessary radiological imaging in a prospective cohort study with a new population of patients. Future research should also focus on how physical examination findings are related to midfacial or mandibular fractures that require immediate intervention. For example, orbital floor fractures are known for the potential entrapment of the inferior rectus muscle, causing ocular movement limitations that require surgical exploration and should therefore not to be missed.

In conclusion, the diagnostic accuracy of physical examination findings was identified for patients with suspected midfacial and mandibular fractures. The construction of a clinical decision aid resulted in a NPV of 83.9 for midfacial trauma patients and a NPV of 98.7 for mandibular trauma patients and may aid in stratifying patients suspected for fractures to reduce unnecessary diagnostic imaging.

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Supplementary table S1: Definition of the physical examination findings

Midface	
Swelling	Any swelling of the midfacial region. A "*yes*" was scored if there was swelling of the midfacial region. A "*no*" was scored if there was no swelling of the midfacial region. A "*not testable*" was scored if swelling of the midfacial region could not be assessed.
Laceration	Any (extra-oral) laceration of the midfacial skin. A "*yes*" was scored if there was any (extra-oral) laceration of the midfacial skin. A "*no*" was scored if there were no (extra-oral) laceration of the midfacial skin. A "*not testable*" was scored if laceration of the midfacial skin could not be assessed.
Facial depression	Unilateral flattening or depression of the malar eminence, cheek or zygomaticomaxillary complex. A "*yes"* was scored if there was unilateral facial depression. A "*no*" was scored if there was no unilateral facial depression. A "*not testable"* was scored if unilateral facial depression could not be assessed, for example in situations where physical examination was not possible due severe swelling or excessive pain during palpation.
Peri-orbital hematoma	Any hematoma localized within or around the orbital or zygomaticomaxillary area that is not defined as raccoon eyes. A "*yes*" was scored if there was a peri-orbital hematoma. A "*no*" was scored if there was no peri-orbital hematoma. A "*not testable*" was scored if the presence of a peri-orbital hematoma could not be assessed.
Raccoon eyes	Bilateral ecchymosis or hematoma localized within and around the upper and/or lower eyelids. A "*yes*" was scored for cases with raccoon eyes. A "*no*" was scored if raccoon eyes were not present. A "*not testable*" was scored if the presence of raccoon eyes could not be assessed.
Epistaxis	A unilateral or bilateral active or passed nosebleed. A "*yes*" was scored for cases with (past) epistaxis. A "*no*" was scored if there was no (past) epistaxis. A "*not testable*" was scored if the presence of epistaxis could not be assessed.
Subconjunctival hemorrhage	A sharply circumscribed bleeding or hemorrhage of the conjunctiva in one or both globes. A "*yes*" was scored if there was subconjunctival hemorrhage. A "*no*" was scored if there was no subconjunctival hemorrhage. A "*not testable*" was scored if the presence of a subconjunctival hemorrhage could not be assessed, for example where severe swelling or hematoma of the eye could not be visualized, even with active help.
Ocular movement limitation	Any restricted gazing or limitation of the eye movements in any direction. A "*yes*" was scored if there were ocular movement limitations. A "*no*" was scored if there were no ocular movement limitations. A "*not testable*" was scored if ocular movements could not be assessed, for example in case of severe swelling and/or hematoma or if patient's state of consciousness hindered active instruction of the patient.
Diplopia	Double vision (a situation where the patients sees a single object in duplicate), either passive or induced during the assessment of the ocular movements. A "*yes*" was scored in case of diplopia. A "*no*" was scored if there was no diplopia. A "*not testable*" was scored if the presence of diplopia could not be assessed, for example when the patient's state of consciousness hindered communication.
Infra-orbital nerve paresthesia	Any numbness, change or loss of sensation of the infraorbital nerve innervation area (e.g., the lower eyelid, nasal vestibule, part of the cheek, the upper lip, upper incisor, canine and premolars). A "*yes*" was scored if there was infra-orbital nerve paresthesia. A "*no*" was scored if there was no infra-orbital nerve paresthesia. A "*not testable*" was scored if the presence of infra-orbital nerve paresthesia could not be assessed, for example if the patient's state of consciousness hindered communication.
Subjective malocclusion	Misalignment or incorrect relation between the teeth of the two dental arches as experienced by the patient that emerged after the trauma. A "*yes*" was scored if the patient experiences the presence of malocclusion. A "*no*" was scored if the patient did not experience malocclusion. A "*not testable*" was scored if subjective malocclusion could not be assessed, for example in a situation where the patient's state of consciousness hindered communication, or in edentulous patients.

Supplementary table S1 *(continued)*

Objective malocclusion	Traumatic misalignment or incorrect relation between the teeth of the two dental arches as objectively identified by the assessor during intra-oral examination assessment. A "*yes*" was scored in there was malocclusion. A "*no*" was scored if there was no malocclusion. A "*not testable*" was scored if the occlusion could not be assessed, for example if the patient had dentures, was edentulous or if the patient was intubated and sedated.
Tooth mobility or avulsion	Mobility or avulsion of any maxillary tooth elements (e.g., first (11-18) and second (21-28) quadrant tooth elements). A "*yes*" was scored in case of tooth mobility or avulsion. A "*no*" was scored if there was no tooth mobility or avulsion. A "*not testable*" was scored if the presence of tooth mobility or avulsion could not be assessed, for example if the patient could not be suitably instructed.
Palpable step-off	The presence of a bony step-off, step defect or discontinuity found when palpating any of the following midfacial anatomical landmarks: (1) zygomatic arch, (2) infra-orbital rim, (3) supra and lateral orbital rim, (4) nasal bridge and (5) zygomaticalveolar crest intra orally. A "*yes*" was scored if there was a palpable step-off. A "*no*" was scored if there was no palpable step-off. A "*not testable*" was scored if the presence of a palpable step-off could not be assessed, for example in case where swelling and/or hematoma hindered full palpable examination of the midface.
Maxillary mobility	Mobility of the complete alveolar process of the maxilla during active lateral or frontal palpation after fixation of the midface. A "*yes*" was scored in case of maxillary mobility. A "*no*" was scored if there was no maxillary mobility. A "*not testable*" was scored if maxillary mobility could not be assessed.
Mandible	
Swelling	Any swelling of the mandibular region. A "*yes*" was scored if was swelling of the mandibular region. A "*no*" was scored if there was no swelling of the mandibular region. A "*not testable*" was scored if swelling of the mandibular region could not be assessed.
Extra-oral laceration	Any extra-oral laceration of the skin of the mandibular region. A "*yes*" was scored if there was any laceration of the mandibular cheek or chin. A "*no*" was scored if there were no laceration of the mandibular cheek or chin. A "*not testable*" was scored if laceration of the mandibular cheek or chin could not be assessed.
Jaw movement pain	The presence of pain during opening, protrusion or lateral movement(s) of the mandible. A "*yes*" was scored if there was pain with jaw movement(s). A "*no*" was scored if there was full range movement of the jaw without pain. A "*not testable*" was scored if pain during jaw movements could not be tested, for example when the patient's state of consciousness hindered adequate communication.
Mouth opening limitations	The reported inability to open the mouth fully or a measured restriction of the mouth opening of 35mm or less during opening of mandible. A "*yes*" was scored in case of mouth opening limitations. A "*no*" was scored if there were no mouth opening limitations. A "*not testable*" was scored if the mouth opening limitations could not be assessed, for example when the patient's state of consciousness hindered adequate communication.
Inferior alveolar nerve paresthesia	Any numbness, change or loss of sensation of the inferior alveolar nerve innervation area (e.g., skin of the lower lip and chin, the mucosa and the gingiva of the inferior vestibule). A "*yes*" was scored if there was inferior alveolar nerve paresthesia. A "*no*" was scored if there was no inferior alveolar nerve paresthesia. A "*not testable*" was scored if the presence of inferior alveolar nerve paresthesia could not be assessed, for example when the patient's state of consciousness of the patient hindered sufficient communication.
Intra-oral hematoma	Any intra-orally localized hematoma either in the mucosa or gingival tissue, including sublingual hematoma. A "*yes*" was scored if there was an intra-oral hematoma. A "*no*" was scored if there was no intra-oral hematoma. A "*not testable*" was scored if the presence of an intra-oral hematoma could not be assessed.

Supplementary table S1 *(continued)*

Intra-oral laceration	Any intra-orally localized gingival, sublingual or mucosal laceration. A "*yes*" was scored if there was an intra-oral laceration. A "*no*" was scored if there was no intra-oral laceration. A "*not testable*" was scored if the presence of an intra-oral laceration could not be assessed.
Palpable step-off	The presence of a palpable bony step-off, step defect or discontinuity in the mandible, with any of any of the following landmarks: (1) alveolar mandibular process intra-orally, (2) inferior mandibular ridge extra-orally and (3) angular, ramus and condylar mandibular process extra-orally. A "*yes*" was scored if there was a palpable step-off. A "*no*" was scored if there was no palpable step-off. A "*not testable*" was scored if the presence of a palpable step-off could not be assessed, for example in cases where swelling and/or hematoma hindered full palpable examination of the mandible.
Tooth mobility or avulsion	Mobility or avulsion of any mandibular tooth element (e.g., third (31-38) and fourth (41-48) quadrant tooth elements). A "*yes*" was scored in case of tooth mobility or avulsion. A "*no*" was scored if there was no tooth mobility or avulsion. A "*not testable*" was scored if the presence of tooth mobility or avulsion could not be assessed, for example if the patient could not be suitably instructed.
Subjective malocclusion	Misalignment or incorrect relation between the teeth of the two dental arches as experienced by the patient that emerged after the trauma. A "*yes*" was scored if the patient experiences the presence of malocclusion. A "*no*" was scored if the patient did not experience malocclusion. A "*not testable*" was scored if the presence of subjective malocclusion could not be assessed, for example a situation where the patient's state of consciousness hindered communication.
Objective malocclusion	Traumatic misalignment or incorrect relation between the teeth of the two dental arches as objectively identified by the assessor during intra-oral examination assessment. A "*yes*" was scored in there was malocclusion. A "*no*" was scored if there was no malocclusion. A "*not testable*" was scored if the occlusion could not be assessed, for example if the patient had dentures, the patient was edentulous or if the patient was intubated and sedated.
Angular compression test pain	Noteworthy presence of pain complaints in the symphyseal or parasymphyseal region induced by simultaneous bilateral pressure of the mandibular angle also known as the angular compression test. A "*yes*" was scored in case of noteworthy presence of pain during the angular compression test. A "*no*" was scored if there was no pain during the angular compression test. A "*not testable*" was scored when the angular compression test could not be conducted, for example if communication with the patient was not possible.
Axial chin pressure test pain	Noteworthy unilateral or bilateral presence of pain complaints of the condylar or temporomandibular region induced by axial pressure on the chin. A "*yes*" was scored in case of noteworthy pain during the axial chin pressure test. A "*no*" was scored if there were no pain during the axial chin pressure test. A "*not testable*" was scored when the axial chin pressure test could not be conducted, for example if communication with the patient was not possible.
Tongue blade bite test	The patient's ability to maintain bilateral intermaxillary fixation of a uniform wooden spatula or tongue depressor (150 x 18 x 1.6 mm) while it was broken by a medial rotation by the assessor. A "*yes*" was scored if the patient was not able to maintain bilateral fixation of the wooden spatula during the tongue blade bite test. A "*no*" was scored if the patient was able to maintain bilateral fixation of the wooden spatula during the tongue blade bite test. A "*not testable*" was scored if the tongue blade bite test could not be conducted, for example in a situation where the patient could not be instructed.

4b

CHAPTER 4b

A clinical decision aid to discern patients without and with midfacial and mandibular fractures that require treatment (the REDUCTION-II study): a prospective multicentre cohort study

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Submitted
Adapted version of the manuscript

Abstract

Objective: To assess the diagnostic accuracy of physical examination findings and to construct clinical decision aids to discern emergency department patients without and with midfacial and mandibular fractures that require treatment.

Methods: A prospective multicentre cohort study was conducted in four hospitals in the Netherlands. Consecutive maxillofacial trauma patients were included whereupon each patient underwent a standardized physical examination consisting of fifteen and fourteen findings for midfacial and mandibular trauma, respectively. The primary outcome was the decision whether to treat during the emergency department stay or within 24 hours of admission. The diagnostic accuracy was calculated for the individual physical examination findings and ensuing clinical decision aids with the focus being on detecting midfacial and mandibular fractures that require active treatment.

Results: A total of 766 midfacial trauma patients were identified of whom 339 (44.3%) had midfacial fractures. Of those, 74 (21.8%) required active treatment. A total of 280 mandibular trauma patients were identified of whom 66 (23.6%) had mandibular fractures. Of those, 37 (56.0%) required active treatment. The decision aid for midfacial trauma consisting of facial depression, epistaxis, ocular movement limitation, palpable step-off, objective malocclusion and tooth mobility or avulsion had a sensitivity of 97.3 (90.7-99.3), a specificity of 38.6 (35.0-42.3), and a negative predictive value of 99.3 (97.3-99.8). The decision aid for mandibular trauma consisting of mouth opening limitation, jaw movement pain, objective malocclusion and tooth mobility or avulsion resulted in a sensitivity of 100.0 (90.6-100.0), a specificity of 39.1 (33.2-45.4), and a negative predictive value of 100.0 (96.1-100.0).

Conclusion: The clinical decision aids successfully identified midfacial and mandibular trauma patients requiring active fracture treatment and so may be useful in preventing unnecessary radiological procedures in the future.

Introduction

Midfacial and mandibular fractures are frequently found in trauma patients in the emergency department [1,2]. Missing these fractures may have major long term morphological, functional and aesthetic consequences. Upon entering the emergency department, each patient should be subjected to a structured assessment of the maxillofacial region and the observed findings should be used to identify which maxillofacial patients may have midfacial or mandibular fractures [1].

Although various studies have focused on how physical examination findings can be used to predict midfacial and mandibular fractures [3–13] and to stratify patients at risk of fractures and subsequently requiring radiological imaging of the maxillofacial region, studies on identifying patients that require treatment are limited [10,11]. In today's emergency department landscape, the primary assessment of trauma patients is mostly performed by emergency physicians and specialized trauma surgeons and, if maxillofacial fractures are diagnosed, an oral and maxillofacial surgeon is consulted to assess the need for active treatment. Therefore, early recognition of any fractures by all these health care professionals from the physical examination findings is required to deliver more accurate patient management. Moreover, it allows prioritization of other injuries and optimization of emergency department workflows. A clinical decision aid using physical examination findings could be used as a fast bedside strategy to single out patients with maxillofacial fractures that require treatment but, to date, no such clinical decision aid has been published.

Hence, this prospective multicenter REDUCTION II study (*RED*ucing *U*nnecessary *C*omputed *T*omography *I*n *M*axill*O*facial I*N*jury) was initiated with a twofold aim. First, to identify the diagnostic accuracy of physical examination findings in identifying midfacial and mandibular fractures that require treatment. Second, the construct a clinical decision aid with the focus being on successfully ruling out patients with these findings.

Material and Methods

Study design

A prospective observational cohort study was conducted of all emergency department patients suspected of midfacial and mandibular trauma between the period of May 2018 and October 2019. The Medical Ethical Committee of the University Medical Center Groningen confirmed that the Medical Research Involving Human Subjects Act did not apply (METc code 2017/249) and local feasibility was approved for the participating hospitals. The study was performed in compliance with the Declaration of Helsinki and according to the FEDERA (Foundation Federation of Dutch Medical Scientific Societies) code of conduct. The study was registered at ClinicalTrials.gov (NCT03314480) and reported according to the STARD guidelines (Standards for Reporting of Diagnostic Accuracy Studies) and Methodologic Standards for Interpreting Clinical Decision Rules in Emergency Medicine [14,15].

Inclusion and exclusion criteria

All consecutive emergency department patients presenting with midfacial or mandibular trauma at the University Medical Center Groningen (level I), Isala hospital Zwolle (Level I), Isala Diaconessenhuis hospital Meppel (level III) and Nij Smellinghe hospital Drachten (level III) were included. Patients younger than 18 years of age and patients admitted for a second time for maxillofacial trauma within the period of inclusion were excluded. Patients were also excluded if the initial assessment was performed in another hospital or access to medical records was declined.

Physical examination and radiological imaging

All eligible patients received a standardized full physical examination of the midfacial or mandibular region. The physical examination consisted of fifteen findings for midfacial trauma, and fourteen findings for mandibular trauma. The findings were consulted during the primary or secondary assessment of the patient, and standardized for all the included patients according to a tripartite strategy consisting of an individual hands-on instruction, online educational tool and bedside use of a pocket card. Details regarding the process of standardization were provided previously by our research group. Patients suspected of midfacial fractures were examined using Computed Tomography (CT) or Cone Beam Computed Tomography (CBCT). Midfacial fractures were defined as any fracture of the frontal sinus, orbital rim and walls, maxillary sinus, zygomaticomaxillary complex, nasoorbitoethmoid (NOE) complex, nasal bone, Le Fort I, II, III complex, and maxillary dentoalveolar complex. Patients suspected of mandibular fractures were diagnosed with CT, CBCT or orthopantomography (OPT). Mandibular fractures were defined as any fracture of the symphyseal or parasymphyseal area, corpus, angle, ramus, coronoid process, condylar process and dentoalveolar complex. Radiological interpretation was performed without knowledge of the radiological imaging outcome and the classification of fractures was performed by a board certified oral and maxillofacial surgeon (BvM).

Treatment and outcome measures

The primary outcome was the decision for treatment of midfacial or mandibular fractures as intended during the emergency department stay or within 24 hours of admission. The decision of treatment was determined by a consultant oral and maxillofacial surgeon or otorhinolaryngologist. Decisions were made according to the usual care in agreement with the treatment protocols of the Dutch Society of Oral and Maxillofacial Surgery (NVMKA) or Dutch Association of Otorhinolaryngology and Head & Neck Surgery (NVKNO) as consulted within the period of inclusion. The decision of fracture treatment was assigned to either a conservative or active intend. Conservative treatment included adequate analgesics, avoidance of nose blowing or holding the nose when sneezing, a soft non-chewing diet, and watchful observation. Active treatment was divided into closed or open treatment. Closed treatment included reduction of nasal fractures under local anesthesia, nasal packing, intermaxillary fixation, rigid and flexible splinting or appliances for dental injury. Open treatment included any surgical intervention in which the patient underwent open reduction and internal fixation in an operation theatre.

Secondary outcomes included the presence of skull fractures and dental injury. Skull fractures were defined as any fracture of the skull base, frontal, temporal, parietal or occipital bone diagnosed with a CT. Dental injury was defined as any clinical observed avulsion, luxation or fracture of the maxillary or mandibular teeth.

Statistical analyses

The Statistical Package for the Social Sciences was used for the data analyses (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). Fracture outcomes were presented as frequencies and percentages. The individual physical examination findings were presented as the proportion of patients diagnosed with a fracture, and patients diagnosed with any fracture requiring active treatment. For the subtypes of fractures, the physical examination findings were presented as the proportion of total diagnosed midfacial and mandibular fractures. The diagnostic accuracy was calculated for each individual physical examination finding.

Principle component analysis (PCA) was used to construct clinical decision aids consisting of physical examination findings, with the focus being on ruling out patients that require active treatment for midfacial or mandibular fractures. The PCA analysis was performed with subsequent promax rotation and Kaiser normalization and used to identify the underlying structure of the physical examination findings. The Barlett's test of sphericity and the Kaiser-Meyer-Olkin measure of sampling adequacy were conducted to test whether the variables were uncorrelated in the correlation matrix and factors with Eigenvalues greater than one were initially retained for the analysis.

The physical examination findings selected to construct the clinical decision aids were based on a combination of factor loadings and the clinical considerations of findings related to fractures that require active treatment by two board certified oral and maxillofacial surgeons (MD and BvM). Objective malocclusion and tooth mobility or avulsion were intentionally included in both clinical decision aids because they are essential findings for each patient suspected of midfacial and mandibular fractures requiring treatment. The contingency tables for the clinical decision aids were constructed with absent findings being recorded as 'negative' whereas present, not testable and missing findings were recorded as 'positive'.

Regarding the outcome of interest, a 'positive outcome' was defined as a patient whose fractures underwent active treatment (e.g. closed or open treatment), and a 'negative outcome' was defined as patients whose fractures were treated conservatively or patients who had been diagnosed as not having a fracture. The diagnostic accuracy and corresponding 95 per cent confidence interval outcomes included: prevalence, pre-test probability, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+) and negative likelihood ratio (LR-).

Results

Patient characteristics

A total of 993 patients were eligible for inclusion. Among this population, 766 patients had suffered a midfacial trauma and 280 patients had suffered a mandibular trauma. From the total population, 263 patients were identified with both a midfacial and mandibular trauma. Skull fractures were observed in 51 (5.1%) patients. Dental injury of the maxillary teeth was observed in 83 (8.4%) patients, and dental injury of the mandibular teeth was found in 28 (2.8%) patients.

Treatment of midfacial fractures

Midfacial fractures were diagnosed in 44.3% (n=339) of the patients. Zygomaticomaxillary complex fractures (n=134), nasal bone fractures (n=126) and orbital rim and wall fractures (n=96) were the most common (Table 1). Among those diagnosed with a midfacial fracture, 265 (78.2%) patients were treated conservatively, 32 (9.7%) received closed treatment and 42 (12.4%) received open treatment. The treatment outcomes of the midfacial fracture subtypes are presented in Table 1. Conservative treatment occurred most commonly for patients suffering fractures of the frontal sinus (64.0%), orbital rim and walls (84.4%), maxillary sinus (86.7%), zygomaticomaxillary complex (79.9%), nasoorbitoethmoid complex (70.6%) and the nasal bone (70.6%). Le Fort type fractures were generally treated surgically.

Table 1: Fracture outcomes

Fracture type	Total (n)	Conservative treatment (n (%))	Closed treatment (n (%))	Surgical treatment (n (%))
Midface fractures	339	265 (78.2)	32 (9.4)	42 (12.4)
Frontal sinus	25	16 (64.0)	0 (0.0)	9 (36.0)
Orbital rim and walls	96	81 (84.4)	4 (4.2)	11 (11.5)
Maxillary sinus	30	26 (86.7)	2 (6.7)	2 (6.7)
Zygomaticomaxillary complex	134	107 (79.9)	0 (0.0)	27 (20.1)
Nasoorbitoethmoid complex	17	12 (70.6)	1 (5.9)	4 (23.5)
Nasal bone	126	89 (70.6)	24 (19.0)	13 (10.3)
Le Fort I	9	4 (44.4)	1 (11.1)	4 (44.4)
Le Fort II	8	2 (25.0)	0 (0.0)	6 (75.0)
Le Fort III	6	3 (50.0)	0 (0.0)	3 (50.0)
Dentoalveolar complex	15	6 (40.0)	8 (53.3)	1 (6.7)
Mandible fractures	66	29 (43.9)	4 (6.1)	33 (50.0)
Symphyseal or parasymphyseal	24	6 (25.0)	0 (0.0)	18 (75.0)
Corpus	17	5 (29.4)	2 (11.8)	10 (58.8)
Angular	8	0 (0.0)	0 (0.0)	8 (100.0)
Ramus	7	4 (57.1)	0 (0.0)	3 (42.9)
Coronoid	4	1 (25.0)	0 (0.0)	3 (75.0)
Condylar process	44	21 (47.7)	4 (9.1)	19 (43.2)
Dentoalveolar complex	1	0 (0.0)	0 (0.0)	1 (100.0)

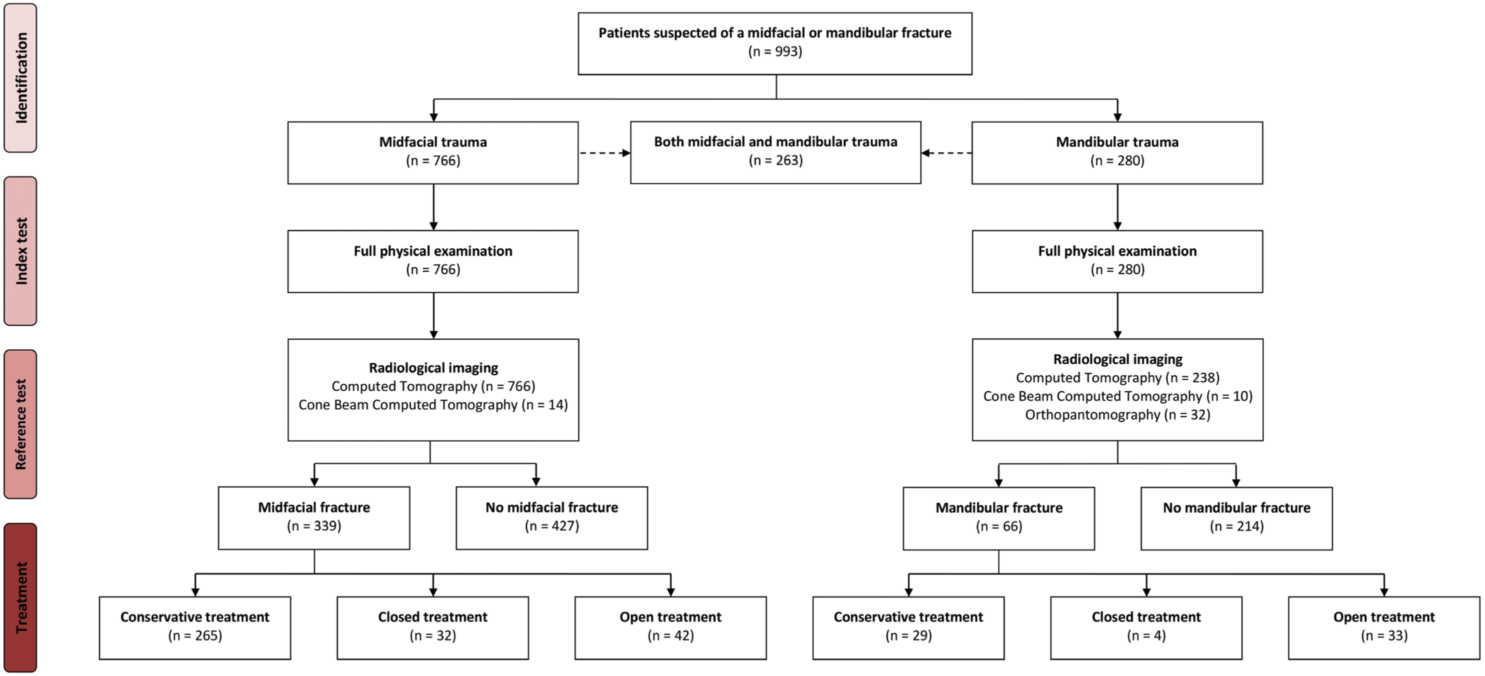

Figure 1: Flowchart of study patients.

Findings related to midfacial fractures requiring treatment

Facial depression (93.9%), ocular movement limitation (92.3%), infra-orbital nerve paresthesia (80.6%) and palpable step-off (91.2%) were the physical examination findings most often associated with the presence of a midfacial fracture (Table 2). The physical examination findings that were often seen with midfacial fractures requiring active treatment were facial depression (46.9%), palpable step-off (41.2%), objective malocclusion (39.1%), tooth mobility or luxation (35.4%) and ocular movement limitation (30.8%). The physical examination finding outcomes midfacial fracture subtypes requiring surgical treatment are presented in Table 2.

Treatment of mandibular fractures

Mandibular fractures were diagnosed in 23.6% (n=66) of the patients. Symphyseal or parasymphyseal (n=24), corpus (n=17) and condylar process (n=44) fractures were the most common mandibular fracture subtypes observed (Table 1). Regarding the patients that were diagnosed with a mandibular fracture, 29 (43.9%) were treated conservatively, 4 (6.1%) received closed treatment and 33 (50.0%) received open treatment. The treatment outcomes of the different mandibular fracture subtypes are presented in Table 1. Ramus (57.1%) and condylar process (47.7%) fractures were often treated conservatively. Open treatment was commonly observed for patients with fractures of the symphyseal or parasymphyseal area (75.0%), angle (100.0%), coronoid process (75.0%) and dentoalveolar complex (100%).

Findings related to mandibular fractures requiring treatment

Mouth opening limitation (61.4%), palpable step-off (94.1%), tooth mobility or avulsion (61.1%), objective malocclusion (66.7%), a positive axial chin pressure test (61.0%), and positive tongue blade bite test (68.2%) were the physical examination findings most often associated with the presence of a mandibular fracture (Table 2). The physical examination findings that were commonly seen with a mandibular fracture requiring surgical treatment were palpable step-off (82.4%), tooth mobility or avulsion (44.4%), objective malocclusion (42.9%), a positive tongue blade bite test (40.3%) and a positive axial chin pressure test (40.2%). The outcomes of physical examination findings for the specific mandibular fractures subtypes requiring active treatment are presented in Table 3.

Table 2: Physical examination findings associated with midfacial fractures requiring active treatment

		Midfacial fractures (n (%)) ^{1}		Midfacial fracture subtypes requiring active treatment (n (%)) ^{2}									
Physical examination findings	Total observed	Fractures identified	Fractures requiring active treatment	Frontal sinus	Orbital rim and wall	Maxillary sinus	Zygomatico-maxillary complex	Naso-orbitoethmoid complex	Nasal bone	Le Fort I	Le Fort II	Le Fort III	Dento-alveolar complex
Swelling	621	294 (47.3)	63 (10.1)	9 (14.3)	15 (23.8)	3 (4.8)	23 (36.5)	5 (7.9)	34 (54.0)	4 (6.3)	4 (6.3)	3 (4.8)	7 (11.1)
Laceration	430	200 (46.5)	37 (8.6)	5 (13.5)	9 (24.3)	2 (5.4)	12 (32.4)	5 (13.5)	21 (56.8)	3 (8.1)	3 (8.1)	2 (5.4)	7 (18.9)
Facial depression	49	46 (93.9)	23 (46.9)	3 (13.0)	3 (13.0)	0 (0.0)	18 (78.3)	2 (8.7)	6 (26.1)	3 (13.0)	3 (13.0)	1 (4.3)	1 (4.3)
Peri-orbital hematoma	355	199 (56.1)	38 (10.7)	7 (18.4)	11 (28.9)	3 (7.9)	16 (42.1)	5 (13.2)	21 (55.3)	3 (7.9)	3 (7.9)	3 (7.9)	2 (5.3)
Raccoon eyes	55	35 (63.6)	7 (12.7)	2 (28.6)	2 (28.6)	2 (28.6)	0 (0.0)	0 (0.0)	6 (85.7)	1 (14.3)	0 (0.0)	2 (28.6)	0 (0.0)
Epistaxis	285	194 (68.1)	49 (17.2)	5 (10.2)	8 (16.3)	4 (8.2)	17 (34.7)	5 (10.2)	34 (69.4)	4 (8.2)	4 (8.2)	2 (4.1)	2 (4.1)
Subconjunctival hemorrhage	69	52 (75.4)	10 (14.5)	2 (20.0)	3 (30.0)	2 (20.0)	4 (40.0)	3 (30.0)	6 (60.0)	1 (10.0)	1 (10.0)	1 (10.0)	1 (10.0)
Ocular movement limitation	13	12 (92.3)	4 (30.8)	1 (25.0)	2 (50.0)	1 (25.0)	3 (75.0)	1 (25.0)	2 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Diplopia	20	13 (65.0)	5 (25.0)	1 (20.0)	1 (20.0)	0 (0.0)	4 (80.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infra-orbital nerve paresthesia	62	50 (80.6)	13 (21.0)	0 (0.0)	3 (23.1)	0 (0.0)	11 (84.6)	1 (7.7)	3 (23.1)	1 (7.7)	0 (0.0)	0 (0.0)	0 (0.0)

Table 2 *(continued)*

		Midfacial fractures (n (%)) [1]		Midfacial fracture subtypes requiring active treatment (n (%)) [2]									
Physical examination findings	Total observed	Fractures identified	Fractures requiring active treatment	Frontal sinus	Orbital rim and wall	Maxillary sinus	Zygomatico-maxillary complex	Naso-orbitoethmoid complex	Nasal bone	Le Fort I	Le Fort II	Le Fort III	Dento-alveolar complex
Subjective malocclusion [3]	47	27 (57.4)	14 (29.8)	1 (7.1)	4 (28.6)	0 (0.0)	6 (42.9)	0 (0.0)	1 (7.1)	2 (14.3)	2 (14.3)	0 (0.0)	5 (35.7)
Objective malocclusion [3]	23	14 (60.9)	9 (39.1)	0 (0.0)	1 (11.1)	0 (0.0)	2 (22.2)	0 (0.0)	1 (11.1)	2 (22.2)	2 (22.2)	0 (0.0)	5 (55.6)
Tooth mobility or avulsion	48	33 (68.8)	17 (35.4)	1 (5.9)	2 (11.8)	1 (5.9)	1 (5.9)	1 (5.9)	6 (35.3)	1 (5.9)	4 (23.5)	1 (5.9)	9 (52.9)
Palpable step-off	68	62 (91.2)	28 (41.2)	5 (17.9)	9 (32.1)	2 (7.1)	13 (46.4)	3 (10.7)	11 (39.3)	3 (10.7)	2 (7.1)	2 (7.1)	3 (10.7)
Maxillary mobility	36	20 (55.6)	10 (27.8)	2 (20.0)	2 (20.0)	0 (0.0)	2 (20.0)	1 (10.0)	6 (60.0)	4 (40.0)	4 (40.0)	1 (10.0)	2 (20.0)

[1] Presented as the number of patients from the total number of patients with a positive physical examination finding.

[2] Presented as the number of patients from the total number of patients diagnosed with a midfacial fracture.

[3] Excluding patients with both a midfacial and mandibular trauma.

Table 3: Physical examination findings associated with mandibular fractures requiring treatment

		Mandibular fractures (n (%)) [1]		Mandibular fractures requiring active treatment (n (%)) [2]						
Physical examination finding	Total observed	Fractures identified	Fractures requiring active treatment	Symphyseal or parasym-physeal	Corpus	Angular	Ramus	Coronoid	Condylar process	Dento-alveolar complex
Swelling	105	50 (47.6)	25 (23.8)	12 (48.0)	7 (28.0)	8 (32.0)	2 (8.0)	3 (12.0)	14 (56.0)	1 (4.0)
Extra-oral laceration	101	36 (35.6)	19 (18.8)	9 (47.4)	6 (31.6)	0 (0.0)	1 (5.3)	2 (10.5)	16 (84.2)	1 (5.3)
Jaw movement pain	129	59 (45.7)	34 (26.4)	18 (52.9)	10 (29.4)	7 (20.6)	2 (5.9)	1 (2.9)	22 (64.7)	0 (0.0)
Mouth opening limitation	88	54 (61.4)	30 (34.1)	16 (53.3)	10 (33.3)	5 (16.7)	2 (6.7)	1 (3.3)	20 (66.7)	0 (0.0)
Inferior alveolar nerve paresthesia	8	4 (50.0)	3 (37.5)	1 (33.3)	1 (33.3)	1 (33.3)	0 (0.0)	0 (0.0)	2 (66.7)	0 (0.0)
Intra-oral hematoma	35	19 (54.3)	12 (34.3)	6 (50.0)	5 (41.7)	2 (16.7)	1 (8.3)	1 (8.3)	7 (58.3)	1 (8.3)
Intra-oral laceration	62	24 (38.7)	18 (29.0)	8 (44.4)	7 (38.9)	5 (27.8)	1 (5.6)	1 (5.6)	10 (55.6)	1 (5.6)
Palpable step-off	17	16 (94.1)	14 (82.4)	6 (42.9)	6 (42.9)	4 (28.6)	2 (14.3)	3 (21.4)	7 (50.0)	1 (7.1)
Tooth mobility or avulsion	18	11 (61.1)	8 (44.4)	6 (75.0)	1 (12.5)	1 (12.5)	0 (0.0)	0 (0.0)	6 (75.0)	0 (0.0)
Subjective malocclusion [3]	69	37 (53.6)	23 (33.3)	15 (65.2)	6 (26.1)	3 (13.0)	2 (8.7)	1 (4.3)	16 (69.6)	0 (0.0)
Objective malocclusion [3]	42	28 (66.7)	18 (42.9)	10 (55.6)	5 (27.8)	3 (16.7)	1 (5.6)	1 (5.6)	12 (66.7)	0 (0.0)
Angular compression test pain	96	51 (53.1)	33 (34.4)	17 (51.5)	10 (30.3)	7 (21.2)	2 (6.1)	1 (3.0)	21 (63.6)	0 (0.0)
Axial chin pressure pain	82	50 (61.0)	33 (40.2)	17 (51.5)	10 (30.3)	7 (21.2)	2 (6.1)	1 (3.0)	22 (66.7)	0 (0.0)
Tongue blade bite test	22	15 (68.2)	12 (54.5)	7 (58.3)	4 (33.3)	2 (16.7)	0 (0.0)	0 (0.0)	9 (75.0)	0 (0.0)

[1] Presented as the number of patients from the total number of patients with a positive physical examination finding.

[2] Presented as the number of patients from the total number of patients diagnosed with a midfacial fracture.

[3] Excluding patients with both a midfacial and mandibular trauma.

Diagnostic accuracy

The diagnostic accuracy of the individual physical examination findings for both the midfacial and mandibular trauma patients who needed fracture treatment is presented in Table 4. The sensitivity of the findings for midfacial trauma patients was high for swelling, and specificity was found high for almost all physical examination findings except for swelling, laceration, peri-orbital hematoma and epistaxis. The NPV was high for all findings. The sensitivity of the findings for mandibular trauma patients was high for jaw movement pain, the angular compression test and the axial chin pressure test. High specificity was found for inferior alveolar nerve paresthesia, intra-oral hematoma, palpable step-off, tooth mobility or avulsion, and a positive tongue blade bite test. For jaw movement pain, a NPV of 100.0 and infinitesimal LR- was found. NPV was also found high for all other findings.

Clinical decision aids

Clinical decision aids were successfully constructed to discern patients with midfacial or mandibular fractures that require treatment. For midfacial trauma patients, the clinical decision aid consisted of facial depression, epistaxis, ocular movement limitation, palpable step-off, objective malocclusion, and tooth mobility or avulsion. The aid had a sensitivity of 97.3 (90.7-99.3), a specificity of 38.6 (35.0-42.3), a NPV of 99.3 (97.3-99.8), and a LR- of 0.1 (0.0-0.3) when all the physical examination findings were observed as being absent. The decision aid helped in accurately picking out 34.9% (n=267) of the patients who required active treatment for midfacial fractures. A total of 2 (0.3%) fracture patients were not identified, both of whom had nasal fractures. The clinical decision for mandibular trauma patients consisted of mouth opening limitation, jaw movement pain, objective malocclusion, and tooth mobility or avulsion, and had a sensitivity of 100.0 (90.6-100.0), a specificity of 39.1 (33.2-45.4), a NPV of 100.0 (96.1-100.0) and an infinitesimal LR-. The details of the clinical decision aids are presented in Table 5.

Discussion

Maxillofacial injury is frequently observed in patients admitted to the emergency department with trauma. Early recognition of maxillofacial fractures in these patients is essential, in particular because missing these fractures may lead to a decrease in aesthetic and functional outcomes in the long term. Moreover, missing fractures that require surgical intervention could necessitate a secondary reconstruction, leading

Table 4: Accuracy of physical examination findings for midfacial and mandibular trauma patients requiring active treatment.

	Statistics					
Midface	Sens. (CI)	Spec. (CI)	PPV (CI)	NPV (CI)	LR+ (CI)	LR- (CI)
Swelling	85.1 (75.3-91.5)	19.4 (16.6-22.5)	10.1 (8.0-12.8)	92.4 (86.9-95.7)	1.1 (1.0-1.2)	0.8 (0.4-1.4)
Laceration	50.0 (38.9-61.1)	43.2 (39.6-46.9)	8.6 (6.3-11.6)	89.0 (85.2-91.9)	0.9 (0.7-1.1)	1.2 (0.9-1.5)
Facial depression	33.3 (23.4-45.1)	96.1 (94.4-97.4)	46.9 (33.7-60.6)	93.4 (91.3-95.0)	8.6 (5.2-14.3)	0.7 (0.6-0.8)
Peri-orbital hematoma	51.4 (40.2-62.4)	54.2 (50.5-57.9)	10.7 (7.9-14.4)	91.2 (88.1-93.6)	1.1 (0.9-1.4)	0.9 (0.7-1.1)
Raccoon eyes	9.7 (4.8-18.7)	93.1 (90.9-94.7)	12.7 (6.3-24.0)	90.8 (88.5-92.7)	1.4 (0.7-3.0)	1.0 (0.9-1.0)
Epistaxis	68.1 (56.6-77.7)	65.4 (61.8-68.9)	17.2 (13.3-22.0)	95.1 (92.8-96.7)	2.0 (1.6-2.4)	0.5 (0.3-0.7)
Subconjunctival hemorrhage	15.2 (8.4-25.7)	91.0 (88.6-93.0)	14.5 (8.1-24.7)	91.5 (89.1-93.4)	1.7 (0.9-3.1)	0.9 (0.8-1.0)
Ocular movement limitation	6.3 (2.5-15.0)	98.6 (97.3-99.3)	30.8 (12.7-57.6)	91.3 (88.9-93.1)	4.4 (1.4-13.9)	1.0 (0.9-1.0)
Diplopia	8.1 (3.5-17.5)	97.6 (96.1-98.6)	25.0 (11.2-46.9)	91.6 (89.2-93.4)	3.4 (1.3-9.1)	0.9 (0.9-1.0)
Infra-orbital nerve paresthesia	20.0 (12.1-31.3)	92.2 (89.9-94.1)	21.0 (12.7-32.6)	91.8 (89.4-93.7)	2.6 (1.5-4.5)	0.9 (0.8-1.0)
Subjective malocclusion [1]	12.5 (5.0-28.1)	97.2 (94.8-98.5)	30.8 (12.7-57.6)	91.8 (88.4-94.3)	4.5 (1.5-13.8)	0.9 (0.8-1.0)
Objective malocclusion [1]	0.0 (0.0-11.0)	98.5 (96.5-99.3)	0.0 (0.0-43.4)	91.2 (87.8-93.7)	1/∞	1.0 (1.0-1.0)
Tooth mobility or avulsion	23.0 (14.9-33.7)	95.4 (93.6-96.8)	35.4 (23.4-49.6)	91.9 (89.7-93.7)	5.0 (2.9-8.7)	0.8 (0.7-0.9)
Palpable step-off	38.9 (28.5-50.4)	93.9 (91.8-95.5)	41.2 (30.3-53.0)	93.4 (91.2-95.0)	6.4 (4.2-9.7)	0.7 (0.5-0.8)
Maxillary mobility	15.4 (8.6-26.1)	96.0 (94.2-97.3)	27.8 (15.8-44.0)	91.9 (89.6-93.7)	3.9 (1.9-7.6)	0.9 (0.8-1.0)
Mandible						
Swelling	67.6 (51.5-80.4)	67.1 (60.9-72.7)	23.8 (16.7-32.8)	93.1 (88.4-96.0)	2.1 (1.5-2.7)	0.5 (0.3-0.8)
Extra-oral laceration	51.4 (35.9-66.6)	66.3 (60.1-71.9)	18.8 (12.4-27.5)	89.9 (84.7-93.5)	1.5 (1.1-2.2)	0.7 (0.5-1.0)
Jaw movement pain	100.0 (89.8-100.0)	59.9 (53.6-65.9)	26.4 (19.5-34.6)	100.0 (97.4-100.0)	2.5 (2.1-2.9)	1/∞
Mouth opening limitation	88.2 (73.4-95.3)	75.7 (69.9-80.7)	34.1 (25.0-44.5)	97.8 (94.6-99.2)	3.6 (2.8-4.7)	0.2 (0.1-0.4)
Inferior alveolar nerve paresthesia	9.1 (3.1-23.6)	97.8 (95.0-99.1)	37.5 (13.7-69.4)	88.1 (83.6-91.6)	4.1 (1.0-16.5)	0.9 (0.8-1.0)

Table 4 *(continued)*

	Statistics					
Intra-oral hematoma	40.0 (24.6-57.7)	90.2 (85.7-93.4)	34.3 (20.8-50.8)	92.1 (87.9-95.0)	4.1 (2.3-7.3)	0.7 (0.5-0.9)
Intra-oral laceration	56.3 (39.3-71.8)	81.4 (75.9-85.8)	29.0 (19.2-41.3)	93.2 (88.9-95.9)	3.0 (2.0-4.5)	0.5 (0.4-0.8)
Palpable step-off	42.4 (27.2-59.2)	98.7 (96.3-99.6)	82.4 (59.0-93.8)	92.5 (88.5-95.1)	33.4 (10.1-110.0)	0.6 (0.4-0.8)
Tooth mobility or avulsion	22.2 (11.7-38.1)	95.8 (92.4-97.7)	44.4 (24.6-66.3)	89.1 (84.6-92.3)	5.3 (2.2-12.5)	0.8 (0.7-1.0)
Subjective malocclusion [1]	89.5 (68.6-97.1)	64.1 (48.4-77.3)	54.8 (37.8-70.8)	92.6 (76.6-97.9)	2.5 (1.6-3.9)	0.2 (0.0-0.6)
Objective malocclusion [1]	68.4 (46.0-84.6)	77.5 (62.5-87.7)	59.1 (38.7-76.7)	83.8 (68.9-92.3)	3.0 (1.6-5.8)	0.4 (0.2-0.8)
Angular compression test pain	97.1 (85.1-99.5)	73.0 (66.9-78.3)	34.4 (25.6-44.3)	99.4 (96.8-99.9)	3.6 (2.9-4.5)	0.0 (0.0-0.3)
Axial chin pressure pain	97.1 (85.1-99.5)	78.3 (72.5-83.2)	40.2 (30.3-51.1)	99.4 (96.9-99.9)	4.5 (3.5-5.8)	0.0 (0.0-0.3)
Tongue blade bite test	75.0 (50.5-89.8)	93.5 (88.5-96.4)	54.5 (34.7-73.1)	97.3 (93.3-98.9)	11.6 (6.0-22.4)	0.3 (0.1-0.6)

Abbreviations: Prev. prevalence; Sens. Sensitivity; Spec. specificity; Pr. pre-test probability; PPV positive predictive value; NPV negative predictive value; LR+ positive likelihood ratio; LR- negative likelihood ratio

[1] Excluding patients with both a midfacial and mandibular trauma

Table 5: Clinical decision aid for discerning patients with fractures that require active treatment

			Contingency table outcomes		Cumulative diagnostic accuracy					
Clinical decision aid	Physical examination findings	Definitions	TN (%)	FN (%)	Sens. (CI)	Spec. (CI)	PPV (CI)	NPV (CI)	LR+ (CI)	LR- (CI)
Midfacial trauma	Facial depression	Unilateral flattening of the malar eminence or zygomaticomaxillary complex.	647 (84.5)	46 (6.0)	37.8 (27.6-49.2)	93.5 (91.4-95.1)	38.4 (28.1-49.8)	93.4 (91.3-95.0)	5.8 (3.9-8.7)	0.7 (0.6-0.8)
	Epistaxis	A unilateral or bilateral active or past nosebleed.	434 (56.7)	14 (1.8)	81.1 (70.7-88.4)	62.7 (59.1-66.2)	18.9 (14.9-23.5)	96.9 (94.8-98.1)	2.2 (1.9-2.5)	0.3 (0.2-0.5)

Table 5 *(continued)*

			Contingency table outcomes		Cumulative diagnostic accuracy					
Clinical decision aid	Physical examination findings	Definitions	TN (%)	FN (%)	Sens. (CI)	Spec. (CI)	PPV (CI)	NPV (CI)	LR+ (CI)	LR- (CI)
	Ocular movement limitation	Unilateral restricted gazing or limitation of the eye movements in any direction.	405 (52.9)	12 (1.6)	83.8 (73.8-90.5)	58.5 (54.8-62.1)	17.8 (14.1-22.1)	97.1 (95.0-98.3)	2.0 (1.8-2.3)	0.3 (0.2-0.5)
	Palpable step-off	The presence of a bony step-off found during palpation of the zygomatic arch, infra-orbital rim, supra and lateral orbital rim, nasal bridge and zygomaticoalveolar crest intra-orally.	378 (49.3)	8 (1.0)	89.2 (80.1-94.4)	54.6 (50.9-58.3)	17.4 (13.9-21.5)	97.9 (96.0-98.9)	2.0 (1.8-2.2)	0.2 (0.1-0.4)
	Objective malocclusion	Objectively identified traumatic misalignment of the maxillary and mandibular dental arches.	278 (36.3)	5 (0.7)	93.2 (85.1-97.1)	40.2 (36.6-43.9)	14.3 (11.4-17.7)	98.2 (95.9-99.2)	1.6 (1.4-1.7)	0.2 (0.1-0.4)
	Tooth mobility or avulsion	Mobility or avulsion of any maxillary tooth element.	267 (34.9)	2 (0.3)	97.3 (90.7-99.3)	38.6 (35.0-42.3)	14.5 (11.7-17.9)	99.3 (97.3-99.8)	1.6 (1.5-1.7)	0.1 (0.0-0.3)
Mandible trauma	Mouth opening limitation	The reported inability to fully open the mouth or a measured mouth opening of less than 35mm.	181 (64.6)	4 (1.4)	89.2 (75.3-95.7)	74.5 (68.7-79.6)	34.7 (25.9-44.7)	97.8 (94.6-99.2)	3.5 (2.7-4.5)	0.1 (0.1-0.4)
	Jaw movement pain	Evident presence of pain during opening, protrusion or lateral movement of the mandible.	137 (48.9)	0 (0.0)	100.0 (90.6-100.0)	56.4 (50.1-62.5)	25.9 (19.4-33.6)	100.0 (97.3-100.0)	2.3 (2.0-2.6)	1/∞
	Objective malocclusion	Objectively identified traumatic misalignment of the maxillary and mandibular dental arches.	101 (36.1)	0 (0.0)	100.0 (90.6-100.0)	41.6 (35.5-47.8)	20.7 (15.4-27.2)	100.0 (96.3-100.0)	1.7 (1.5-1.9)	1/∞
	Tooth mobility or avulsion	Mobility or avulsion of any mandibular tooth element.	95 (33.9)	0 (0.0)	100.0 (90.6-100.0)	39.1 (33.2-45.4)	20.0 (14.9-26.3)	100.0 (96.1-100.0)	1.6 (1.5-1.8)	1/∞

Abbreviations: TN true negatives; FN false negatives; NPV negative predictive value; LR- negative likelihood ratio; Sens. sensitivity to additional healthcare costs, increased burden and, potentially, a poor outcome. Subjecting each maxillofacial trauma patient to a structural physical examination may help in identifying or ruling out these fractures at an early stage of treatment. In this prospective multicenter study, we assessed the diagnostic accuracy of the physical examination findings for midfacial and mandibular fractures requiring active treatment. Clinical decision aids were constructed focusing discerning patients with these type of fractures, resulting in a NPV of 99.3% for midfacial trauma patients, and a NPV of 100.0% for mandibular trauma patients. When all the related physical examination findings in these clinical decision aids are absent means one can successfully rule out patients with midfacial and mandibular fractures requiring treatment.

Our study identified how individual physical examination findings are associated with different subtypes of midfacial and mandibular fractures that require active treatment. For example, midfacial fractures were found in almost every patient with facial depression and almost 50% of the treated fractures were associated with fractures of the zygomaticomaxillary complex. Another example is that mandibular fractures were frequently found in patients with malocclusion, most of whom had to be treated. Most of these patients presented with symphyseal, parasymphyseal and condylar process subtype fractures, supporting the fact that displacement of fractures in these regions cause traumatic misalignment of the dental arches. Specific physical examination findings can be highly effective in the diagnosis of maxillofacial fracture subtypes requiring treatment in emergency department patients, and radiological imaging should therefore be strongly considered for them. Understanding these individual physical examination findings can be useful for early identification of a patient at risk of midfacial or mandibular fractures.

In this study, we found that the sensitivity remained low for physical examination findings related to midfacial trauma whereas the sensitivity of the findings for mandibular trauma patients was high for jaw movement pain, a positive angular compression test and a positive axial chin pressure chin test. The specificity was high for most of the midfacial and mandibular physical examination findings, indicating that these findings are commonly absent among patients whose fractures can be treated conservatively or do not have a fracture. This is supported by the fact that almost all the physical examination findings produced an exceptionally high NPV and, contrarily, a low PPV. Our results suggest that the absence of these physical examination findings means the unlikelihood of a midfacial or mandibular fracture that requires treatment. Therefore, these individual findings can be used to stratify patients into low or high risk fracture groups.

Although individual physical examination findings can be useful, it is of particular interest how a combination of findings can perform as a clinical decision aid in the emergency department. In our study, clinical decision aids were constructed with the aim to differentiate patients without or with midfacial or mandibular fractures that require active treatment (e.g., closed or surgical treatment). An approach was chosen in which the physicians assessed the physical examination findings not knowing the outcome of interest, representing a blinded clinical workflow of assessing emergency department patients. The clinical decision aid constructed for midfacial trauma patients consisted of facial depression, epistaxis, ocular movement limitation, palpable step-off, malocclusion, and tooth mobility or avulsion. The absence of all these findings produced a sensitivity of 97.3%, a specificity of 38.6, and a NPV of 99.3%. The clinical decision aid only misdiagnosed two patients (i.e., false negatives) with nasal fractures that required a closed treatment protocol. These two patients were missed despite including palpation of the nasal bridge and epistaxis in the nasal related physical examination findings. Nasal fractures are commonly found in maxillofacial trauma patients, emphasizing the need to consider these fractures for each patient suffering any maxillofacial trauma. Moreover, because the nose projects from the face, any nasal fracture displacements may have important aesthetic consequences. Nevertheless, the clinical decision aid accurately picked out the majority of patients with midfacial fractures that required active treatment. Previous research is limited and preliminary focused on the diagnosis of orbital fractures requiring treatment. The authors of a prospective cohort study of 2262 emergency department patients with blunt orbital trauma constructed an orbital fracture risk score focusing on the need for emergent surgical intervention [5]. One point was assigned for: orbital rim tenderness, periorbital emphysema, subconjunctival hemorrhage, impaired extra-ocular movement, painful extra-ocular movement and epistaxis. The authors stated the risk score was successful as only three patients had been misdiagnosed. In another retrospective cohort study of 912 orbital trauma patients, an orbital fracture risk score was constructed to predict the need for surgery [11]. One point was given for periorbital emphysema and male sex, and two points for diplopia and infra-orbital nerve paresthesia. A cut-off of two points was defined as the best compromise for the risk of surgical intervention, producing a NPV of 92.1% and a sensitivity of 82.5%.

The clinical decision aid we constructed for mandibular trauma patients consisted of mouth opening limitation, jaw movement pain, malocclusion, tooth mobility or avulsion. The clinical decision aid correctly discerned all the patients who did not require active treatment for mandibular fractures through the absence of the physical examination findings. To the best of our knowledge, no studies have been conducted focusing on such a clinical decision aid. Our clinical decision aids were only constructed with physical examination findings. The main advantage is that the decisions are consistent, also for patients with unclear or unverifiable components such as age, sex or mechanism of injury. The clinical decision aids allow for early bedside management during an early stage of the primary or secondary assessment. Maxillofacial trauma patients often have concomitant injuries and our clinical decision aids might help in stratifying which injuries require prioritization for resuscitation. Moreover, the clinical decision aids can be used to identify the patients requiring a consultation with an oral and maxillofacial surgeon or an otolaryngologist.

The study has several limitations. First, only those patients who had undergone radiological imaging were included. Nevertheless, we focused on patients who required active treatment and one would expect those not needing radiological imaging as having low fracture risks. Second, the physical examination findings were assessed by emergency department physicians with varying years of experience. Although we tried to define each physical examination finding clearly, trained oral and maxillofacial surgeons have more experience in the assessment of maxillofacial trauma patients and are often faced with patients that require treatment. Third, the treatment decision was established using Dutch treatment protocols. However, other international treatment protocols for maxillofacial and mandibular fractures might be different, which confines the generalizability of the clinical decision aids. Thus, these clinical decision aids should be validated by future research with a new population of patients.

In conclusion, the physical examination findings in the clinical decision aids focusing on patients with midfacial or mandibular fractures that require active treatment are diagnostically accurate and thus can be used to stratify patients at an early stage of assessment.

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5

CHAPTER 5

Maxillofacial fractures in electric and conventional bicycle related accidents

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Submitted
Adapted version of the manuscript

Abstract

Objective: The aim of this study was to assess the incidence and severity of midfacial and mandibular fractures following e-bike and conventional bicycle accidents.

Methods: A retrospective cohort study was conducted of all the consecutive patients with maxillofacial trauma due to e-bike and conventional bicycle accidents. Maxillofacial injury severity was assessed using the Maximum Abbreviated Injury Scale (MAIS) and Facial Injury Severity Scale (FISS). Binary logistic regression analysis was applied to assess differences in the risk of maxillofacial injury and for severe maxillofacial fractures between the conventional bicycle group and the e-bike group.

Results: In total, 311 patients were included (73 e-bikers and 238 conventional cyclists). E-bikers sustained midfacial fractures more frequently (47% vs. 34%, p=0.04), whereas conventional cyclists more often had mandibular fractures (1% vs. 11%, p=0.01). Although the median MAIS and FISS scores did not differ, the severe maxillofacial fractures (FISS score ≥ 2) were observed significantly more often in the conventional cyclists (45% vs. 25%, p=0.04). Logistic regression analysis did not show any differences between e-bikers and conventional cyclists regarding the incidence of midfacial and mandibular fractures as well as the severe fractures when correcting for age and comorbidities.

Conclusion: Both the distribution and the severe maxillofacial fractures differed between the e-bike and conventional bicycle accident patients. Patient specific characteristics, such as age and comorbidities may have a greater influence on sustaining maxillofacial injuries than the type of bicycle ridden.

Introduction

Bicycles are becoming an increasing popular means of transport. Electric bicycles or 'e-bikes' have been categorised as assisted physical pedalling with electric power, with the capacity to travel at higher speeds of up to 25 km/h or 15mph. With the increased use of both conventional bicycles and e-bikes on Dutch cycling paths, the number and proportion of bicycle-related trauma has increased accordingly [1].

Bicycle-related accidents are frequently associated with head and facial injuries. Facial trauma has been seen in 34% of the injured cyclists admitted to the emergency department (ED) [2]. E-bike accidents also seem to frequently lead to facial injury [3,4]. A study comparing both types of bicycle-related accidents reported that 31% of the e-bikers suffered facial injury compared to 38% of the conventional cyclists, with equal severity [5]. Another study focusing on e-bike related maxillofacial injuries showed that zygomaticomaxillary complex fracture was the most frequent observed injury followed by soft tissue injuries [4]. Consequently, several studies suggested that helmet use can decrease the risk of, or even prevent, facial injury in bicycle accidents [6,7]. As bicycle related accidents are considered one of the major causes of maxillofacial fractures, recommendations have been made to make wearing a helmet mandatory for cyclists [8]. With the increased presentation of patients at the ED after bicycle accidents, research focusing on the epidemiological factors of the sustained maxillofacial injury is becoming increasingly more important.

However, there is a lack of epidemiological data on maxillofacial injuries following e-bike and conventional bicycle accidents as well as evidence of the differences in the types and severity of maxillofacial trauma between these bicycle types. A-priori data on midfacial and mandibular fractures may assist ED personnel when assessing maxillofacial trauma due to conventional bicycle and e-bike accidents. Therefore, the aim of this study was to compare the incidence and severity of midfacial and mandibular fractures after conventional bicycle and e-bike related accidents.

Material and Methods

Study design

A retrospective cohort study was conducted of all the patients selected from our research group's database containing patients with midfacial or mandibular trauma attending the ED of four hospitals in the north of the Netherlands between May 2018 and October 2019. The Institutional Review Board of the University Medical Centre Groningen (Groningen, the Netherlands) confirmed that the Medical Research Involving Human Subjects Act does not apply (METc code 2017/249) and local feasibility was approved by all the hospitals.

Patient population

All the patients aged 18 years or older presenting with midfacial or mandibular trauma at the ED following a conventional bicycle or an e-bike accident were included. Patients suffering maxillofacial trauma due to other types of bicycles (e.g., speed pedelecs, racing bicycles or mountain bikes) were excluded. Patients who declined access to their medical records were also excluded.

Data extraction

Data was collected from the electronic patient files and the Dutch Trauma Registry (DTR). The DTR is based on the Major Trauma Outcome Study (MTOS+) and includes patient demographics, vital signs on admission, injury mechanism, anatomical injury characteristics and outcome [9]. The demographic parameters included age, gender, alcohol use, co-morbidities, and 30-day mortality. The injury characteristics collected from the electronic patient files and radiographs consisted of the presence and classification of midfacial and mandibular fractures, dental injury, skull fractures, treatment decisions, concomitant injuries diagnosed at the ED, discharge destination after the ED and days hospitalised.

Outcome measures

The primary outcome was the incidence and severity of midfacial and mandibular fractures. Midfacial fractures were categorised as: the frontal sinus, orbital, maxillary sinus, zygomaticomaxillary complex, nasoorbitoethmoid, nasal, Le Fort type fractures, and dentoalveolar fractures of the maxilla [10]. Mandibular fractures were categorised as: symphyseal and parasymphyseal, corpus, angular, ramus, coronoid, condyle and dentoalveolar [11].

The severity of the maxillofacial trauma was assessed using the Maximum Abbreviated Injury Scale (MAIS) of the facial region [12]. The MAIS is the Abbreviated Injury Scale (AIS) score of the most severe injury sustained. The AIS is an anatomically-based injury severity scoring system that classifies each injury according to body region on a

6-point scale with higher scores indicating higher injury severity. The maxillofacial AIS scores go from 1 to 4. The MAIS facial region score is used as a representation of the severity of the maxillofacial trauma. Maxillofacial fracture severity was scored using the Facial Injury Severity Scale (FISS), on which each maxillofacial fracture subtype has a score of 1 to 6 points [13]. The FISS score is the summation of the points of the observed maxillofacial fractures. FISS scores were categorised into minor (FISS score = 1) or severe maxillofacial fractures (FISS score ≥ 2). Patients without a maxillofacial fracture (FISS score = 0) were excluded from the analyses regarding maxillofacial fractures. The overall injury severity was measured according to the Injury Severity Score (ISS), which is the sum of the squares of the three highest AIS scores of the studied body regions [14]. Severe multitrauma is defined as an ISS > 15. Dental injury involved: (sub) luxation, avulsion or a fracture of the teeth or tooth. Skull fractures were defined as: frontal, temporal, parietal or occipital, or skull base fracture. Alcohol usage was scored as either yes (alcohol use, irrespective of the number of alcohol units) or no (no alcohol use or alcohol use was not noted in the electronic patient file). The Functional Comorbidity Index (FCI) was used to score the presence of 18 comorbid conditions [see reference], resulting in a total score between 0 to 18. A higher FCI score implies greater comorbidity and correlates with reduced physical function [15].

Statistical analysis

The Statistical Package for the Social Sciences was employed for the data analysis (IBM Corp. Released 2015, IBM SPSS Statistics for Windows, Version 23.0). The categorical variables were presented as frequencies and percentages. Regarding the continuous variables, the normally distributed variables were displayed as means with the standard deviation, and the non-normally distributed variables were represented as the median with the interquartile range. Pearson's $\chi 2$ test or Fischer's exact test were used to test the differences in maxillofacial injury incidence between the conventional bicycle group and the e-bike group. The Mann-Whitney U test was used to test differences in the non-normally distributed data. Binary logistic regression analysis was applied to assess differences in the risk of maxillofacial injury and for severe maxillofacial fractures between the conventional bicycle group and the e-bike group. Separate analyses were conducted for the midfacial fractures, mandibular fractures, skull fractures, dental injury and maxillofacial fractures with a FISS score ≥ 2 (i.e., severe maxillofacial fractures). Age, alcohol use and FCI score were added to the analyses as potential cofounders. The FCI score was dichotomised for these analyses; the patients either had no or one comorbidity (FCI ≤ 1) or two or more comorbidities (FCI ≥ 2). Age was categorised into 18-54, 55-74 and 75+ years. A p-value of ≤ 0.05 was used to indicate statistical significance.

Results

Patient characteristics

The details of the patient characteristics are presented in Table 1. A total of 311 patients were included. Of those, 238 patients had suffered a conventional related bicycle accident (77%), and 73 an e-bike related accident (23%). The e-bike group was significantly older with a median age of 66 years compared to the conventional bicycle group's median age of 53 (*p*< 0.001). Gender distribution was equal in both groups. The presence of comorbidities (*p*<0.001) and the total number of comorbidities (p<0.001) was found to be significantly higher for e-bike cyclists than for conventional cyclists. Alcohol use frequency was significantly higher in the conventional bicycle group (32%) than in the e-bike group (16%) (*p*=0.008).

Table 1: Patient characteristics

	Total	Conventional bicycle	E-bike	*p-value*
Patients (n)	311	237	74	
Male gender (n (%))	141 (45)	108 (46)	33(45)	0.88
Age in years (median (IQR))	56 (35)	53 (38)	66 (18)	< 0.001*
FCI				
Comorbidities present (n (%))	123 (40)	80 (34)	43 (58)	< 0.001*
Comorbidities number (median (IQR))	0 (1)	0 (1)	1 (2)	< 0.001*
Alcohol use (n (%))	88 (28)	76 (32)	12 (16)	0.008*
ISS				
Score (median (IQR))	5 (7)	4 (4)	6 (10)	0.001*
Severe multitrauma (n (%)) [1]	14 (5)	11 (5)	3 (4)	1
Discharge destination				
Hospital (n (%))	123 (40)	81 (34)	42 (57)	0.001*
Admission duration in days (median (IQR))	2 (2)	2 (1)	3 (4)	0.01*
ICU (n (%))	8 (3)	4 (2)	4 (5)	0.1
Admission duration in days (median (IQR))	3 (6)	3.5 (8)	3 (6)	0.76
Thirty-day mortality (n (%))	1 (0)	1 (0)	0 (0)	1

Abbreviations: IQR; Inter Quartile Range, FCI; Functional Comorbidity Index, ISS; Injury Severity Score, ICU; Intensive Care Unit

[1] ISS score > 15 is considered severe multitrauma

* p < 0.05

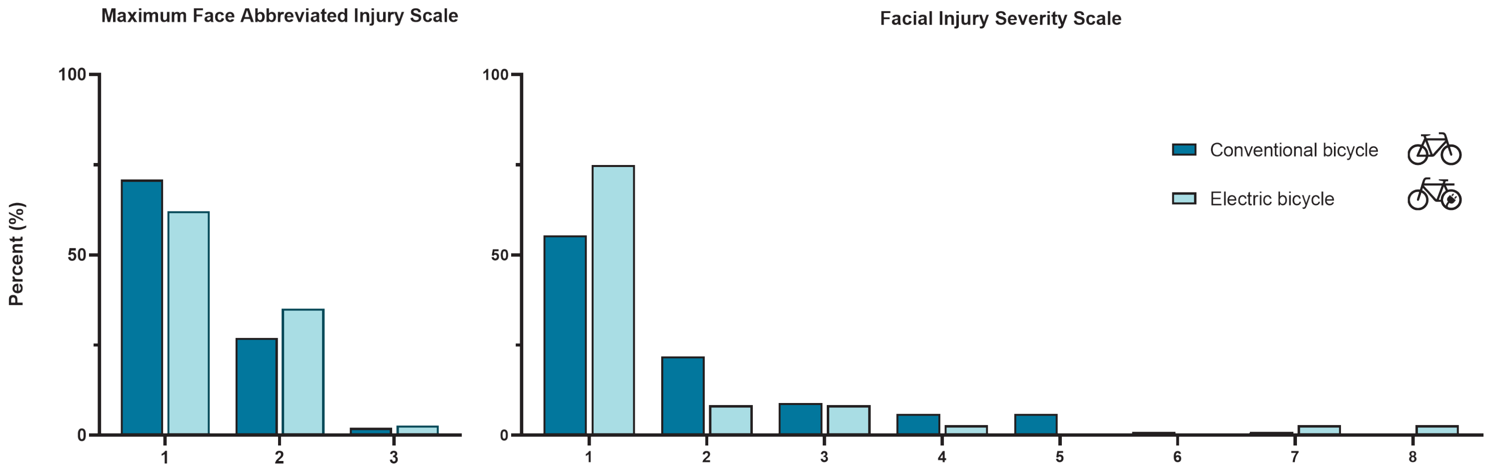

Figure 1: Maximum Abbreviated Injury Scale (MAIS) and Facial Injury Severity Scale (FAIS) scores

Maxillofacial trauma outcome

The distribution and severity of maxillofacial injuries are presented in Figure 1 and Table 2. Midfacial fractures were observed significantly more often in the e-bike group (47% vs 33%, *p*=0.03). Mandibular fractures were observed significantly more often in the conventional bicycle group (11% vs 1%, *p*=0.01). There were no significant differences in the median MAIS and FISS scores between the two groups. The severe maxillofacial fractures (FISS score ≥ 2) were found significantly more often in the conventional bicycle group (45% vs. 25%, *p*=0.04).

Table 2: Midfacial and mandibular trauma outcomes and severity

	Total	Conventional bicycle	E-bike	*p-value*
Midfacial fractures				
Patients (n (%))	114 (37)	79 (33)	35 (47)	0.03*
Conservative treatment (n (%))	95 (83)	64 (81)	31 (87)	
Active treatment (n (%))	19 (17)	15 (19)	4 (11)	0.32
Closed	12 (11)	11 (14)	1 (3)	
Surgical	7 (6)	4 (5)	3 (9)	
Mandibular fractures				
Patients (n (%))	26 (8)	25 (11)	1 (1)	0.01*
Conservative treatment (n (%))	12 (46)	11 (44)	1 (100)	
Active treatment (n (%))	14 (54)	14 (56)	0 (0)	0.46
Closed	4 (15)	4 (16)	0 (0)	
Surgical	10 (39)	10 (40)	0 (0)	
Dental injury (n (%))	48 (15)	43 (18)	5 (7)	0.02*
Skull fractures (n (%))	30 (10)	19 (8)	11 (15)	0.08
MAIS Face				
Score (median (IQR))	1(1)	1(1)	1(1)	0.16
MAIS score of 1 (n (%))	214 (69)	168 (71)	46 (62)	0.16
MAIS score of 2 (n (%))	90 (29)	64 (27)	26 (35)	0.18
MAIS score of 3 (n (%))	7 (2)	5 (2)	2 (3)	0.76
FISS				
Score (median (IQR))	1 (1)	1 (1)	1 (1)	0.07
FISS score = 1 (n (%))	83 (61)	56 (55)	27 (75)	0.04*
FISS score ≥ 2 (n (%))	54 (39)	45 (45)	9 (25)	

Abbreviations: MAIS; Maximum score on the Abbreviated Injury Scale, FISS; Facial Injury Severity Scale
* P < 0.05

Fracture types

The midfacial and mandibular fracture outcomes are presented in Table 3. Zygomaticomaxillary complex fractures (19%) were the most frequently observed maxillofacial fracture type, followed by orbital fractures (10%) and nasal fractures (9%). Regarding the conventional bicycle related accidents, the most reported fractures were zygomaticomaxillary complex (19%), nasal (9%), orbital floor and rim (8%) and condyle process and head fractures (8%). In the e-bike group, the most reported fractures were zygomaticomaxillary complex (20%), orbital floor and rim (19%) and nasal fractures (8%). Significantly more symphyseal fractures were found in the conventional bicycle group (*p*=0.03), while significantly more orbital (*p*=0.005) and Le Fort II (*p*=0.04) fractures were seen in the e-bike group.

Table 3: Incidence of midfacial and mandibular fractures

	Total	Conventional bicycle	E-bike	*p-value*
Midfacial fractures (n (%))				
Frontal sinus	5 (2)	5 (2)	0 (0)	0.60
Orbital floor and rim	32 (10)	18 (8)	14 (19)	0.005*
Zygomaticomaxillary complex	58 (19)	43 (18)	15 (20)	0.68
Nasoorbitoethmoid	5 (2)	3 (1)	2 (3)	0.34
Maxillary sinus	8 (3)	6 (3)	2 (3)	1
Nasal	28 (9)	22 (9)	6 (8)	0.76
Le Fort I	5 (2)	3 (1)	2 (3)	0.34
Le Fort II	4 (1)	1 (0)	3 (4)	0.04*
Le Fort III	1 (0)	0 (0)	1 (1)	0.24
Dentoalveolar process	8 (3)	8 (3)	0 (0)	0.21
Mandibular fractures (n (%))				
Symphyseal and parasymphyseal	14 (5)	14 (6)	0 (0)	0.03*
Corpus	6 (2)	6 (3)	0 (0)	0.34
Angular	1 (0)	1 (0)	0 (0)	1
Ramus	3 (1)	3 (1)	0 (0)	1
Coronoid	1 (0)	1 (0)	0 (0)	1
Condyle process and head	19 (6)	18 (8)	1 (1)	0.05
Dentoalveolar process	0 (0)	0 (0)	0 (0)	n/a

* $P < 0.05$

Logistic regression analysis

The logistic regression analyses results are presented in Table 4. After correcting for relevant confounding factors, there were no significant differences in the risk of sustaining midfacial fractures, mandibular fractures, skull fractures, dental injury and severe maxillofacial fractures between the e-bikers and conventional cyclists.

Table 4: Logistic regression analysis of differences in the risk of maxillofacial trauma between e-bikers and conventional cyclists

Outcome [1]	B	SE	*P*	OR	95% CI
Midfacial fractures [2]	0.27	0.29	0.35	1.31	0.74 to 2.30
Mandibular fractures [3,4]	-1,17	1.08	0.28	0.31	0.04 to 2.54
Skull fractures [2]	0.47	0.43	0.28	1.60	0.69 to 3.74
Dental injury [2]	-0.73	0.52	0.16	0.48	0.18 to 1.34
Severe maxillofacial fractures (FISS ≥ 2) [2]	-0.83	0.48	0.08	0.48	0.17 to 1.11

Abbreviations: FCI; Functional Comorbidity Index, B; Logistic Regression Coefficients, SE; Standard Error, *P*; P-value, OR; Odds Ratio, CI; Confidence Interval, FISS; Facial Injury Severity Score

[1] Conventional cyclists were used as the reference group

[2] Corrected for age, alcohol use and comorbidities (FCI)

[3] Corrected for age and alcohol use

[4] Comorbidities (FCI) was not a relevant cofounder

Discussion

Bicycle-related accidents often result in maxillofacial injury [8]. With the increased use of e-bikes, there is a need to study the epidemiological characteristics of the maxillofacial injuries. Thus, the aim of the present study was to compare the incidence and severity of maxillofacial fractures after conventional bicycle and e-bike related accidents. This study showed that midfacial fractures were found more frequently in e-bike accidents whilst mandibular fractures were observed more in conventional bicycle accidents. Maxillofacial trauma and fracture severity did not differ between both groups. However, the severe maxillofacial fractures were found more often in the conventional bicycle group.

Although both the median score and the differences in maxillofacial trauma severity were not significant, the MAIS indicated that the maxillofacial injuries due to e-bike accidents appeared more severe than on conventional cyclists. A trend was observed that e-bikers suffered fewer minor (MAIS 1) but more moderate maxillofacial injuries (MAIS 2) compared to conventional cyclists. The potential factors involved could be the higher speed of an e-bike or that the e-bike group was significantly older. Previous research stated that elderly cyclists have a higher chance of more severe injuries [16]. However, serious (MAIS 3) and severe maxillofacial trauma (MAIS 4) were uncommon in both groups. Overall, there was no statistically significant difference in median maxillofacial fracture severity even though the e-bike related accidents resulted in a higher FISS score than the conventional bicycle group. However, after a distinction was made between minor (FISS =1) and severe maxillofacial fractures (FISS ≥ 2), we saw that the incidence of severe maxillofacial fractures was significantly higher among the conventional cyclists. In other words, the e-bikers' maxillofacial fractures were less severe but were sustained more frequently whereas the conventional cyclists sustained maxillofacial fractures less frequently but, if they did, the fractures were more severe. A study focusing on patients hospitalised due to electric-powered bike accidents reported that the majority of oral- and maxillofacial-related injuries were moderate (MAIS 2) followed by minor (MAIS 1) [17]. Two studies on patients who sustained maxillofacial fractures due to conventional bicycle accidents reported a mean FISS score as a representation of severity, namely 1.9 and 2.0, respectively [18,19]. Our study reports a median FISS of 1 for both conventional and e-bike related accidents. In general, maxillofacial injury severity seems to be comparable between the two types of cyclists. Both sustained minor maxillofacial injuries more frequently, followed by moderate maxillofacial injuries. Likewise, both groups of cyclists had more maxillofacial fractures with a FISS score of 1 followed by maxillofacial fractures with a FISS score of 2. This seems to be in line with the results of a study where the e-bike accident injury patterns are more comparable with conventional bicycle accidents than with motorcycle accidents [20]. The mechanisms that are frequently involved in bicycle accidents and injury are loss of balance, falling while mounting or dismounting, or getting spooked by other traffic. The cycling velocity in such cases may be low and the resulting fall takes place on a level surface, thus rarely leading to severe maxillofacial trauma [19]. These low energy falls are known to frequently lead to soft-tissue injuries, such as abrasions, haematoma's and lacerations, all of which are minor maxillofacial injuries [21–23].

This study showed that the most frequent fractures seen in both groups were zygomaticomaxillary complex fractures, orbital fractures and nasal fractures. Mandibular fractures were observed less frequently and, remarkably, only one mandibular fracture was reported in the e-bike group. The results of the present study are in line with previous studies which reported zygomaticomaxillary complex fractures and orbital fractures as the most frequently seen midfacial fractures following conventional bicycle accidents [18,19,24,25]. The incidence of mandibular fractures in our study is also in accordance with that seen by previous studies whereby conventional bicycle accidents frequently lead to mandibular fractures, with condyle fractures being the most common subtype [18,19,24,25]. Two studies presented zygomaticomaxillary complex fractures as the most frequent midfacial fracture due to e-bike accidents [4,17]. There could be various reasons for the higher incidence of midfacial fractures and a lower incidence of mandibular fractures among e-bike related accidents. A potential explanation is the heavier weight of an e-bike, with more chance of falling sideways than toppling over the handlebar with low speed trauma. In addition, the e-bike cohort was significantly older and low speed trauma mechanisms, including sudden stops and losing balance, are known to be more common among elderly cyclists [26,27]. A study showed that the majority of the midface fractures due to conventional bicycle accident were situated in the lateral region [25]. However, if e-bikers are more likely to fall sideways than conventional cyclists, then the lateral structures will be more frequently affected, possibly resulting in more midfacial fractures and fewer mandibular fractures among e-bikers. In contrast, toppling over the handlebar leads to potential frontal impact on the chin which can result in fractures in the symphyseal region and indirect fractures of the condyles, a common sequel to falling off a bicycle [18,24]. This is also reflected in the mandible fractures seen among our group of conventional cyclists, with the most reported subtypes being condyle and symphyseal fractures.

Another important finding of this study was that the bicycle type is not significantly associated with an increased risk of midfacial fractures, mandibular fractures, skull fractures and dental injury, and severe maxillofacial fractures. This suggests that cyclist characteristics, such as age, alcohol use and comorbidities, play an important part in sustaining maxillofacial fractures as well as the severe cases. The use of a helmet for conventional cyclists has been proven to reduce head injury and has a protective effect on facial injuries and fractures [7]. A study also showed more severe brain injuries among e-bikers compared to conventional cyclists [5]. Considering that this study found that e-bikers were more frequent to suffer fractures to the skull and presented that the cyclist characteristics are strongly of influence for the maxillofacial injury, helmet use is strongly advised for e-bikers as well for vulnerable and elderly cyclists.

The primary strength of this study is the use of data from a large multicentre cohort, and reporting on both the incidence and the severity of maxillofacial injuries sustained in e-bike related accidents compared to conventional bicycle related accidents. The participating hospital EDs cover a range of hospital trauma levels (level 1-3), populations and geographical differences, thereby reducing forms of selection bias. The second strength of this research is correcting for possible confounders to assess the true effect of the type of bicycle on various maxillofacial fractures.

This study has a number of limitations. First, the distribution among the two bicycle groups was disproportionate as the number of e-bike related accident patients was limited. Another limitation is that the outcome measures are only a limited representation of severity. The AIS for maxillofacial injury ranges from 1 to 4 and the 3 and 4 scores were uncommon in both of our groups. In other words, the AIS offers only a limited degree of distinction for facial injuries. The FISS is unable to assess minor maxillofacial traumas as it consists almost exclusively of maxillofacial fractures. Nevertheless, both scales were used side by side to assess the trauma as thoroughly as possible. Moreover, instead of a quantitative method a binary registration of facial fractures was used, which may have over- or underrepresented several fracture types. However, The FISS does take the number of fractures into consideration, minimizing the over- and under-representation when assessing the severity of these fractures.

Future research on maxillofacial facial injuries after e-bike and conventional bicycle accidents should increase the sample size, especially after e-bike accidents. Increasing the sample size allows to provide more data on injury differences between both bicycle types. Moreover, prospective research on maxillofacial injury after bicycle accidents could focus on specific influences such as helmet use, quantifying alcohol use and the mechanism of injury. The advantages of a helmet as a protective measure for e-bikers, as well as for vulnerable and elderly cyclists, should be advocated and then investigated further given the fact that e-bikers suffered fractures to the skull more frequently, and that cyclist characteristics could influence maxillofacial injury.

In conclusion, e-bikers suffered midfacial fractures significantly more often, and mandibular fractures less often, than conventional cyclists. The difference in both maxillofacial trauma and maxillofacial fracture severity between both groups was not significant in this study. However, severe maxillofacial fractures were found significantly more frequently among the conventional cyclists. Patient specific characteristics, such as age and comorbidities may have a greater influence on sustaining maxillofacial injuries than the type of bicycle ridden.

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PART II

Radiological advancements

6

CHAPTER 6

Substantial CT radiation dose reduction does not affect the preference for CT over direct digital radiography to diagnose isolated zygomaticomaxillary fractures: a study in human cadavers

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Published in Radiography
Volume 22, Issue 4, November 2016, Pages e228-e232
Adapted version of the manuscript

Abstract

Objective: Zygomaticomaxillary fractures can be diagnosed with either computed tomography (CT) or direct digital radiography (DR). The aim of the present study was to assess the effect of CT dose reduction on the preference for facial CT versus DR for accurate diagnosis of isolated zygomaticomaxillary fractures.

Methods: Eight zygomaticomaxillary fractures were inflicted on four human cadavers with a free fall impactor technique. The cadavers were scanned using eight CT protocols, which were identical except for a systematic decrease in radiation dose per protocol, and one DR protocol. Single axial CT images were displayed alongside a DR image of the same fracture creating a total of 64 dual images for comparison. A total of 54 observers, including radiologists, radiographers and oral and maxillofacial surgeons, made a forced choice for either CT or DR.

Results: Forty out of 54 observers (74%) preferred CT over DR (all with $P<0.05$). Preference for CT was maintained even when radiation dose reduced from 147.4 μSv to 46.4 μSv (DR dose was 6.9 μSv). Only a single out of all raters preferred DR ($P=0.0003$). The remaining 13 observers had no significant preference.

Conclusion: This study demonstrates that preference for axial CT over DR is not affected by substantial (~70%) CT dose reduction for the assessment of zygomaticomaxillary fractures.

Introduction

The orbito-zygomatic area represents the major fracture site among maxillofacial traumas [1–4]. Traffic accidents and assault have been described as the main causes of zygomaticomaxillary fractures [1,4–6]. It has been demonstrated that early and correct diagnosis are important factors determining treatment outcome [7–9]. Both clinical examination and diagnostic imaging are used for the assessment of potential zygomaticomaxillary fractures. Isolated zygomaticomaxillary fractures are suspected after midface trauma with low clinical index of suspicion for orbital or visual complications. Computed tomography (CT), direct digital radiography (DR) and Cone Beam Computed Tomography (CBCT) are the current imaging modalities to assess zygomaticomaxillary fractures [9–11]. This study focuses on the use of CT and DR due the current lack of CBCT accessibility in the emergency department.

In many cases, DR is first choice to check bone integrity after facial trauma. It is quick, easy accessible in most hospitals and associated with low radiation dose [11]. Apart from these benefits, DR has a few imperative disadvantages. First, the positioning of the head can be difficult causing discomfort to the patient. Second, the images are relatively difficult to interpret due to superimposition of bone structures. Finally, if the assessment is inconclusive, patients need to undergo an additional CT scan, thereby adding to radiation burden. Nowadays, in most emergency room (ER) settings CT is very easily accessible. Compared to DR, multidetector CT requires considerable less time, is safer, and more comfortable for patients [12–15].

The question however remains whether or not the high radiation dose is justified in cases of non-complex maxillofacial trauma, like zygomaticomaxillary fractures. The use of low dose CT might combine the advantages of CT and DR, but it is unclear to what extend low dose CT images are preferred compared to DR for diagnosing zygomaticomaxillary fractures. The aim of the present study therefore was to assess the effect of CT dose reduction on the preference of radiographers, radiologists and oral and maxillofacial (OMF) surgeons for facial CT versus DR for accurate diagnosis of isolated zygomaticomaxillary fractures.

Material and Methods

Research design

Zygomaticomaxillary fractures were inflicted on four human cadaver heads. Subsequently, both CT and DR images were generated. Multi spiral CT scans were performed with linear dose reduction as achieved by raising the noise index for eight different CT protocols. Evaluation of the images was performed by a panel of 54 independent observers, consisting of 37 radiographers, 13 radiologists and 4 OMF surgeons. Selection criterion for participating in the observer group was to have clinical experience in generating and technically evaluating both CT and DR images for their diagnostic value in clinical practice for at least one 2)year. Observers compared CT images with DR images in random order during a double blind forced choice comparison test, *i.e.* both the researchers and observers were blinded for the scan parameters that were used to generate the presented CT image.

Human cadaver heads

Four fresh Caucasian adult human cadavers (two males and two females) were used in this study. Their age ranged from 72 to 87 yr. The human cadavers were purchased from and provided by the section anatomy of the Department of Neurosciences of the University Medical Center Groningen, Groningen, the Netherlands. Legal and ethical approval for the use of the human cadavers was provided by the section anatomy of the Department of Neurosciences of the University Medical Center Groningen, Groningen, the Netherlands. All experiments were conducted in collaboration with the conservators of the Anatomy Section and were executed according to standards for working with human cadavers as provided by Dutch law.

Infliction of zygomaticomaxillary fractures

A blunt trauma was systematically inflicted using 2.0 kg weights and a free fall impact in attempt to inflict zygomaticomaxillary fractures typically found in clinical practice. During a vertical drop, a 160 cm tube guided the weights to the malar eminence (Figure 1). A calculation based on the biomechanical tolerance force of the zygomatic bone indicated a minimal drop height of 72 cm [16]. The human cadaver heads were placed on a 52 degree wooden wedge to ensure perpendicular impact on the malar eminence (Figure 2). An OMF surgeon clinically examined the midface of the specimen after impact, focusing on flattening of the cheek and steps at the infraorbital rim or at the location of the zygomatic alveolar crest in order to confirm the zygomaticomaxillary fractures. Fractures were inflicted on both the left and the right zygomaticomaxillary complex for each cadaver head.

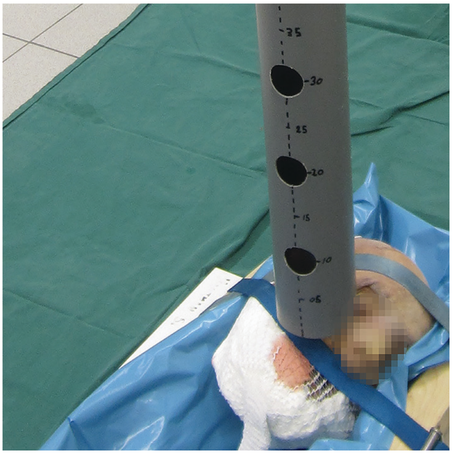

Figure 1: Infliction of the zygomaticomaxillary fractures.

Figure 2: Positioning of the human cadaver heads.

Computed Tomography

The zygomatic-orbital fractures were scanned using a GE Lightspeed Ultra 8 Slice CT (General Electric Co., Fairfield, Connecticut, United States). Facial multidetector CT was performed using the acquisition parameters as reported in Table 1. Linear dose reduction was achieved by raising the noise index for eight different CT protocols (Table 1). The effective dose was calculated using dose length products (DLP) and conversion factors according to the European guidelines on quality criteria for computed tomography [17].

Direct digital radiography

DR images were generated using a calibrated Oldelft Canon Triathlon DR (Oldelft Benelux Ltd., Veenendaal, The Netherlands). Details regarding the acquisition parameters were provided in Table 2. For each specimen four different DR images were taken. The cadaver heads were positioned on a bed for occipitomental projection. From this position DR images were generated 15 degrees craniocaudal, perpendicular vertical (Waters), 15 and 30 degrees caudocranial to ensure a full view of the midface anatomy. Effective dose normalization to dose area products (mSv/Gy·cm^2) was derived from report NRPB-R262 of the British National Radiological Protection Board (IRCP-60) [18].

Table 1: General Electric Lightspeed Ultra 8 Slice Computed Tomography scanner acquisition parameters for the eight different scan protocols.

Scan type	Helical
Tube voltage	100 kV
Noise index range	24.00 – 60.00
Slice thickness	0.625 mm
Position increment	0.625 mm
Collimation	8 x 0.625mm
Average scan range	109 mm
Pitch	1.0
Rotation time	1.0 s
Exposure time	1.3 s
Grayscale depth	16 bit
Field of View (FOV)	250.0 mm
Matrix	512 x 512
Reconstruction type	Filtered Back Projection
Convolution kernel	BonePlus

Table 2: Oldelft Canon Triathlon DR acquisition parameters

Tube voltage	70 kV
Exposure control mode	AEC
Focal Distance	100 cm
Filtration	0.1 mm Cu
Grayscale depth	12 bit
Grid ratio	8:1 (focussed)
Detector type	Scintillation Flat panel
Pixels	2208 * 2688 pixels
Pixel pitch	160 * 160 microns
Spatial resolution	160 micron

Abbreviations: DR Digital radiography; AEC Automatic Exposure Control

Image assessment

For forced comparison, a representative DR image as well as a single and representative CT image from each of the eight different dose protocol scans was selected by an experienced and independent radiologist, who was subsequently excluded from the image assessment for this research study. The single slice that was chosen was at the same level of anatomy for each scan protocol. For each human cadaver head the eight different CT images were randomly paired with the corresponding DR image. A heterogeneous group of observers consisting of 37 radiographers, 13 radiologists and 4 OMF surgeons from the University Medical Center Groningen (Groningen, NL), Deventer hospital (Deventer, NL), and the Nij Smellinghe hospital (Drachten, NL) rated each of the 64 comparisons (specimen (1-4), side (left/right), and CT protocol (1-8). Each observer was forced to select a preferred image from a randomly paired comparison of a CT- and DR image of the same fracture (Figure 3). The observer was asked to select the image in which the fracture was better visualized, so either DR or CT. Images were evaluated on a dual 3MP Eizo Radiforce GS310 or dual 5MP Eizo Radiforce G51 monochrome AAPM validated monitor (Eizo Nanao Co., Hakusan, Japan).

Statistical analysis

The null hypothesis of .50 CT preference was tested against its two-sided alternative by the proportions test [19,20]. The proportion of preference for CT was computed separately per profession, side, specimen and CT dose together with its 95 percent confidence interval. Finally, a generalized estimation approach was used to model the preference responses by generalized mixed models (repeated logistic regression) using observers as random effects in order to test for possible effects of side, profession, specimen and CT dose [21,22]. With respect to the latter, the degree of noise was centered and added as a co-variate to the model. P-values <0.05 were considered statistically significant.

Figure 3: Randomly paired comparison of a CT- and DR image of the same fracture. Representative examples of CT, minimal dose CT and DR images of a zygomatic fracture (arrows). The rater was forced to select either the CT or the DR image of the same fracture in which the fracture was better visualized.

Results

Forced choice comparison test

All 54 observers completed the forced choice comparison test. A total number of 40 out of 54 observers had a significant preference for CT over DR. Only a single observer (a radiologist) had a significant preference for DR. The remaining 13 observers had no significant preference. An overview of all preferences is shown in Table 3. The proportion of preference for CT was computed separately per profession, side, specimen and CT dose (Table 2). Under all experimental conditions there is a significant preference for CT (proportion > 0.5 and all 95% confidence intervals are to the right hand side of 0.5). The preference for CT sustained after substantial (~70%) dose reduction from 147.4 μSv to 46.4 μSv (Table 4 and 5). DR dose was 6.9 μSv (Table 5).

Table 3: Significant versus non-significant modality preference per profession [a]

	Radiographers	OMF surgeons	Radiologists	Total
Significant CT preference	29	4	7	40
Non-Significant CT preference	6	0	4	10
Significant DR preference	0	0	1	1
Non-Significant DR preference	2	0	1	3
Total	37	4	13	54

Abbreviations: DR Direct Digital radiography (DR); CT Computed Tomography; OMF Oral and Maxillofacial

[a] P values < 0.05 were considered significant

Table 4: Radiation dose results for each of the eight Computed Tomography scan protocols on average for the four human cadaver specimen.

Protocol	Noise index	Exposure (mA)	Tube current (mAs)	Scan range (mm)	$CTDI_{vol}$ (mGy)	DLP (mGy*cm)	Eff. Dose (μSv)
1	24.00	27.3 ± 8.3	14.3 ± 4.3	109	5.52	64.09	147.4
2	25.55	14.3 ± 4.3	13.3 ± 4.3	109	4.85	56.27	129.4
3	27.40	22.5 ± 8.0	12.0 ± 4.4	109	4.20	48.73	112.1
4	29.73	19.0 ± 6.9	10.0 ± 3.2	109	3.56	41.33	95.0
5	32.81	15.0 ± 5.3	8.3 ± 2.5	109	2.92	33.84	77.8
6	37.00	11.0 ± 2.9	6.0 ± 1.9	109	2.36	27.61	63.5
7	43.50	9.0 ± 0	4.3 ± 0.4	109	1.91	22.16	51.0
8	60.00	5.3 ± 2.2	3.3 ± 0.4	109	1.74	20.19	46.4

Abbreviations: CTDI Computed Tomography Dose Index Volume; DLP Dose Length Product; Eff. Dose Effective dose

Table 5: Proportion of CT preference with left and right limit of 95 percent confidence interval for profession, specimen, side and CT dose. DR dose was 6.9 μSv.

	Proportion	95% CI
Profession		
Radiographers	0.77	0.75 - 0.79
Radiologists	0.67	0.64 - 0.70
OMF surgeons	0.89	0.84 - 0.92
Specimen		
1	0.74	0.71 - 0.77
2	0.84	0.81 - 0.86
3	0.77	0.74 - 0.80
4	0.68	0.65 - 0.71
Side		
Left	0.78	0.76 - 0.80
Right	0.73	0.71 - 0.75
Effective CT Dose (μSv)		
147.4	0.76	0.72 - 0.80
129.4	0.76	0.71 - 0.80
112.1	0.77	0.73 - 0.81
95.1	0.79	0.75 - 0.83
77.8	0.75	0.71 - 0.79
63.5	0.75	0.71 - 0.79
51.0	0.73	0.69 - 0.77
46.4	0.73	0.68 - 0.77

Abbreviations: CT Computed Tomography; DR Direct Digital Radiography; CI Confidence Interval; OMF Oral and Maxillofacial

Logistic regression analysis

In order to correct for inter-dependencies within observers a repeated logistic regression was performed (Table 6) [21,22]. The resulting difference in log odds between right and left sides of the cadaver head is not significant ($p=0.67$). This indicates that there was no difference in preference for either CT or DR within the cadaver heads, though there were difference between the four cadaver heads. For this reason the preferences were not analyzed statistically for each individual fracture. Instead, fractures within one human cadaver head were analyzed, resulting in an N=4 sample size instead of N=8. There was a difference in log odds between human cadaver head 2 and 4 compared to human cadaver head 1. Reduction of CT radiation dose by ~70% did not influence the preference for CT; observers consistently preferred

CT for fracture detection even after lowering radiation dose. After correcting for profession, side, specimen and CT dose, the estimated odds of the CT preference of OMF surgeons is exp(.77) = 2.16 times that of a radiographer, which is in line with the ratio of odds 0.89/(1-.89)/(0.77/(1-.77)) = 2.42 obtained from the proportions in table 5. The difference in log odds between radiographers and radiologists is not significant, whereas that between radiographers and OMF surgeons is (Table 6).

Table 6: Estimated effects of profession, side, specimen corrected for the noise index of CT by repeated binary logistic regression based upon fitting generalized estimating equations.

	EE	SE	Wald	p-value
(Intercept)	1.19	0.21	32.07	0.00
Radiologist	-0.41	0.31	1.72	0.19
OMF surgeon	0.77	0.20	14.66	0.00
Right side	0.07	0.17	0.18	0.67
Specimen 2	1.13	0.37	9.55	0.00
Specimen 3	-0.36	0.24	2.29	0.13
Specimen 4	-0.81	0.17	24.01	0.00
Centered noise index	0.00	0.00	0.00	0.98

Abbreviations: CT Computed Tomography; EE Estimated Effect; SE Standard Error; OMF Oral and Maxillofacial

Discussion

The increased radiation dose of CT as compared to DR is a significant consideration weighing the risks versus benefits of CT as a primary diagnostic tool for the assessment of isolated zygomaticomaxillary fractures. To our knowledge, the current study is the first to describe a significant preference for CT over DR, even after substantial (~70%) CT radiation dose reduction. These results support the applicability of low dose CT as a primary diagnostic tool for the assessment of isolated zygomaticomaxillary fractures. The lowest CT dose was higher than that of DR (46,4 µSv versus 6.9 µSv respectively), but both are substantially lower than the baseline CT dose (147.4 uSv).

Three aspects of this study design will be discussed. The number of observers and the skew distribution of professions may be seen as a limitation of this study. However, the generalizability of the study was enhanced by double blindness of the design and conducting the experiment in three different hospitals in the Netherlands. The group of observers was heterogeneous as it represented the professions involved in the assessment of zygomaticomaxillary images, i.e. radiographers (37), radiologists (13) and OMF surgeons (4). Although the group of OMF surgeons was small in number, it demonstrated a homogeneous preference for CT. Our results are consistent in the a vast majority of the observers preferred CT to DR, with a single clear exception. Second, a certain degree of 'observer weariness' may have occurred after evaluating 64 image combinations. However, due to the random design of the forced choice comparison it seems safe to exclude such an effect. The third aspect is the fact that for this research a single axial CT slide only was used as opposed to the clinical practice where multiplanar reconstructions (MPR) are being used. MPR increase the effectiveness of visualization of fractures, especially in inferior orbital wall fractures [23]. Coronal reconstructions contribute to the diagnostic process of maxillofacial fractures [23,24]. Furthermore, volume rendering CT recreates the surgeon's complex mental process of visualizing fractures in operative planning [24]. Volume rendering does not only give a more accurate diagnostic reading of radiographs, surgeons value it as a front line tool in the evaluation and management of acute facial trauma [14]. However, experienced radiologists and OMF surgeons continue to prefer and interpret 2D CT [11]. MPR and volume rendering can be seen as a valuable addition when choosing CT as primary diagnostic modality. Therefore, we expect that the use of MPR and volume rendering would result in an even a higher actual CT preference in clinical practice than demonstrated in this experimental study.

Although DR may still be preferred to assess anatomic integrity after facial trauma, evidence to support the use of CT to diagnose bone trauma increases, especially if a zygomatic trauma is part of the differential diagnosis. It has been demonstrated that when choosing CT no additional radiographic imaging is needed, while patients often need additional facial imaging following DR. Therefore, the use of CT as primary diagnostic tool reduced facial imaging and as a consequence, radiation dose [2]. However, DR images may well be preferred in situations in which pre- and post-operative evaluation is required. In addition to the decrease in additional imaging when choosing CT as primary diagnostic tool, several other advantages have been described previously [1,2,13,25]. CT requires considerable less time and can be performed with less potentially hazardous positioning of injured patients as compared to DR [2,13]. As manipulation of the head in the unconscious multi-trauma patient is not advisable, CT is safer and more comfortable for the patient [2,15]. Maxillofacial fractures are often associated with brain injury and/or edema.

Therefore, a major benefit of CT over DR is that CT enables assessment of fractures despite the presence of edema, of injuries involving the brain, eyeballs, optic nerves and other soft tissue structures [13,25–27]. Concerning diagnostic accuracy, it has been demonstrated that facial CT imaging is more accurate compared to DR, as CT is superior in displaying fracture lines and the orientation of fracture fragments [13]. Tanrikulu *et al.* found no significant difference between axial CT, coronal CT and DR for the diagnosis of zygomaticomaxillary fractures when assessed independently by two examiners [9]. Nevertheless, CT was preferred because of two reasons. First, the exact diagnosis of displacement of each of the five major articulations of the zygomaticomaxillary complex can be better evaluated which facilitates the selection of the best surgical approach [28]. Second, depression of the zygomatic arch may trap the coronoid process of the mandible and this complication is more easily appreciated using CT [29].

In conclusion, the current study shows that low dose CT images are preferable over DR images for the assessment of isolated zygomaticomaxillary fractures. This conclusion adds to an increasing amount of evidence on the advantages of CT over DR. The data presented in this study justifies more research into the use of low dose CT as primary diagnostic tool for the assessment of zygomaticomaxillary fractures.

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CHAPTER 7

Diagnostic reliability of low dose Multidetector Computed Tomography and Cone Beam Computed Tomography in maxillofacial trauma: an experimental blinded and randomized study

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Published in Dentomaxillofacial Radiology
Volume 47, Issue 8, December 2018
Adapted version of the manuscript

Abstract

Objective: To assess the diagnostic reliability of low dose Multidetector Computed Tomography (MDCT) and Cone Beam Computed Tomography (CBCT) for zygomaticomaxillary fracture diagnosis.

Methods: Unilateral zygomaticomaxillary fractures were inflicted on four out of six fresh frozen human cadaver head specimens. All specimens were scanned using four MDCT and two CBCT imaging protocols of which the radiation exposure was systematically reduced. A blinded diagnostic routine was simulated at which 16 radiologists and 8 oral and maxillofacial (OMF) surgeons performed 144 randomized image assessments. We considered the findings during an open operative approach of the zygomatic region as the gold standard.

Results: Zygomaticomaxillary fractures were correctly diagnosed in 90.3% (n=130) of the image assessments. The zygomatic arch was most often correctly diagnosed (91.0%). The zygomatic alveolar crest showed the lowest degree of correct diagnosis (65.3%). Dose reduction did not significantly affect the objective visualization of fractures of the zygomaticomaxillary complex. The sensitivity and specificity also remained consistent among the low dose scan protocols. Dose reduction did not decrease the ability to assess dislocation, comminution, orbital volume, volume rendering and soft tissues. OMF surgeons considered the low dose protocols sufficient for treatment planning.

Conclusion: Dose reduction did not decrease the diagnostic reliability of MDCT and CBCT for the diagnosis of zygomaticomaxillary fractures.

Introduction

Multidetector Computed Tomography (MDCT) and Cone Beam Computed Tomography (CBCT) are the imaging modalities of choice in midfacial trauma diagnostics and treatment planning [1–3]. Both modalities are utilized to detect and characterize midfacial fractures [2,4,5]. The zygomaticomaxillary buttress represents the most common site of facial fractures [6,7]. Disruption of the zygomatic position can cause an aesthetic and functional deficit. It is therefore mandatory that zygomatic bone injuries are properly diagnosed and adequately managed [8].

Although CBCT is considered to produce a generally lower radiation dose, there are some clinical considerations for the common use of MDCT to evaluate blunt facial trauma [1,9]. First, there is limited availability of CBCT within the emergency department, where the majority of the patients are presented initially. Second, additional traumatic injuries may impede examinations using CBCT in which the patient is scanned in a natural head position. Third, only MDCT allow soft tissue reconstructions, which are appreciated for the ability to detect associated soft tissue injury in midfacial trauma [10].

However, there is an increasing concern regarding the potential radiation induced risks due to the exponentially increased use of MDCT and CBCT in medicine [1,11]. Keeping the radiation dose as low as reasonably achievable, remains the most important strategy for limiting the risks [12,13]. There is limited evidence regarding the effect of dose reduction for the diagnosis of maxillofacial trauma. In two studies, evidence for the potential of substantial dose reduction for the diagnosis of midface fractures was successfully provided [14,15]. However, these studies were not randomized and the observers were not blinded for the outcome of interest. The aim of the present study was to assess the diagnostic reliability of low dose MDCT and low dose CBCT for zygomaticomaxillary fractures using a randomized approach with blinded observers.

Material and Methods

Study subjects

Six fresh frozen human cadaver heads were obtained from the section anatomy of the Department of Neurosciences of the University Medical Center Groningen (Groningen, NL). These cadavers have been donated for medical research and educational purposes according to the legal and ethical guidelines of the Dutch uniform anatomical gift act. Their age ranged from 60 to 96 years old. Thawing the cadaver specimens to room temperature occurred 48 hours prior to experimentation. The specimens were isolated at the craniovertebral junction keeping the intracranial contents intact.

Experimental design

An experiment was designed to systematically inflict unilateral zygomaticomaxillary fractures on four out of six specimens. A blunt facial trauma was simulated using a guided free fall method as an impact model (Figure 1) [15–17]. The specimens were placed horizontally on a solid wedge for stabilisation. The direction of impact was chosen at a 40 degree angle from the mid sagittal section plane in order to obtain perpendicular impact on the malar eminence. A cylindrical 2.0 kg impactor with a flat impacting surface was used as a free falling mass. A drop height estimation of 70 cm was calculated using biomechanical fracture tolerance data where power of collision was measured in dynamic loads [17–19]. An independent consultant oral and maxillofacial (OMF) surgeon physically examined the zygomaticomaxillary complex for fracture presence after impact. The drop height was raised with 10 cm consequently if no discernible evidence for a fracture was found.

Figure 1: Impact model used to inflict unilateral zygomaticomaxillary fractures.

Diagnostic imaging

All specimens were scanned using four MDCT and two CBCT protocols (Figure 2). The scan field of view (FOV) was standardized from the maxillary dentition up to the superior orbital rim of the frontal sinus. MDCT imaging was performed using a third generation Siemens SOMATOM Force scanner (Siemens Healthcare AG, Erlangen, Germany). Automatic exposure control (AEC) was used for radiation dose optimization adapting tube current (CARE Dose4D, Siemens) and tube voltage (CARE kV, Siemens). For each specimen the tube voltage was fixed for consecutive scans made from the baseline protocol. Quality reference mAs was used as the only variable to systemically reduce the radiation dose for each MDCT scan protocol. Each specimen was scanned using a quality reference mAs of 50, 40, 30 and the lower limit of 20. Scan parameter details for MDCT are found in Table 1. The raw data was reconstructed into 0.6 mm bone and soft tissue volume datasets using the Siemens Hr59d and Hr32d kernels respectively. CBCT imaging was performed using the ProMax 3D Mid (Planmeca Oy, Helsinki, Finland). Each specimen was scanned using two 0,4 mm isotropic scan protocols. One of these datasets was scanned using the ultra-low dose (ULD) mode. Scan parameter details for CBCT are found in Table 2. For both MDCT and CBCT the bone volumetric datasets were reconstructed into a 3D volume rendering batch using a bone template. This data was presented in a dynamic 360 degree rotational view round a fixed vertical axis providing the spatial relationship of the osseous midfacial anatomy. All data was exported in a Digital Imaging and Communications in Medicine (DICOM) standard.

Table 1: Siemens SOMATOM Force MDCT scan parameters.

Tube voltage modulation [a]	CARE kV					
Specimen (1-6) fixed kV	90	100	80	90	80	90
Tube current modulation [b]	CARE Dose4D					
Scan protocol	1	2	3	4		
Quality reference mAs	50	40	30	20		
Average effective mAs	77	52	40	29		
Average $CTDI_{vol}$ (mGy)	4.6	3.5	2.7	1.8		
Average DLP (mGy*cm)	61.9	48.8	37.2	24.6		
ADMIRE Strength	1					
Field of view	220.0 mm					
Collimation	192 x 0,6 mm					
Average scan length	118 mm					
Slice thickness	0.6 mm					
Position increment	0.4 mm					
Grayscale depth	12 bit					
Pitch	0.6					
Rotation time	0.5 s					
Exposure time	0.5 s					
Scan time	3,4 s					
Matrix	512 x 512					

Abbreviations: MDCT Multidetector Computed Tomography; ADMIRE Advanced Modelled Iterative Reconstruction; $CTDI_{vol}$ Volume Weighted Computed Tomography Dose Index; DLP Dose Length Products

a For each specimen the tube voltage was fixed for consecutive scans made from the baseline protocol
b The quality reference mAs was used to systemically reduce the radiation dose for four different scan protocols

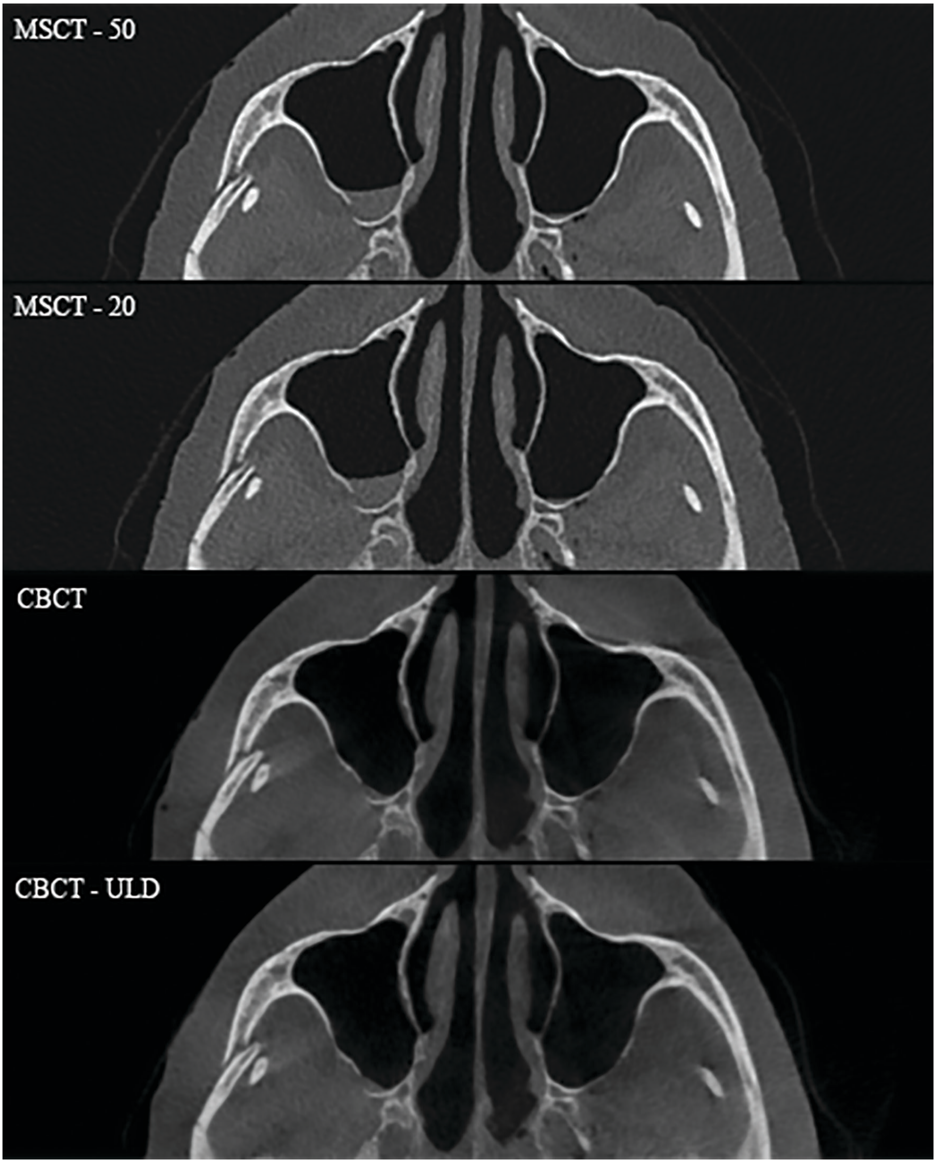

Figure 2: A right sided zygomaticomaxillary fracture in the zygomatic arch, the anterior and posterior sinus maxillary wall. The baseline (A+C) and the lowest dose (B+D) protocols for both Multidetector Computed Tomography and Cone Beam Computed Tomography are compared consecutively.

Table 2: Planmeca Promax 3D mid CBCT scan parameters for the baseline and ULD protocol.

Tube voltage	90 kV
Tube current	10 mA
DAP (mGy)	15.6
Tube current ULD	7 mA
DAP ULD (mGy)	3.2
Exposure time	13,6 s
Exposure time ULD	4,5 s
Grayscale depth	12 bit
Scan time	18-26 s
Field of view	200 x 100
Radiation source	Pulsed
Rotation degree	Single 200 degree rotation
Projections per rotation	300
Detector type	Flat panel detector
Voxel size (x,y,z)	0,4 mm^3
Matrix	512 x 512

Abbreviations: CBCT Cone Beam Computed Tomography; DAP Dose Area Product; ULD Ultra Low Dose

Gold standard

A gold standard was created in a consensus meeting between a European certified head and neck radiologist (HW) and an OMF surgeon with specific craniomaxillofacial trauma experience (BM). Both were not included in the image assessment procedure. The presence of fractures of the zygomatic region were recorded by the radiologist who had access to all scanned MDCT and CBCT data. These findings were validated by the OMF surgeon using a combined local transcutaneous and maxillary vestibular approach of the specimen's zygomaticomaxillary complex (Figure 3). Discrepancies were discussed and advocated.

Assessment setup

The diagnostic quality of all scan protocols was read in 144 image assessments by a group of 24 observers consisting of radiologists (n=16) and OMF surgeons (n=8) from the University Medical Center Groningen (Groningen, NL), Isala hospital (Zwolle, NL), Nij Smellinghe hospital (Drachten, NL), Tjongerschans hospital (Heerenveen, NL) and Sionsberg hospital (Dokkum, NL). Each observer performed image assessments for all six patient cases. One of the six scan protocols was randomly allocated for each

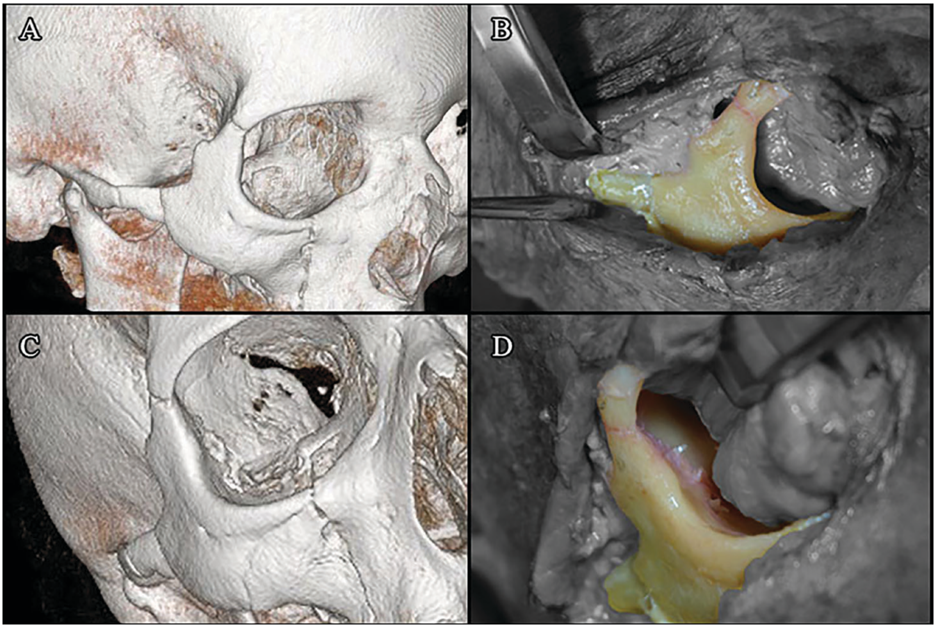

Figure 3: Approach used as gold standard. For this specimen the 3D volume rendering (A+C) is compared to the surgical approach (B+D) from the same projection. Fractures were recorded in the zygomatic arch, frontozygomatic suture, infra-orbital rim, anterior maxillary sinus wall and lateral orbital wall.

of these patient cases using a research randomizer [20]. The order in which the patient cases were assessed was also randomized. Each image assessment was simulated as a diagnostic routine where each specimen was presented as a fictive patient case with a suspected zygomaticomaxillary fracture. The observer was blinded for the outcome of interest and all scan parameters. The use of a medical diagnostic display was set as a condition for radiologist. These displays all met the acceptance and constancy tests following the American Association of Physicists in Medicine (AAPM) Task Group 18 (TG18) guidelines [21]. The DICOM datasets were provided on a mobile TeraRecon Aquarius iNtuition DICOM Viewer (TeraRecon, Foster City, California, United States). This viewer application allowed the features and functionalities that a medical professional would use in the daily clinical care. MDCT patient cases were provided with two datasets using a bone and soft tissue reconstruction kernel. Each CBCT patient case was provided with the single reconstruction dataset. The volume rendering batch was available for both acquisition modalities. The observer was allowed to adjust window width and window level from a 2000/250 bone and 400/40 soft tissue preset. Volume datasets were presented into orthogonal axial, sagittal and coronal plane where free angle adjustment using the multi planar reconstruction (MPR) module was allowed.

Image assessment

Each patient case was provided with fictive personal particulars, mechanism of injury, clinical presentation and physical examination findings. Each image assessment was divided into an objective and subjective analysis. The objective analysis consisted of a fracture diagnosis including a location determination using a predefined selection of zygomaticomaxillary fracture associated anatomical sites. The gold standard was used to verify the correctness of these observations. The subjective analysis was used to study the sufficiency of the image quality to assess parameters relevant to diagnosing fractures in the maxillofacial region. Also, the acceptability of the image quality for 3D volume rendering and soft tissue reconstructions was assessed. All parameters of the image assessment are summarized in Table 3 in detail.

Table 3: Objective and subjective image assessment parameters used to assess the diagnostic reliability for each of the scan protocols.

Objective (presence and location) *Question; do the following anatomical sites of the midface comprise a fracture?* **(yes/no/inconclusive)**	**Subjective** (scan protocol sufficiency) *Question; is the image quality sufficient to assess the following parameters?* **(sufficient/not sufficient)**
Frontozygomatic suture	Fracture dislocation
Lateral orbital wall	Fracture comminution
Zygomatic arch	Orbital volume
Orbital floor	Volume rendering
Zygomatic alveolar crest	Soft tissue [a]
Anterior maxillary sinus wall	Treatment management sufficiency [b]
Posterior maxillary sinus wall	Fracture assessment sufficiency [c]
Zygomatic corpus	

[a] Soft tissue reconstructions were only available for Multidetector Computed Tomography
[b] This parameter was only assessed by oral and maxillofacial surgeons
[c] This parameter was only assessed by radiologists

Effective dose estimations

Effective dose estimations were only accessible for MDCT using volume weighted CT dose indices ($CTDI_{vol}$) and Dose Length Products (DLP) provided by the scanner. Head conversion coefficients (0.0021 mSv mGy^{-1} cm^{-1}) quoted by the AAPM were used to convert DLP to effective dose [22].

Statistics

Data analysis was performed using the R environment for statistical computing and graphics (version 3.3.3) [23]. A generalized linear mixed model (GLMM) was constructed to assess the effect of dose reduced scan protocols for the objective fracture detectability outcome. The analysis was performed separately for MDCT and CBCT and the baseline protocols were used as intercept. The diagnostic accuracy of the eight fractures sites, as verified by the gold standard, was used as response variable (Table 3). The variable was defined binary and inconclusive reported data was statistically handled as an incorrect diagnostic finding as it would otherwise result in an distorted skew towards a diagnostic reliable outcome. The scan protocol covariate was included as a fixed effect and the observer, patient case and fracture location covariates nested within the patient case were included as random effects to account for the correlation among the repeated measurements. The significance level was set at 5%. As an additional outcome for the overall diagnostic reliability, the sensitivity and specificity were calculated for each scan protocol by pooling the verified assessment outcomes for all the anatomical sites of the zygomaticomaxillary complex.

Results

Zygomaticomaxillary fractures were successfully inflicted on all four specimens in varying degree of severity. The consensus meeting corresponded that the baseline protocols of MDCT and CBCT appeared sufficient to visualize all fractures of the anatomical sites selection of the midface. Over the total of 144 image assessments, 90.3% (n=130) of the zygomaticomaxillary fractures were correctly diagnosed and 7.6% (n=11) were misdiagnosed. In another 2.1% (n=3) the diagnosis was reported as inconclusive. The four specimens that sustained a fracture were diagnosed correctly by all 24 observers (100%). From the two specimens without a fracture, one was diagnosed correctly by 23 observers (95.8%) whilst the other was diagnosed correctly by 11 observers (45.8%). The objective detectability percentages varied substantially among the assessed anatomical sites (Table 4). Zygomatic arch fractures were most often diagnosed correctly (91.0%). On average, the highest degree of misdiagnosis was found for zygomatic alveolar crest fractures. For patient case four there was an outlying degree of misdiagnosis for the anterior and posterior maxillary sinus wall and the orbital floor. In the consensus meeting, these fractures were found to be minimal and non-dislocated. For patient case six, there was a high degree of zygomaticomaxillary fracture misdiagnosis when compared to the other patient

Table 4: Percentage correctly diagnosed fracture sites subdivided for each patient case.

	Patient case [a]												
	1		2		3		4		5		6		Mean
Fracture presence [b]	100	Y	100	Y	100	Y	100	Y	95.8	N	45.8	N	90.3
Frontozygomatic suture	87.5	Y	95.8	Y	50.0	N	45.8	Y	95.8	N	79.2	N	75.7
Lateral orbital wall	95.8	Y	87.5	Y	91.7	Y	83.3	Y	95.8	N	83.3	N	89.6
Zygomatic arch	100	Y	100	Y	100	Y	100	Y	100	N	45.8	N	91.0
Orbital floor	79.2	Y	100	Y	70.8	Y	8.3	Y	100	N	91.7	N	75.0
Zygomatic alveolar crest	33.3	N	33.3	N	54.2	Y	87.5	N	100	N	83.3	N	65.3
Anterior maxillary sinus wall	100	Y	100	Y	100	Y	16.7	Y	100	N	75.0	N	81.9
Posterior maxillary sinus wall	87.5	Y	83.3	Y	95.8	Y	8.3	Y	100	N	70.8	N	74.3
Zygomatic corpus	62.5	N	62.5	N	62.5	N	79.2	N	100	N	91.7	N	76.4

a For each patient case, the presence of a fracture was verified by the gold standard and provided for each assessed anatomical site of the zygomaticomaxillary complex (Y/N)

b Zygomaticomaxillary fractures were inflicted on the first four patient cases 1-4

Table 5: Objective and subjective image assessment proportion outcomes for the four MDCT and two CBCT protocols.

	Quality reference mAs MDCT protocol				CBCT protocol	
	50	40	30	20	Baseline	ULD
Effective dose (μSv)[a]	129.9 ± 9.2	99.9 ± 12.0	78.3 ± 6.3	51.0 ± 4.2		
Objective analysis[b]						
Fracture presence	21/24 (87.5%)	23/24 (95.8%)	21/24 (87.5%)	22/24 (91.7%)	21/24 (87.5%)	22/24 (91.7%)
Frontozygomatic suture	18/24 (75.0%)	18/24 (75.0%)	17/24 (70.8%)	19/24 (79.2%)	18/24 (75.0%)	19/24 (79.2%)
Lateral orbital wall	21/24 (87.5%)	21/24 (87.5%)	24/24 (100%)	20/24 (83.3%)	22/24 (91.7%)	21/24 (87.5%)
Zygomatic arch	23/24 (95.8%)	22/24 (91.7%)	21/24 (87.5%)	22/24 (91.7%)	21/24 (87.5%)	22/24 (91.7%)
Orbital floor	17/24 (70.8%)	18/24 (75.0%)	18/24 (75.0%)	17/24 (70.8%)	19/24 (79.2%)	19/24 (79.2%)
Zygomatic alveolar crest	15/24 (62.5%)	15/24 (62.5%)	16/24 (66.7%)	18/24 (75.0%)	15/24 (62.5%)	15/24 (62.5%)
Anterior maxillary sinus wall	19/24 (79.2%)	19/24 (79.2%)	19/24 (79.2%)	19/24 (79.2%)	21/24 (87.5%)	21/24 (87.5%)
Posterior maxillary sinus wall	17/24 (70.8%)	19/24 (79.2%)	16/24 (66.7%)	19/24 (79.2%)	17/24 (70.8%)	19/24 (79.2%)
Zygomatic corpus	18/24 (75.0%)	20/24 (83.3%)	19/24 (79.2%)	17/24 (70.8%)	15/24 (62.5%)	21/24 (87.5%)
Subjective analysis[c]						
Dislocation	17/18 (94.4%)	18/18 (100%)	18/19 (94.7%)	17/18 (94.4%)	18/19 (94.7%)	18/19 (94.7%)
Comminution	15/18 (83.3%)	18/18 (100%)	14/19 (73.7%)	17/18 (94.4%)	17/19 (89.5%)	18/19 (94.7%)
Orbital volume	16/18 (88.9%)	18/18 (100%)	17/19 (89.5%)	18/18 (100%)	18/19 (94.7%)	19/19 (100%)
Volume rendering	18/18 (100%)	17/18 (94.4%)	15/19 (78.9%)	17/18 (94.4%)	13/19 (68.4%)	15/19 (78.9%)
Soft tissue	17/18 (94.4%)	17/18 (94.4%)	16/19 (84.2%)	17/17 (94.4%)	-	-
Fracture assessment	13/16 (81.3%)	15/16 (93.8%)	14/16 (87.5%)	16/16 (100%)	13/16 (81.3%)	9/16 (56.3%)
Treatment management	7/8 (87.5%)	8/8 (100%)	8/8 (100%)	7/8 (87.5%)	8/8 (100%)	8/8 (100%)

Abbreviations: MDCT Multidetector Computed Tomography; CBCT Cone Beam Computed Tomography; ULD Ultra Low Dose

a Only provided for MDCT. Effective dose estimations (Mean±SD μSv) were calculated by converting Dose Length Products (DLP) using head conversion coefficients (0.0021 mSv mGy-1 cm-1) quoted by the American Association of Physicists in Medicine (AAPM)[22].

b Reported as correctly diagnosed proportions and percentages as verified by the gold standard.

c Reported as the acceptable reported proportions and percentages. It was only reported when the observer suspected the presence of a zygomaticomaxillary fracture. Soft tissue reconstructions were not available for CBCT. Treatment management was only assessed by oral and maxillofacial surgeons (n=8) whilst the fracture assessment was only assessed by radiologists (n=16).

cases. For the subjective analysis, there was a high degree of conformity that the image quality was sufficient to assess the fracture dislocation (95.5%), comminution (89.2%) and the orbital volume (95.5%). This was also the case for the 3D volume rendering batch (85.6%) and the soft tissue reconstructions or MDCT (91.8%). The agreement remained consistent among the scan protocols (Table 5).

Effect of dose reduction

Both the outcomes of the objective detectability of the eight anatomical fracture sites and the subjective assessed parameters remained consistent among the six scan protocols (Table 5). The GLMM analysis showed that the objective fracture detectability accuracy did not differ significantly between the different MDCT and CBCT scan protocols (Table 6). The sensitivity and specificity also remained consistent among the scan protocols. For radiologists, there was a high agreement for the overall sufficiency of the image quality to asses fractures for the MDCT protocols and the baseline CBCT protocol. The CBCT ULD protocol was found sufficient in 56.3%. For OMF surgeons, the treatment management sufficiency remained consistently high for all scan protocols (Table 5). The effective dose for MDCT examinations (Mean±SD) was reduced by 60.7% from 129.9 ± 9.2 to 51.0 ± 4.2 μSv (Table 5).

Table 6: Generalized linear mixed model outcome and sensitivity and specificity for each scan protocol.

	OR	CI	p-value [a]	Sensitivity (%) [b]	Specificity (%) [b]
MDCT protocol					
50 (intercept)				78	77
40	0.91	0.47 - 1.76	0.78	78	81
30	0.75	0.37 - 1.53	0.44	78	83
20	1.10	0.57 - 2.14	0.78	76	81
CBCT protocol					
Baseline (intercept)				80	79
ULD	1.43	0.76 - 2.70	0.27	82	85

Abbreviations: OR Odds Ratio; CI Confidence Interval; MDCT Multidetector Computed Tomography, CBCT Cone Beam Computed Tomography, ULD Ultra Low Dose

[a] Generalized linear mixed model were used to assess the effect of scan protocols for the outcome of the assessment

[b] The sensitivity and specificity were calculated pooling the verified outcome for all assessed anatomical sites of the zygomaticomaxillary complex

Discussion

In this study, we assessed the diagnostic reliability of low dose MDCT and CBCT for the diagnosis of zygomaticomaxillary complex fractures in a blinded and randomized study design. We showed that dose reduction did not significantly affect the objective visualization of fractures of the zygomaticomaxillary complex. Above that, the sensitivity and specificity remained consistent among the low dose scan protocols. Similar results were found in a previous study in which low dose protocols were considered sufficient for the diagnosis of both dislocated and non-dislocated midface fractures [14].

Despite these findings, detectability percentages varied substantially among the assessed anatomical sites. Potential explanations are discussed. First, patient case six was falsely diagnosed with a zygomatic arch fracture whilst no trauma was inflicted on this specimen. A consolidated fracture was suspected but no medical records were available for verification. Second, the highest degree of misdiagnosis was found for zygomatic alveolar crest fractures. The zygomatic alveolar crest is located in the infrazygomatic region. It is clinically appreciated because the cortical bone thickness provides anchorage for the osteosynthesis screws during surgery [24]. We believe that the determination of a fracture in this region was doubtful for the observer, as the zygomatic alveolar crest is unclearly demarcated in anatomical terms. Third, the low detection rates for the orbital floor, the anterior and posterior maxillary sinus wall for patient case four could be explained by their minimal and non-dislocated characteristics. Although not evaluated in the present study, the clinical consequences of missing non-dislocated fractures could be argued. Nevertheless, the detection variability among the anatomical sites does emphasize that careful reading and adequate anatomical proficiency is a requisite to assess datasets of a suspected midface fracture sufficiently.

Both MDCT and CBCT dose reduced protocols were found sufficient to assess the fracture dislocation, the extend of comminution and the orbital volume. Also, no decrease was found for the diagnostic quality sufficiency of the volume rendering and soft tissue reconstructions. The use of 3D volume rendering provides a visualisation of the spatial relationships of the midface buttresses and is available for both MDCT and CBCT [25]. For MDCT, the soft tissue reconstructions allow evaluation of soft tissue injury which, in case of midfacial fractures, is predominantly utilized to assess the extraocular muscles [10,26,27].

For OMF surgeons, dose reduction did not affect the capability for treatment management. For radiologists, the overall sufficiency to assess the fracture did not decrease for MDCT protocols. Although the objective fracture detectability did not decrease significantly, the ULD protocol of CBCT was only found sufficient subjectively in 56.3% of the assessments. We believe that this is first, due to more evident artefacts in this protocol and second, due to the fact that the application and interpretation of CBCT is dedicated to OMF surgeons. From a clinical perspective, there is a difference in image interpretation between radiologists and OMF surgeons. We think that OMF surgeons predominantly focus on determination of the treatment pathway and planning of potential surgery. This is in contrast to radiologists who are responsible for a correct diagnosis and therefore assess the image quality from a different approach. This allocation of roles should be taken into account when MDCT and CBCT are used for maxillofacial fracture diagnosis.

In this study, effective dose estimations were only provided for MDCT. For CBCT, a previous study used thermoluminescent dosimeters in anthropomorphic Alderson radiation therapy phantoms to estimate effective radiation dose and reported 122μSv and 28μSv for baseline and low dose medium FOV dento-alveolar protocols using the same CBCT device [28]. When compared, the effective dose of MDCT remained well in range of CBCT. Moreover, the effective dose of the MDCT low dose protocols remained below the baseline CBCT protocol. Another study could also successfully confirm dose reduction of MDCT below the levels of CBCT [29]. This data is in contrast to the common believe that MDCT delivers a higher radiation exposure compared to CBCT [1,5,9,30]. The delivered radiation dose is the result of the interplay between a variety of elements. Above all, one should be aware of the large exposure ranges among MDCT and CBCT devices [9,31,32]. For CBCT, a distinction is needed between small-, medium-, and large FOVs [28]. Optimization should be performed using an appropriate scan range determination, tube potential and reconstruction algorithm. For MDCT, some studies propose the use of a full head protocol [9,14]. However, maxillofacial trauma protocols should predominantly be used to visualize the osseous anatomy, requiring lower levels of radiation dose. Also, the use of AEC improves consistency of the image quality and curtails the radiation dose for each individual patient [12]. In this study this was accomplished for both the tube current (CARE Dose4D) and tube voltage (CARE kV). Furthermore, filtered back projection (FBP) is currently the well-established reconstruction type for clinical MDCT protocols. The recent availability of iterative reconstruction (IR) algorithms offers new possibilities for radiation dose reduction [14,33]. In this study FBP was combined with a model-based IR (ADMIRE 1, Siemens). As there is limited evidence regarding the use of IR algorithms for maxillofacial trauma, further research should focus on the potential of dose reduction, the clinical applicability and computational time requirements.

This study has some limitations. First, the post-mortem status of human cadaver specimen carries process changes that may affect the interpretability of the scans. Second, trauma patients may have indirect predictive CT findings, such as sinus opacification and periorbital contusion, that have discriminatory benefits for predicting midface fractures in trauma patients [34]. These findings are absent in human cadavers. Nevertheless, we believe that, as a surrogate model, it is the most accurate approach of a maxillofacial trauma patient.

Another limitation is that we were only able to use six human cadavers as a representation of a midface trauma patient population. Therefore, the statistical power is limited and there was a lack of variability of fracture patterns. This study focuses on the diagnosis of zygomaticomaxillairy fractures only, whilst clinicians are faced with a broad range of fracture patterns such as Le Fort or naso-orbitoethmoid fractures that were not assessed with the present study design. However, we believe that the experimental approach of this study provided substantial evidence to further study the clinical applicability of low dose maxillofacial trauma protocols in human subjects.

In conclusion, the results of this human cadaver study show that dose reduction did not decrease the diagnostic reliability of MDCT and CBCT for the diagnosis of zygomaticomaxillary fractures. Low dose protocols were also considered sufficient for treatment management according OMF surgeons. Further research should focus on the potential of IR algorithms and the applicability of low dose MDCT and CBCT protocols in a clinical environment.

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8

CHAPTER 8

Iterative reconstruction and deep learning algorithms for enabling low dose computed tomography in midfacial trauma

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Published in Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology
Volume 132, Issue 2, August 2021, Pages 247-254
Adapted version of the manuscript

Abstract

Objectives: To quantitatively assess the image quality of advanced modeled iterative reconstruction and the PixelShine™ deep learning algorithm for the optimization of low dose CT protocols in midfacial trauma.

Methods: A total of six fresh frozen human cadaver head specimens were CT scanned using both standard and low dose scan protocols. Varying iterative reconstruction strengths were applied to reconstruct bone and soft tissue datasets and these were subsequently applied to a deep learning algorithm. Signal to noise and contrast to noise ratios were calculated for each dataset by using the image noise measurements of ten consecutive image slices from a standardized region of interest template.

Results: The low dose scan protocol resulted in a 61.7% decrease in the radiation dose. Radiation dose reduction significantly reduced and iterative reconstruction and the deep learning algorithm significantly improved contrast to noise ratio for bone and soft tissue datasets. The algorithms improved the image quality after substantial dose reduction. The highest effects of signal to noise and contrast to noise ratio improvement was found using the iterative reconstruction algorithm.

Conclusion: Both advanced modeled iterative reconstruction and deep learning algorithms significantly improve image quality after substantial radiation dose reduction.

Introduction

CT has evolved as the imaging modality of choice for the assessment of maxillofacial injury. In recent years, particular attention has been directed towards the effects of radiation exposure within this population of patients. Novel reconstruction algorithms have been proposed to optimize and reduce the radiation dose of these CT protocols.

In recent years, the iterative reconstruction algorithms and a new deep learning algorithm have emerged to provide substantial image noise reduction in CT datasets [1]. First, the iterative reconstruction (IR) algorithm was introduced as an alternative to the standard Filtered Back Projection (FBP) reconstruction. To this date, CT vendors have released different generations of the IR algorithm [2]. First generation algorithms were based on the image domain only, whereas second generation or sinogram affirmed iterative reconstruction uses both backward and forward projections to compute the differences and compare them with the actual measured CT. The newest generation, called the full or advanced modeled iterative reconstruction is a more complex algorithm that also removes geometric imperfections and has system and noise modeling to further decrease the image noise, reduce artifacts and improve spatial and contrast resolution [3].

Second, a deep learning based procedure was initiated as a post-processing denoising algorithm. This so called PixelShine™ (PS) algorithm is a software technology developed and based on an artificial neural network which is a deep machine learning technique (AlgoMedica Inc., Sunnyvale, California, USA). The algorithm is proprietary. Typical deep learning techniques for medical imaging often include convolutional neural networks, such as U-Net17 or V-Net16, which are used for medical image segmentation [4,5]. The network classifies each voxel as part of a region of interest or background. The network is trained at pixel level and detects voxel patterns at different resolution scales to determine whether a pattern is noise or a relevant structure. The few published research papers propose that the algorithm denoise datasets substantially [6,7]. This deep learning type of algorithm initiates a completely new concept regarding image quality optimization and should be further explored.

As generally known, adequate radiation exposure is needed to produce acceptable image quality. This is a prerequisite for the visualization of fractures in midfacial trauma CT, as well as for the assessment of soft tissue injury and subsequent treatment management. Yet, the patient radiation dose should be kept as low as reasonably possible. The IR and PS algorithms potentially improve the image quality of CT datasets but not much research has been reported on this topic. The purpose of this study was to quantitatively assess the image quality of IR and PS algorithms for CT protocols in midfacial trauma imaging after substantially reducing the radiation dose.

Material and Methods

The workflow of the material and method section of this study is summarized in Figure 1's infographic.

Study subjects (I)

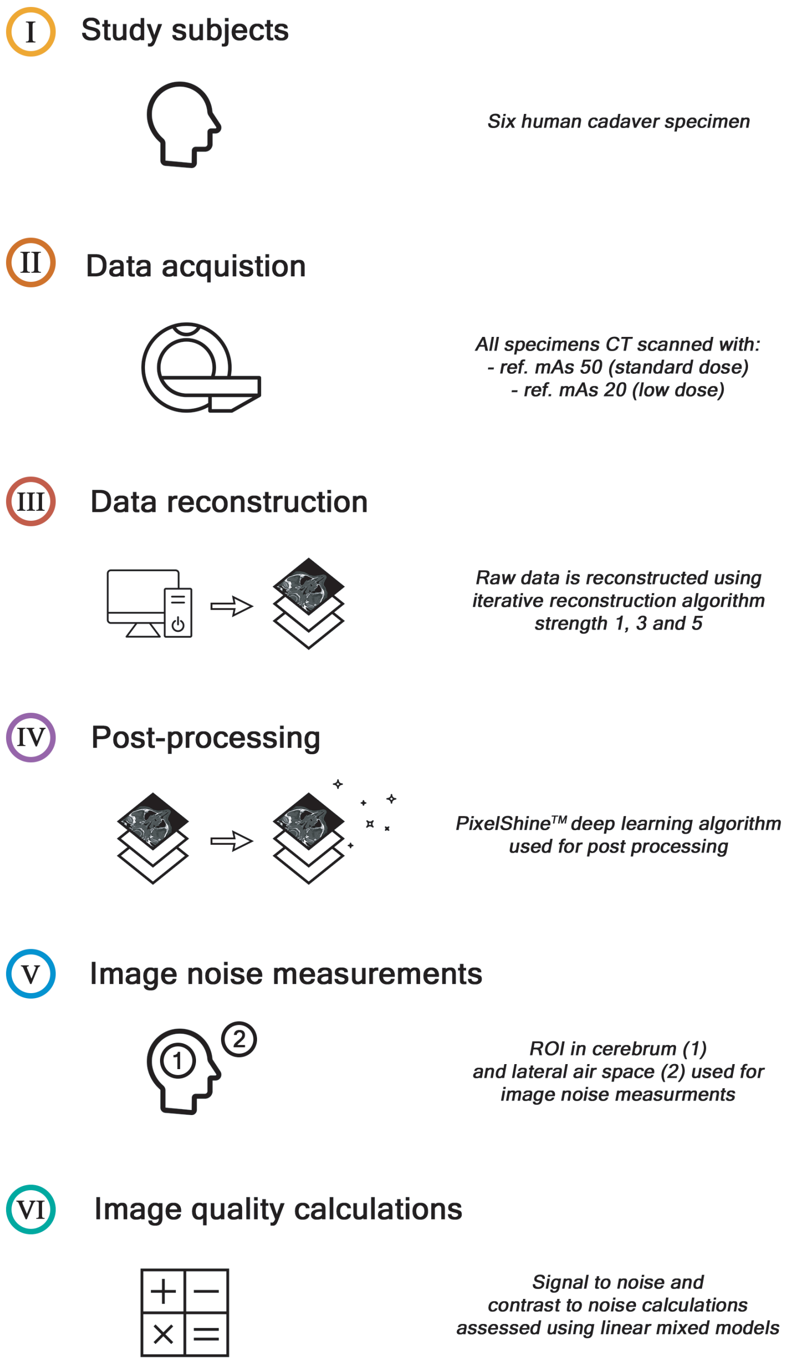
Six fresh frozen human cadaver heads were obtained from the anatomy section of the Department of Neurosciences of the institution (University Medical Center Groningen). The specimens were obtained according to the local legal and ethical guidelines as previously described in a different study by our research group [8].

Data acquisition (II)

All the specimens were scanned using a third generation Siemens SOMATOM Force scanner (Siemens Healthcare AG, Erlangen, Germany). Each specimen was situated in a fixed position and scanned using a multitude of standardized scans of the midfacial region. The scan range was set from the upper border of the frontal sinus to the complete maxilla. Scans were produced in both the standard (ref. mAs 50) and radiation reduced (ref. mAs 20) scan protocol. All scan parameter details are given in Table 1.

Data reconstruction (III)

All the raw datasets were reconstructed using a model-based iterative reconstruction algorithm set at strength one, three and five (ADMIRE, Siemens Healthcare AG). ADMIRE has up to five strength levels that result in less noise and reflect how aggressively the algorithm is using IR over FBP during the raw data reconstruction. All the data was reconstructed using both a bone (Hr59d) and soft tissue (Hr32d) convolution kernel.



I Study subjects

Six human cadaver specimen

II Data acquistion

All specimens CT scanned with:
- ref. mAs 50 (standard dose)
- ref. mAs 20 (low dose)

III Data reconstruction

Raw data is reconstructed using
iterative reconstruction algorithm
strength 1, 3 and 5

IV Post-processing

PixelShine™ deep learning algorithm
used for post processing

V Image noise measurements

ROI in cerebrum (1)
and lateral air space (2) used for
image noise measurments

VI Image quality calculations

Signal to noise and
contrast to noise calculations
assessed using linear mixed models

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Figure 1: Workflow of the material and methods.

Table 1: CT protocol and reconstruction parameters.

Tube voltage	80 kV
Tube current modulation	CARE Dose4D
Quality reference mAs	50 & 20
ADMIRE strength	1, 3 & 5
Field of view	220.0 mm
Collimation	192 x 0,6 mm
Average scan length	118 mm
Slice thickness	0.6 mm
Position increment	0.4 mm
Grayscale depth	12 bit
Pitch	0.6
Rotation time	0.5 s
Exposure time	0.5 s
Scan time	3,4 s
Matrix	512 x 512
Reconstruction kernels	Bone Hr59d & Soft Tissue Hr32d
Post-processing	PixelShine^{TM} deep learning processing

Abbreviations : CT Computed Tomography, ADMIRE Advanced Modeled Iterative Reconstruction.

Post-processing (IV)

All the reconstructed datasets were submitted to the deep learning PS algorithm (v.1.2.57) for additional image quality optimization. Both the post-processed and original datasets were included for data analysis. All datasets were exported in a Digital Imaging and Communications in Medicine (DICOM) standard.

Image quality measurements (V)

Image noise was assessed as HU and standard deviation. ROI measurements were performed using a standardized template for each specimen and scan protocol using the Python software application (Python Software Foundation, Wilmington, Delaware, USA. Python Language Reference, version 3.6.1. Available at http://www.python.org). The standardized template consisted of two homogenous circular ROI within each image slice as similary performed in a previous study [9]. The first ROI of 10.0 cm^2 was positioned in the posterior fossa of the cerebrum and the second ROI of 2.5 cm^2, the background reference, was positioned in the lateral airspace. This Measurements were performed for 10 image consecutive slices.

Image quality calculations (VI)

Signal to noise ratios (SNR) and contrast to noise ratios (CNR) were calculated using image noise measurements [9,10]. SNR is a common way to quantify image noise and CNR reflects how noise affects the ability to see an object in an image. The SNR was defined as the mean attenuation of the cerebrum ROI divided by its standard deviation. The CNR was defined as the difference in the mean attenuation of the cerebrum ROI and the air space ROI divided by the square root of the sum of their variances.

$$\mathrm{SNR} = \frac{\text{Mean HU}_{\text{cerebrum}}}{\text{SD HU}_{\text{cerebrum}}}$$

$$\mathrm{CNR} = \frac{\text{Mean HU}_{\text{cerebrum}} - \text{Mean HU}_{\text{air}}}{\sqrt{\frac{SD_{cerebrum}{}^{2} + SD_{air}{}^{2}}{2}}}$$

Radiation dose estimations

An estimation of radiation dose was calculated by extracting the radiation exposure parameters from the DICOM header for each dataset. The Computed Tomography Dose Index (CTDI_{vol}) and scan range for each specimen was used to calculate the Dose Length Products (DLP) to compare the radiation dose outcome.

Statistical analysis

The data was analyzed with the Statistical Package for the Social Sciences was used for data analysis (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0.) Boxplots were used to visualize the SNR and CNR outcomes. SNR and CNR normalities were examined via the Kolmogorov-Smirnov test and the Q-Q plots. Linear mixed models were used to predict the fixed effects of radiation dose reduction, IR strength and the use of the PS algorithm on image quality outcomes while accounting for repeated measures within each unique dataset. The reference categories of the analyses were: low dose reference mAs 20 scan protocol, ADMIRE strength 1 and no use of PS. The significance level was set at 5%.

Results

A total of 24 unique datasets were reconstructed for each specimen. Repeated image noise measurements were taken from a total of 1440 image slices.

SNR and CNR outcomes

The means and standard deviations of the noise, SNR and CNR outcomes are presented in Table 2. Dose reduction, IR strength and the PS algorithm influenced the HU. The SNR and CNR outcomes of the soft tissue datasets were superior to the bone datasets. Overall, a radiation dose reduction from the reference mAs 50 to the reference mAs 20 protocol resulted in decreased SNR and CNR outcomes. The SNR of the bone datasets tended to increase slightly. The reduced radiation dose was equivalent to a 61.7% decrease of the DLP (Table 2). Raising the IR strength improved the SNR and CNR outcomes of all the datasets, especially the soft tissue datasets. The use of the PS algorithms further increased the SNR and CNR of all the datasets (Figure 2). These effects are clearly illustrated in Figure 3 by the boxplots of the SNR and CNR comparison of each scan protocol. The IR strength five reconstructed datasets and the additional use of the PS algorithm gave the best SNR and CNR outcomes. The IR and PS algorithm improved the SNR and CNR to an extent that the outcomes for the reduced radiation protocol were well in range of the standard protocol.

Linear mixed model analysis outcomes

The results of the linear mixed models analysis are presented in Table 3. A radiation dose reduction, from the standard to the low dose protocol, did not decrease the SNR of the bone datasets significantly, but it certainly decreased the CNR significantly. Raising the IR strength from one to three and from one to five was significantly associated with both the SNR and CNR of the bone datasets. Also, the use of the PS algorithm was significantly associated with both the SNR and CNR bone dataset outcomes. Based on the estimates, the effects of IR strength and use of PS far outreach the effects of radiation dose on SNR and CNR outcome.

Regarding the soft tissue datasets, there was a significant association between both SNR and CNR and radiation dose reduction, raising the IR strength and the use of the PS algorithm. Based on the estimates, the effects of these predictors are substantially larger for the soft tissue datasets than for the bone datasets. The highest estimates were found on raising the IR strength from one to five.

Table 2: Radiation dose, noise, SNR and CNR outcomes for all CT datasets.

Reference mAs	50			20		
Average effective mAs	116.00 ± 10.30			36.00 ± 2.87		
Average CTDIvol (mGy)	5.26 ± 0.48			1.65 ± 0.13		
Average DLP (mGy*cm)	54.22 ± 5.30			20.79 ± 1.46		
ADMIRE strength	1	3	5	1	3	5
Bone						
Conventional processing						
Noise (HU)	31.84 ± 110.87	39.60 ± 89.10	42.00 ± 56.66	32.10 ± 109.42	39.47 ± 87.69	41.43 ± 56.59
SNR	0.289 ± 0.040	0.446 ± 0.057	0.743 ± 0.094	0.294 ± 0.044	0.451 ± 0.058	0.733 ± 0.094
CNR	11.89 ± 0.32	15.17 ± 0.55	23.93 ± 1.10	11.43 ± 0.36	14.73 ± 0.46	22.94 ± 0.71
PS deep learning processing						
Noise (HU)	39.54 ± 90.18	42.12 ± 69.14	42.14 ± 44.31	40.55 ± 83.58	41.96 ± 63.00	42.14 ± 44.31
SNR	0.441 ± 0.070	0.612 ± 0.082	0.956 ± 0.130	0.487 ± 0.071	0.669 ± 0.088	1.019 ± 0.124
CNR	15.71 ± 0.74	20.68 ± 1.28	32.15 ± 2.01	16.46 ± 0.91	21.99 ± 1.26	33.62 ± 1.65
Soft tissue						
Conventional processing						
Noise (HU)	40.67 ± 22.93	40.99 ± 20.58	41.76 ± 18.17	40.52 ± 27.13	40.83 ± 24.33	41.44 ± 21.59
SNR	1.798 ± 0.252	2.024 ± 0.297	2.347 ± 0.366	1.505 ± 0.172	1.692 ± 0.200	1.940 ± 0.239
CNR	59.33 ± 5.91	66.39 ± 7.26	75.67 ± 9.33	48.41 ± 2.98	54.02 ± 3.71	61.03 ± 4.71
PS deep learning processing						
Noise (HU)	39.54 ± 90.18	42.12 ± 69.14	42.14 ± 44.31	40.55 ± 83.58	41.96 ± 62.99	41.57 ± 40.89
SNR	2.006 ± 0.314	2.224 ± 0.362	2.516 ± 0.425	1.696 ± 0.223	1.878 ± 0.251	2.095 ± 0.277
CNR	68.31 ± 8.20	75.06 ± 9.80	83.16 ± 11.89	56.44 ± 4.64	61.79 ± 5.54	67.53 ± 6.17

Abbreviations : CNR Contrast-to-Noise Ratio, SNR Signal-to-Noise Ratio, MDCT Multidetector Computed Tomography, ADMIRE Advanced Modeled Iterative Reconstruction, HU Hounsfield Units, PS PixelShine$^{\text{TM}}$ deep learning

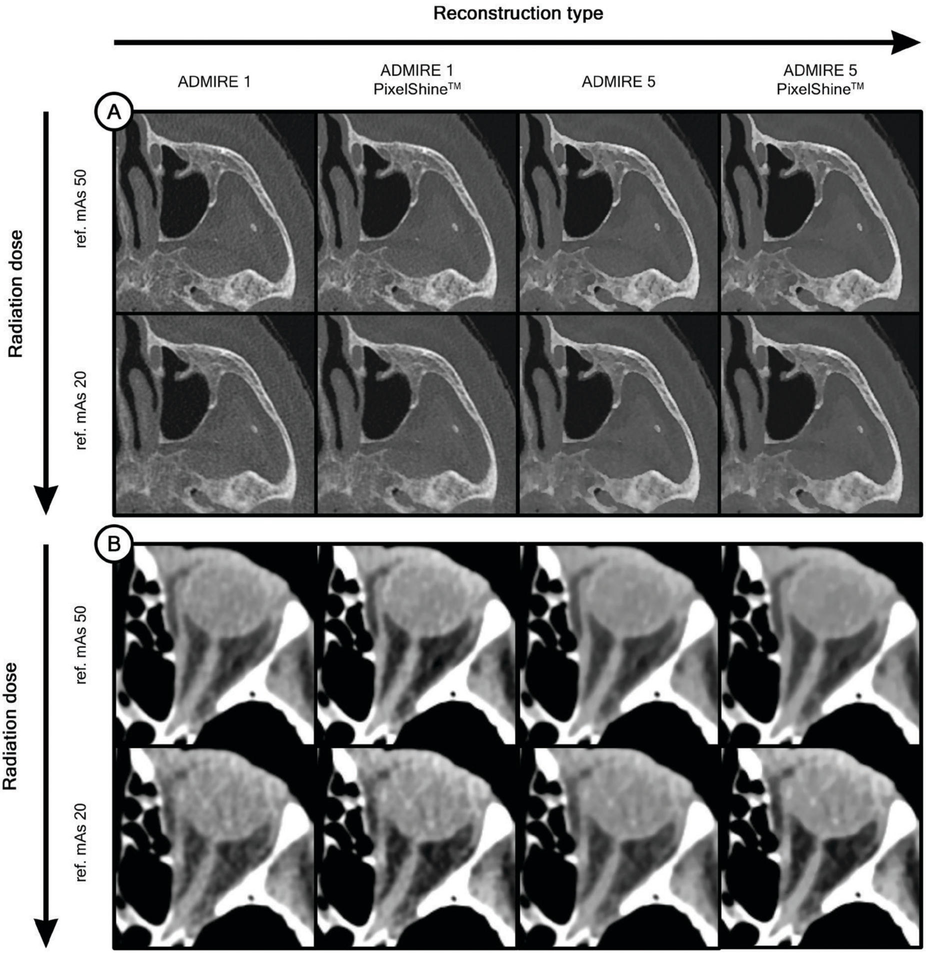

Figure 2: Visual presentation of ADMIRE iterative reconstruction and PixelShine™ deep learning algorithms for bone (A) and soft tissue (B) reconstructed datasets..

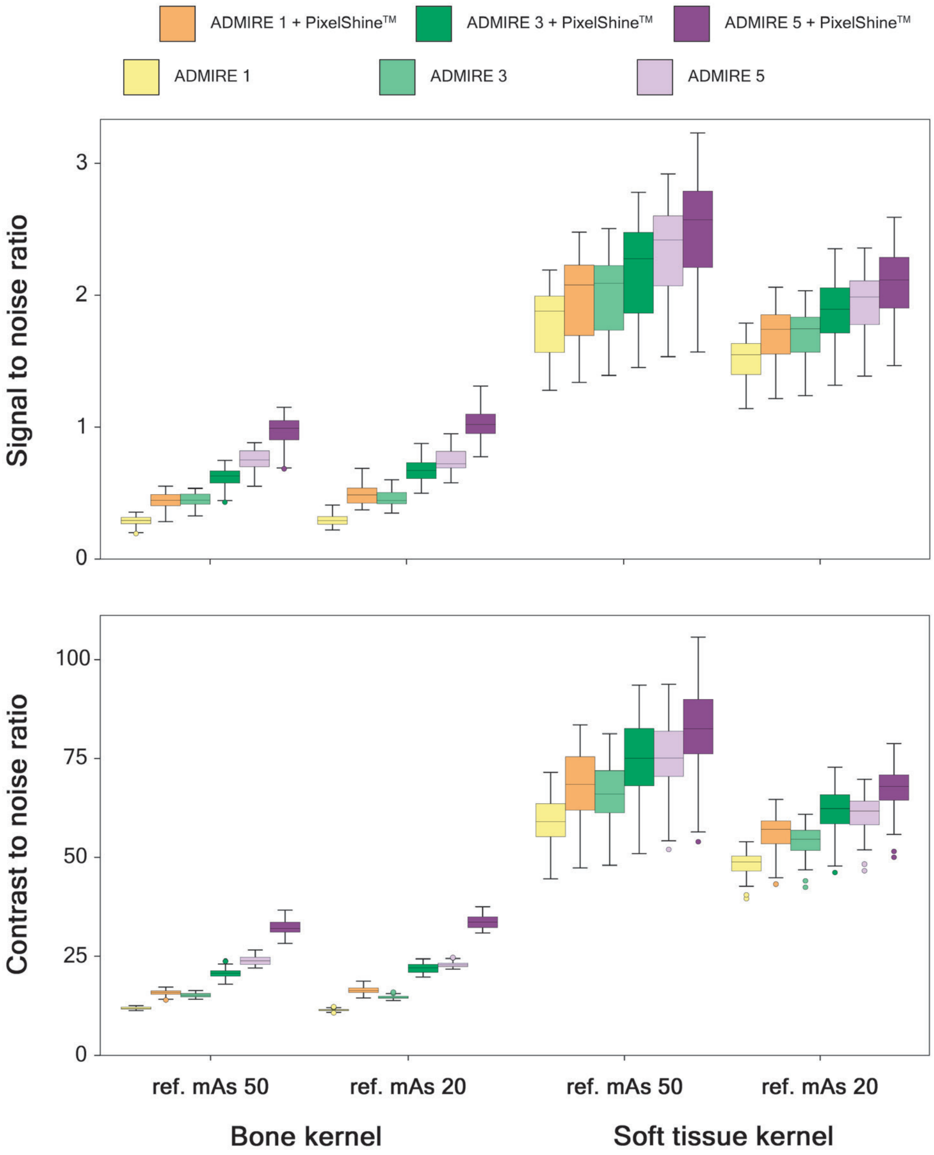

Figure 3: Boxplots comparison of contrast to noise ratio and signal to noise ratio outcomes.

Table 3: Results of the linear mixed model analysis.

Reconstruction type		Bone				Soft tissue			
Parameter		B	SE	95% CI	p-value	B	SE	95% CI	p-value
SNR									
Intercept		0,291	0,010	0,272 – 0,310	0,000	1,804	0,032	1,741 – 1,868	0,000
Radiation dose	Ref. mAs 50								
	Ref. mAs 20	-0,001	0,012	-0,025 – 0,023	0,914	-0,293	0,041	-0.373 – -0.212	0,000
ADMIRE strength	1								
	3	0,155	0,013	0,129 – 0,180	0,000	0,228	0,043	0,142 – 0,313	0,000
	5	0,447	0,013	0,421 – 0,472	0,000	0,559	0,043	0,473 – 0,644	0,000
PS deep learning processing	No								
	Yes	0,145	0,012	0,121 – 0,169	0,000	0,210	0,041	0,129 – 0,290	0,000
CNR									
Intercept		12.03	0,12	11,79 – 12.27	0,000	59.48	0,77	57.96 – 61.00	0,000
Radiation dose	Ref. mAs 50								
	Ref. mAs 20	-0,75	0,16	-1,05 – -0.45	0,000	-11,00	0,98	-12.93 – -9.08	0,000
ADMIRE strength	1								
	3	3,15	0,16	2.82 – 3.47	0,000	7.10	1,04	5.06 – 9.14	0,000
	5	11.72	0,16	11,39 – 12,04	0,000	16.79	1,04	14.75 – 18.83	0,000
PS deep learning processing	No								
	Yes	3.54	0,16	3.23 – 3.84	0,000	9.15	0,98	7.23 – 11.07	0,000

Abbreviations: SNR signal to noise ratio, CNR contrast to noise ratio, B estimate, SE standard error, 95% CI confidence interval upper and lower limit, ADMIRE Advanced Modeled Iterative Reconstruction, PS PixelShine^{TM} deep learning.

Linear mixed model analysis were performed for both bone and soft tissue separately using SNR and CNR as outcome. The radiation dose, the IR strength and the use of PS deep learning processing were added as fixed effects. The reference mAs 20 protocol, ADMIRE strength 1 and no use of PS deep learning processing were used as reference category.

Discussion

This is the first study to assess the use of IR and PS algorithms to improve image quality after substantial radiation dose reduction for CT protocols to assess midfacial trauma. This study demonstrated that radiation dose reduction, raising the IR strength and the use of the PS algorithm were all significantly associated with SNR and CNR as outcomes. Most important, the decrease of SNR and CNR due to radiation dose reduction was substantially improved using the IR and PS algorithms.

In the past decades, CT has grown as a routine imaging method for the assessment of maxillofacial injury. The diagnostic quality and increased availability within the emergency department has led to increased number of CT examinations. As a result, there is an increasing concern regarding the associated radiation exposure within this population of patients [11]. In this study, the estimated radiation dose of the low dose CT protocols were comparable to another human cadaver study where a variety scan protocols for maxillofacial fractures was assessed [12].

We analysed both datasets that were reconstructed using bone and soft tissue kernels. Bone datasets feature higher image noise due to the slices being thinner and the high spatial resolution. Such a sharp characteristic is required to visualise fractures as small bony discontinuities. In this study, the IR and PS improved the SNR and CNR after a substantial reduction in radiation dose. These findings are in line with previous research where a substantial improvement in CNR was found using adaptive statistical and model based IR for bone kernel reconstructed datasets [13]. Image noise improvement is favourable for fracture diagnosis and previous cadaver, phantom and modulation transfer function studies by other IR manufacturers also evidenced that spatial resolution is maintained after radiation dose reduction [14–16]. A known disadvantage of IR reconstructed bone datasets is the longer reconstruction time and that the interpretation is complicated by the waxy or pixelated image appearance [17]. This image appearance is not found when using the PS algorithm. Against expectations, this study only obtained higher SNR and CNR outcomes for the bone datasets on comparing the reduced radiation protocol with the standard protocol. This finding suggests that the denoising capabilities of this algorithm are stronger for datasets with high image noise. As the exact architecture of the PS algorithm is mainly unknown, no clear explanation could be found for this outcome.

Soft tissue datasets are appreciated for the ability to visualize the intra-orbital contents of midfacial trauma. Midfacial fractures are associated with soft tissue related injuries, such as entrapment of the rectus muscles. The low contrast detectability of the soft tissue datasets is necessary in order to differentiate the closely related densities of the intra-orbital anatomy. This study shows that there is also a significant association between radiation dose reduction, IR strength and PS algorithm, and both SNR and CNR for the soft tissue datasets. The soft tissue datasets were more prone to a decrease in SNR and CNR following a decrease in radiation dose, compared to the bone datasets. The decrease in SNR and CNR seems to maintain with the standalone use of the IR, raising the strength from one to five, after radiation dose reduction. A prior study also found that both adaptive statistical IR and model-based IR had a significantly better CNR than FBP for the optic nerve and inferior rectus muscle [18]. Other studies provided a potential for radiation dose reduction using an IR algorithm for soft tissue datasets of cranial CTs [19,20]. Although in this study, the PS algorithm significantly improved the soft tissue datasets, the standalone use did not seem to maintain the image quality after radiation dose reduction. Nevertheless, it provides important evidence that this novel deep learning based technology is able to denoise both bone and soft tissue kernel reconstructed datasets substantially.

This study has limitations. Human cadaver specimens were used as representations of patient cases. The post mortem status of the fresh frozen specimens could have skewed the interpretability of the datasets and the radiation dose outcomes could have been underestimated. Nevertheless, this approach allows a reliable comparison of image quality outcome. Another limitation is that the SNR and CNR were the only used parameters as an outcome of image quality. Although these outcomes are widely accepted when assessing noise related image quality, no direct assumptions can be made regarding the effects on diagnostic outcome. Therefore, future research should focus on how these algorithms affect lesion detectability. A priori knowledge of the algorithm capabilities is needed to optimize the radiation dose of CT protocols in relation to midfacial trauma. Future research should also focus on the use of these algorithms for low dose CT protocols in paediatrics, orthodontics and artefact reduction.

In conclusion, both advanced model based IR and PS algorithms significantly improve SNR and CNR of bone and soft tissue datasets for CT protocols used for midfacial trauma. Improvements in SNR and CNR were particularly found for the soft tissue datasets. The algorithms provide potential to maintain image quality after substantial radiation dose reduction.

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9

CHAPTER 9

Structural similarity analysis of midfacial fractures: a feasibility study

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* These authors contributed equally to this work

Published in Quantitative Imaging in Medicine and Surgery
Volume 12, Issue 2, February 2022, Pages 1571-1578
Adapted version of the manuscript

Abstract

Objective: The structural similarity index metric is used to measure the similarity between two images. The aim here was to study the feasibility of this metric to measure the structural similarity and fracture characteristics of midfacial fractures in CT datasets following radiation dose reduction, iterative reconstruction and deep learning reconstruction.

Methods: Zygomaticomaxillary fractures were inflicted on four human cadaver specimen and scanned with standard and low dose CT protocols. Datasets were reconstructed using varying strengths of iterative reconstruction and the subsequently applying the PixelShine^{TM} deep learning algorithm as post processing. Individual small and non-dislocated fractures were selected for the data analysis. After attenuating the osseous anatomy of interest, registration was performed to superimpose the datasets and subsequently to measure by structural image quality. Changes to the fracture characteristics were measured by comparing each fracture to the mirrored contralateral anatomy.

Results: Twelve fracture locations were included in the data analysis. The most structural image quality changes occurred with radiation dose reduction (0.980036 ± 0.011904), whilst the effects of iterative reconstruction strength (0.995399 ± 0.001059) and the deep learning algorithm (0.999996 ± 0.000002) were small. Radiation dose reduction and iterative reconstruction strength tended to affect the fracture characteristics. Both the structural image quality and fracture characteristics were not affected by the use of the deep learning algorithm.

Conclusion: Evidence is provided for the feasibility of using the structural similarity index metric for the analysis of structural image quality and fracture characteristics.

Introduction

Computed Tomography (CT) is the routine imaging method of choice for the diagnosis of midfacial fractures in emergency department patients [1]. Unfortunately, obtaining a good quality image involves a substantial radiation dose [1,2]. However, iterative reconstruction (IR) and deep learning algorithms have been proposed to maintain image quality on reducing the radiation dose [1,3].

The IR algorithm was developed to improve the image quality of reconstructed datasets by producing image data that accurately corresponds to the measured projection data [4]. The most recent full model-based IR algorithm involves both backward and forward projection. This complex algorithm uses the difference between an estimation of the raw data and the real measured data from the imaging system to reduce the image noise in successive iterations [5].

Recently, deep learning processing was proposed as a completely new strategy to optimize the image quality of reconstructed CT datasets. The proprietary PixelShine™ (PS) algorithm is a software technology based on a deep, artificial neural network (AlgoMedica Inc., Sunnyvale, California, United States). The artificial neural network is trained at pixel level and learns the relationship between baseline and low dose datasets to determine a function that improves the image quality of the dataset.

In a previous study by our research group, we found that both the advanced modeled IR and the PS algorithm substantially improve the noise related image quality of CT protocols for maxillofacial trauma [3]. Although outcomes such as the signal-to-noise and contrast-to-noise ratio quantify image noise, they are not directly related to how the fracture visualization is affected. The same is true for other more complex metrics such as noise power spectrum (NPS), noise equivalent quanta (NEQ), the modulation transfer function (MTF) and detective quantum efficiency (DQE) which are related more to the image formation process of the system [6]. Thus, human observer studies were designed to perform a specific task or to quantify the image quality using a confidence rating scale. However, human observer studies are prone to the natural limitations of perception and observer predictions bias. Therefore, the Structural Similarity Index Metric (SSIM) was developed for the assessment of image quality [7,8].

SSIM measures the similarity between two images. It is based on luminance differences, contrast differences and structural variations and ranges from minus one (opposite contrast) to zero (completely different) to one (completely identical) [6]. Later, a multi-scale structural similarity approach (MS-SSIM) was proposed for the assessment of radiological images. It simulates different spatial resolutions by iterative downsampling and weighting the different values of each component [9]. The aim of our study was to assess the feasibility of this metric to measure the structural image quality and fracture characteristics of midfacial fractures. These measures were assessed with reduced scan radiation dose protocols, and iterative reconstruction and deep learning reconstruction algorithms were used for image quality optimization.

Material and Methods

Human cadaver specimen

A selection of four fresh frozen human cadaver specimens were obtained from the anatomy section of the Department of Neurosciences of the University Medical Center Groningen (University of Groningen, Groningen, the Netherlands), in accordance with our institute's regulations. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Artificial infliction of fractures

Unilateral zygomaticomaxillary fractures were inflicted on each specimen using an experimental design whereby a free-falling mass was used to simulate a blunt facial trauma. In this experiment, the biomechanical tolerance of the zygomaticomaxillary complex to small and non-dislocated fractures was studied. More details regarding this experimental approach were described previously by our research group [10].

Computer Tomography imaging

The specimens were scanned using a third generation Siemens SOMATOM Force Computed Tomography (CT) scanner (Siemens Healthcare AG, Erlangen, Germany). Each specimen was scanned using both a standard maxillofacial trauma protocol (ref mAs 50) and a reduced radiation dose reduced protocol where the reference mAs was reduced to the lowest limit (ref mAs 20). The raw data of both protocols were reconstructed using a model-based iterative reconstruction algorithm with strengths of one, three and five, the latter being the highest strength possible (ADMIRE, Siemens Healthcare AG, Erlangen, Germany) and the Hr59d bone kernel.

Subsequently, all the datasets were subjected to the deep learning PS algorithm (v.1.2.57) to improve the image quality further. The datasets were all exported according to the Digital Imaging and Communications in Medicine (DICOM) standard. The acquisition and reconstruction parameters are summarized in Table 1.

Table 1 : Siemens SOMATOM Force CT acquisition and reconstruction parameters

Tube voltage	80 kV
Tube current modulation	CARE Dose4D
Quality reference mAs	50 & 20
ADMIRE Strength	1, 3 & 5
Field of view	220.0 mm
Collimation	192 x 0,6 mm
Average scan length	118 mm
Slice thickness	0.6 mm
Position increment	0.4 mm
Grayscale depth	12 bit
Pitch	0.6
Rotation time	0.5 s
Exposure time	0.5 s
Scan time	3,4 s
Matrix	512 x 512
Reconstruction kernels	Bone Hr59d
Post-processing	PixelShine^{TM} deep learning processing (v.1.2.57)

CT Computed Tomography, ADMIRE Advanced Modelled Iterative Reconstruction.

Nondisplaced fracture selection

The datasets were assessed by an experienced independent European certified head and neck radiologist (BD) to identify fractures suitable for analysis, with particular attention being paid to minimal and non-dislocated fractures. The standard maxillofacial trauma datasets (ref. mAs 50) were assessed on a medical diagnostic display.

Osseous anatomy attenuation

All the datasets were imported into a Python software application for data analysis (Python Software Foundation. Python Language Reference, version 3.6.1. Available on http://www.python.org). A Hounsfield unit (HU) based sigmoidal soft thresholding function was applied so that only the osseous anatomy of all the datasets was the point of focus, using the following equation:

$$[1 - \exp\left(\frac{HU - 1200}{200}\right)]^{-1} \quad \textbf{(I)}$$

After attenuation, the effects of radiation dose reduction, IR strength and the use of the PS algorithms on fracture visibility were assessed in two experiments (Figure 1).

Structural image quality measurements (I)

In the first experiment, the MS-SSIM was used to assess the effects of radiation dose reduction, IR strength and the use of the PS algorithm on structural image quality. An area of interest was isolated, consisting of a 128^3 pixel cube, using the fracture as the centre. The MS-SSIM was calculated to compare the corresponding areas of interest of the varying radiation dose protocols (ref. mAs 50 & 20), AMDIRE strengths (1,3 & 5) and after applying the PS algorithm (no & yes).

Assessment of fracture characteristics (II)

In the second experiment, the MS-SSIM was used to measure the differences in fracture characteristics by comparing each fracture location with its contralateral anatomy. Using the fracture locations as the centre, a spherical area of interest was isolated using an 8-pixel radius. Accordingly, the uninjured side of the midface was computationally mirrored and superimposed on the side where a fracture had been inflicted. As we only wanted to measure the differences imposed by the inflicted fracture, registration was used to undo misalignment due to anatomical asymmetry and imperfect positioning of the specimens within the gantry during data acquisition. First, solid registration aligned the fracture and uninjured side orthogonally, initialized with manual estimations of the registration angles and offsets. Secondly, elastic registration corrected for misalignments due to global mismatching, solid registration and anatomical asymmetry between the fractured and uninjured sides [11]. The MS-SSIM was calculated and compared for each combination of datasets where the radiation dose, IR strength and PS algorithm had been adjusted. The experiments are summarized in Figure 1.

Statistical analysis

The data were analysed with the Statistical Package for the Social Sciences (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). The MS-SSIM outcomes were presented as means and standard deviations. The normality was tested with Q-Q plots and the Kolmogorov-Smirnov test.

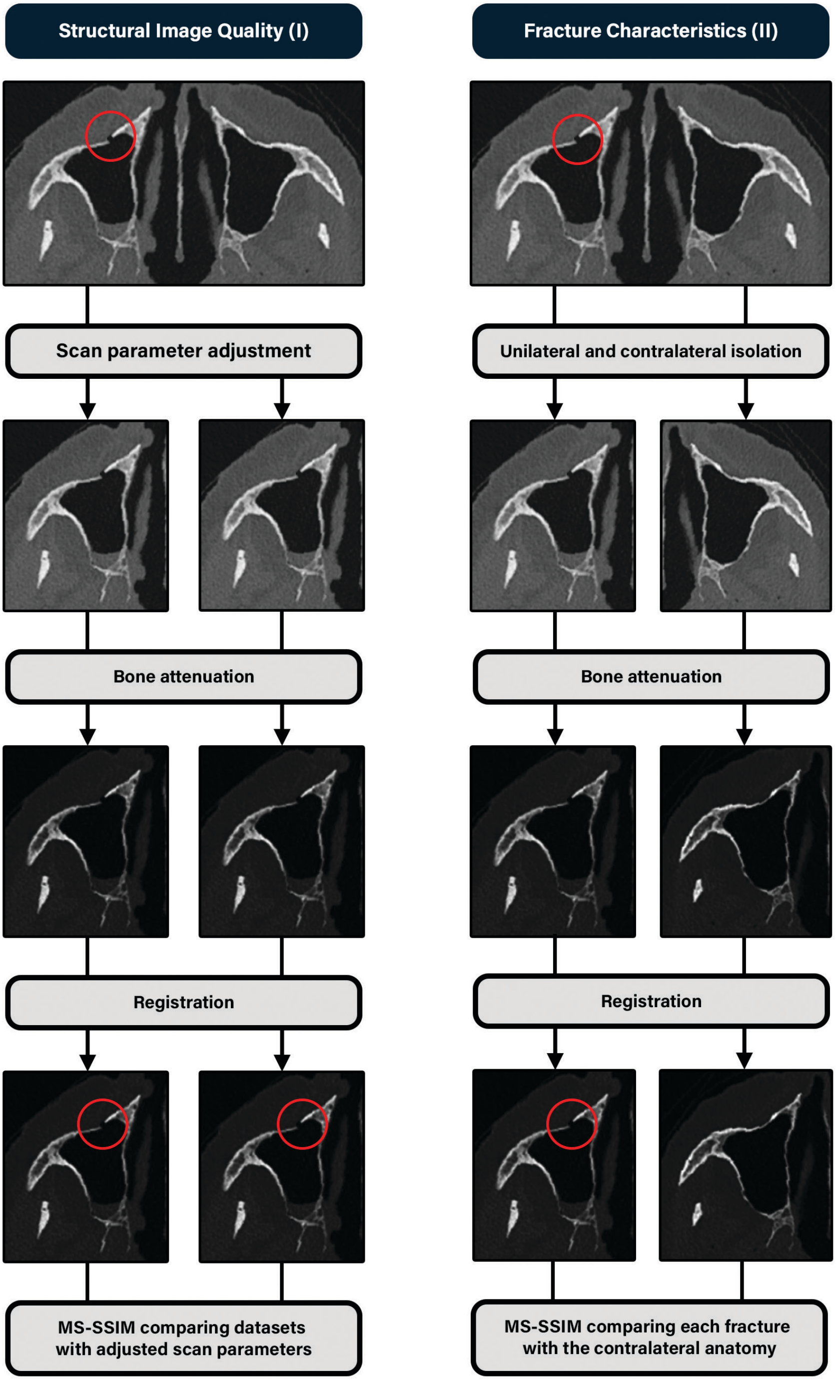

Figure 1: Study workflow for Multiscale structural similarity (MS-SSIM) index measurements (the fracture example is an exaggerated example).

Results

Fractures

Zygomaticomaxillary fractures were successfully inflicted on all four cadavers from which a total of twelve individual fracture locations were selected as eligible for data analysis. The fracture locations included the anterior maxillary sinus (n=6), posterior maxillary sinus (n=3), lateral orbital wall (n=4), and zygomatic arch (n=1).

Structural image quality measurements

The MS-SSIM outcomes are presented in Table 2 and Figure 2. The greatest decrease in structural image quality was found for radiation dose reduction (0.980036 ± 0.011904). Regarding the IR algorithm, a decrease in structural image quality occurred with an increase in strength, whereas the highest effect was found for the 1 to 5 ADMIRE strengths (0.995399 ± 0.001059). The effects of the PS algorithm were minimal because the MS-SSIM outcomes were almost identical to one (0.999996 ± 0.000002).

Table 2: MS-SSIM for structural image quality outcomes

Parameter	Reference	Comparison	MS SSIM (mean ± SD)
Radiation dose protocol [1]	Ref. mAs 50	Ref. mAs 20	0.980036 ± 0.011904
ADMIRE strength [2]	1	3	0.999249 ± 0.000170
	1	5	0.995399 ± 0.001059
	3	5	0.998303 ± 0.000401
PS use [3]	No	Yes	0.999996 ± 0.000002

Abbreviations: MS-SSIM: Multi Scale Structural Similarity Index Metric; SD: Standard Deviation; Ref. mAs: Milliampere-seconds Reference; ADMIRE Advanced Modeled Iterative Reconstruction; PS: PixelShine.

1. Only the ref. mAs 50 radiation dose was adjusted to ref. mAs 20 and the ADMIRE was kept at strength 1 and PixelShine was not used.
2. Only the ADMIRE strength was adjusted from 1 to 3 and 5 and the radiation dose was kept at ref. mAs 50 and PixelShine was not used.
3. Only the PixelShine was used and the radiation dose was kept at ref. mAs 50 and the ADMIRE strength was kept at 1.

Fracture characteristics analysis

The MS-SSIM outcomes are presented in Table 3 and Figure 2. The MS-SSIM outcomes of all the datasets were below 0.90. Regarding radiation dose reduction and the IR algorithm, the MS-SSIM tended to increase, indicating higher structural similarity when comparing the fractured side to the contralateral non-fractured side. No clear trend was observed after applying the PS algorithm.

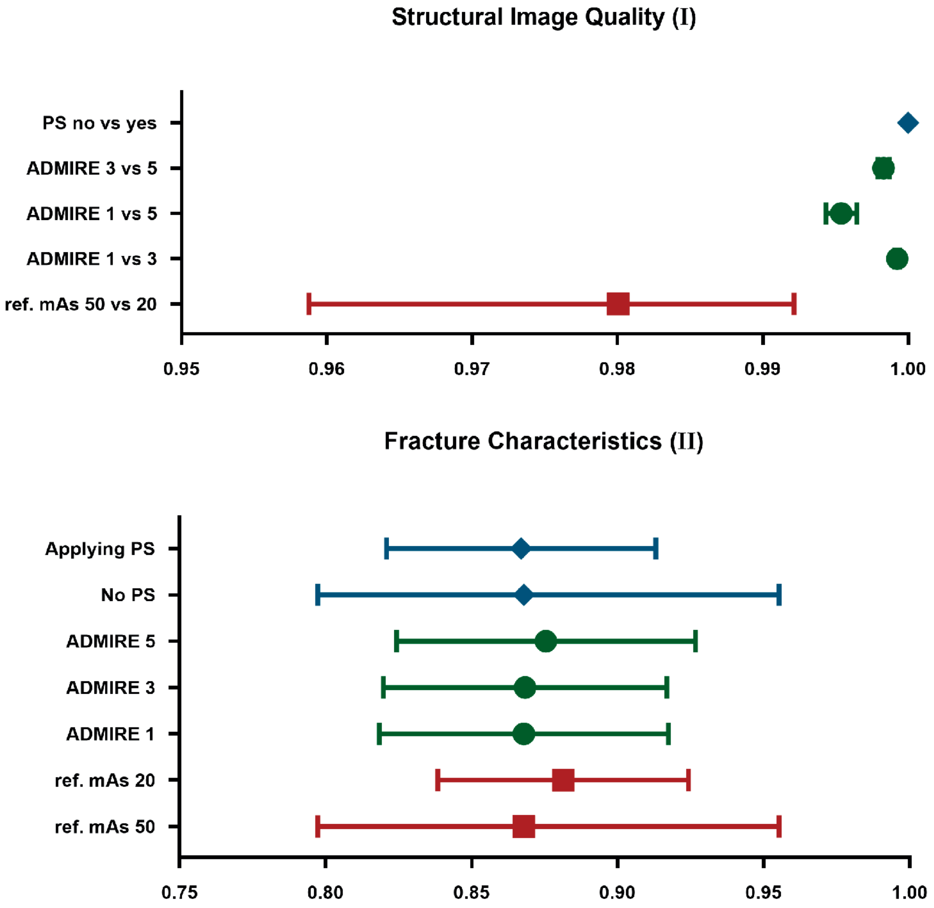

Figure 2: Multiscale structural similarity (MS-SSIM) index means and ranges for structural image quality (I) and fracture characteristics (II) analysis following radiation dose reduction (ref. mAs 50 and ref. mAs 20), Advanced Modeled Iterative Reconstruction strengths 1, 3 and 5 (ADMIRE) and PixelShine deep learning processing (no, yes).

Table 3: MS-SSIM fracture characteristics outcomes

Radiation dose	ADMIRE strength	PS used	MS SSIM (mean ± SD) [1]
Ref. mAs 50	1	No	0.878369 ± 0.043958
Ref. mAs 20	1	No	0.881375 ± 0.042911
Ref. mAs 50	3	No	0.874766 ± 0.047197
Ref. mAs 20	3	No	0.884703 ± 0.046482
Ref. mAs 50	5	No	0.879656 ± 0.037421
Ref. mAs 20	5	No	0.880935 ± 0.037421
Ref. mAs 50	1	Yes	0.866955 ± 0.046103
Ref. mAs 20	1	Yes	0.867904 ± 0.049528
Ref. mAs 50	3	Yes	0.876707 ± 0.046604
Ref. mAs 20	3	Yes	0.868314 ± 0.048533
Ref. mAs 50	5	Yes	0.874656 ± 0.048757
Ref. mAs 20	5	Yes	0.875457 ± 0.051219

Abbreviations: MS-SSIM: Multi Scale Structural Similarity Index Metric; ADMIRE: Advanced Modeled Iterative Reconstruction; PS: PixelShine; SD: Standard Deviation; Ref. mAs: Milliampere-seconds Reference.

[1] The reference category involved the ref. mAs 50 protocol, IR strength 1 and not using the PS algorithm.

Discussion

The concept of structural similarity measurements is based on the assumption that the human visual system is highly adapted to extracting structural information from the scene whereas a measure of structural similarity can provide a good approximation of the perceived image quality [9]. In this study the MS-SSIM was used to study structural image quality and changes to midfacial fracture characteristics. Scan protocols with reduced radiation doses were assessed and the IR and PS algorithms were used to improve the image quality of the outcome measures related to structural similarity. We found that the structural image quality worsened with radiation dose reduction, while the effects of IR and PS were small. Especially the MS-SSIM of the PS algorithm was observed to be exceptionally close to one, indicating a nearly identical structural image compared to datasets where the PS had not been applied.

This result is in line with the fracture characteristics analysis where no clear trend was observed on applying the PS algorithm (Figure 2). This indicates that the PS algorithm denoises the dataset without affecting the fracture characteristics. Radiation dose reduction and IR strength tend to increase the MS-SSIM, indicating a greater similarity between the fracture and the non-fracture side. Although the effects were small, an MS-SSIM tendency towards 'one' indicates a potential smoothing or erasing of the individual fractures. Despite the above results, we found that the MS-SSIM for fracture characteristics' analysis was lower than 0.90 for all the datasets, which might have been caused by the anatomical variance of the contralateral non-fractured side. Even though the variance was reduced to a minimum with solid and elastic registration, the differences in internal bony architecture could have also led to structural dissimilarities. One could consider unilateral analysis of the fracture side before and after inflicting the fracture. However, repositioning the specimen in the gantry can also lead to dissimilarities due to a variance in orthogonal resolution. The results of this feasibility study can be used for the conceptualization of future research to explore the effects of these scan parameters further on structural image quality and changes to fracture characteristics.

In conclusion, this feasibility human cadaver study of a structural similarity analysis of midfacial fractures provides an assessment method for structural image quality and fracture characteristics using the multi-scale structural similarity index metric. Structural image quality tends to be affected the most by radiation dose reduction, whereas the effects of IR and PS tend to be small. Fracture characteristic analyses was confined due to anatomical variances, but the data indicate that reducing the radiation dose and increasing the IR strength negatively affects the MS-SSIM, while the PS algorithm does not tend to affect this measure.

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10

CHAPTER 10

General discussion and future perspectives

General discussion

Maxillofacial injury is frequently presented by trauma patients admitted to the emergency department [1–3]. The injuries range from isolated trauma to the maxillofacial region to a multi-trauma setting where multiple body parts are involved. Thus, each maxillofacial trauma patient admitted to the emergency department should be assessed structurally and systematically to maximize the outcomes and to reduce the risk of undiscovered injuries [4,5]. Early identification of fractures in the maxillofacial region plays a significant role in preventing aesthetic and functional sequelae [6]. As these fractures are known to vary widely in severity, each patient with suspected trauma to the maxillofacial region should receive a full examination to identify whether they require radiological imaging [2,7–10].

The utilization of CT in the emergency department has increased more than threefold in the last few decades [11,12]. Consequently, there is a marked increase in radiation exposure and health care costs among this population of patients [13]. For that reason, there is an increased interest in value-based healthcare regarding radiology with a focus on the unnecessary overutilization of diagnostic imaging and the associated costs [14]. Also, crowding in the emergency department is becoming a major global healthcare issue and there is a great debate on how to optimize the clinical throughput of patients [15,16]. Clinical decision aids have been proposed for emergency department workers to support the justification of radiological imaging or the decision to treat. Although decision making protocols regarding the need for radiological imaging are well established for varying conditions, such as traumatic brain injury and pulmonary embolism, protocols for patients suspected of midfacial or mandibular fractures are lacking [17,18].

The need for these protocols is emphasized by the fact that the majority of patients who sustain trauma to the maxillofacial region do not have fractures. In our systematic review (**Chapter 2**), the prevalence of maxillofacial fractures differs greatly (13.8% to 91.2%) among the patient population. In the REDUCTION-I cohort study (**Chapter 4a**), fracture prevalences of 44.2% and 23.6% were found among the patients who had undergone radiological imaging after being suspected of having a midfacial or mandibular fracture, respectively. Thus, from a theoretical perspective, radiological imaging was redundant in 55.8% of the midfacial trauma patients, and in 76.4% of the mandibular trauma patients. One could even argue that the radiological imaging of patients whose fractures were treated conservatively had been conducted redundantly, as it did not change the management of the treatment. Reflecting on our REDUCTION-II cohort study (**Chapter 4b**), 9.7% and 13.2% of the total patient population were treated actively for midfacial and mandibular fractures, respectively, and it could be stated that radiological imaging was only essential in these situations. However, while our studies focused on the diagnosis of fractures, one should also note that radiological imaging may be required for the assessment of the extraocular muscles and associated soft-tissue injury [19–21]. In other situations, any considerations of scanning the maxillofacial region of patients undergoing CT imaging of the head or cervical spine are based on extending the scan range [22–26]. The need for, and the extent of, radiological imaging has to be re-considered for each individual patient and physical examination findings should be used to identify the high risk fracture patients.

Clinical considerations

Our systematic review and meta-analysis (**Chapter 2**) identified high specificity, but low sensitivity, for most of the physical examination findings related to visual appearance, nasal and ocular assessments, intra-oral assessments, and functional and palpation assessments of midfacial fractures compared to CT scans. These results are in line with our retrospective and prospective cohort studies (**Chapter 3 and 4a**) which suggest that physical examination findings are unlikely to be present if the patients do not have observable fractures. Also, a high positive predictive value (PPV) and positive likelihood ratio (LR+) was found for specific findings such as facial depression, change of globe position, ocular movement limitation, palpable step-off; there is a high likelihood that patients with these findings will have fractures and so radiological imaging should be strongly considered. Although these findings can be particularly useful individually, the question remains how accurately the physical examination findings perform when combined as a clinical decision aid. In our systematic review (**Chapter 2**), clinical decision aids were reported by a total of 8 studies; they appear to be beneficial for predicting the presence of orbital fractures [23,26–28], nasal fractures [29], zygomaticomaxillary complex fracturs [29], or midfacial and mandibular fractures [8,29–31]. However, most of these clinical decision aids were constructed based on retrospective cohort studies and none were successfully validated. Most importantly, none of them were constructed with any midfacial fracture as an outcome. We believe that if patients are strongly suspected of having midfacial fractures or mandibular fractures, radiological imaging should be ordered separately for these anatomical regions. Also, one should realize that physicians are blinded for the outcome of interest when the patient is admitted to the emergency department. Therefore, the full range of potential subtypes of midfacial and mandibular fractures should be carefully considered for each patient during the initial assessment.

In today's emergency department, radiological imaging is easily accessible and therefore easily considered for each patient with maxillofacial trauma. Maxillofacial injury is known for its varying degrees of severity ranging from only soft tissue injury to comminuted fractures with active bleeding requiring immediate airway control [7,32]. Therefore, it is of specific interest how to discern patients without and with midfacial and mandibular fractures and to determine the need for radiological imaging. In this thesis, clinical decision aids were constructed focusing on picking out patients with midfacial and mandibular fractures (**Chapter 4a**) and those that require active treatment (**Chapter 4b**). Regarding picking out patient with fractures, a sensitivity of 89.7% and a specificity of 42.6% for a clinical decision aid constructed based on the presence of any of the following physical examination findings: peri-orbital haematoma, epistaxis, ocular movement limitation, infra-orbital nerve paraesthesia, palpable step-off and tooth mobility or avulsion. The negative predictive value was 83.9% when all of these findings were absent. Although our clinical decision aid picked out the majority of patients correctly, a substantial proportion of patients with orbital, zygomaticomaxillary complex and nasal bone fractures were still missed, indicating the present clinical decision aid was unable to pick out all the patients with midfacial fractures, likely due to the broad range of potential midfacial fracture subtypes. The clinical decision aid for mandibular fractures produced a sensitivity of 98.5% and a specificity of 34.6% for the presence of any of the following physical examination findings: malocclusion, tooth mobility or avulsion and the angular compression test, the axial chin pressure test and the tongue blade test. The NPV was 98.7% when the findings were absent meaning the test could be considered as negative. This clinical decision aid can, potentially, enable the skipping of radiological imaging after a systematic physical examination of a patient suspected of mandibular fractures. Moreover, the clinical decision aid could also direct the diagnosis of specific subtypes of mandibular fractures. For example, symphyseal and parasymphyseal fractures are specifically known to become very painful when applying simultaneous bilateral pressure on the mandibular angle during the angular compression test. Also, fractures of the condylar process are painful when pressure is induced on the chin during the axial chin pressure test.

As far as we know, no previous studies have reported the diagnostic accuracy of these specific tests. In this thesis, sensitivities of 85.0% and 84.7%, and NPVs of 94.7% and 94.9% were found for the angular compression test and the axial chin pressure test, respectively, indicating that these tests can also be useful individually when specific subtypes of mandibular fractures are suspected. The tongue blade bite test produced a sensitivity of 51.7% and a NPV of 90.5%. Although previous studies also reported high NPVs, namely 95.2%, 92% and 100%, the sensitivity rates were substantially higher at 88.5%, 95.0% and 95.7% [33–35]. This thesis extends the limited studies results and evidences that these accurate and easy to perform tests can be used to diagnose each patient suspected of mandibular fractures.

Although our clinical decision aids focus on the diagnosis of maxillofacial fractures, it is also particularly interesting to identify patients requiring active fracture treatment (**Chapter 4b**) because it allows more accurate prioritisation of injuries and one can make a better estimation of whether an oral and maxillofacial surgeon should be consulted in an early stage. Regarding midfacial trauma patients, a clinical decision aid consisting of facial depression, epistaxis, ocular movement limitation, palpable step-off, objective malocclusion, and tooth mobility or avulsion, resulted in a sensitivity of 97.3% and a specificity of 38.6%. A NPV of 99.3% was found when all these findings were absent. Regarding mandibular trauma patients, a sensitivity of 100%, a specificity of 39.1% and a NPV of 100% was found for the following physical examination findings: mouth opening limitations, jaw movement pain, objective malocclusion and tooth mobility or avulsion. Although research focusing on this topic is limited, risk scores were successfully constructed by some for orbital fractures requiring treatment [27,28] but not for all the other midfacial fracture subtypes.

As far as we know, no studies have been published that focus on clinical decision aids for emergency department patients suspected of mandibular fractures that require active treatment. The clinical decision aids provided in this thesis were only built with physical examination findings (**Chapter 4b**). The main advantage of this approach is that these findings can be tested during the initial bedside assessment of a patient, and therefore allows for early decision making at the emergency department.

Each patient suffering midfacial or mandibular trauma should, however, be assessed with specific patient characteristics in mind such as age, sex, comorbidities, mechanism of injury and concomitant injury. Insights into these epidemiological characteristics can be used by emergency department physicians as a priori knowledge to estimate which patients are at risk of midfacial or mandibular fractures. Assault, sports, motor vehicle accidents, and falls are common mechanisms of injury although the order of importance varies between the different studies and regions [36–39]. For example, in our REDUCTION cohort, 33.6% of the patients suffered a maxillofacial injury due to bicycle related accidents (**Chapter 4**). Other studies also state that bicycles are an increasing popular mode of transport [40–42] leading thus to a substantial increase in related accidents [43]. In line with our study, maxillofacial injuries caused by both conventional and electric-bicycle related accidents were commonly observed in other studies. Maxillofacial injury following a conventional bicycle accident was observed in 42.0% of the patients, whereas for electric-bicycles this was 40.3% [42]. We found that the electric-bicycle related accident patients suffered more midfacial fractures and fewer mandibular fractures compared to conventional cyclists. Moreover, a trend was observed that the electric bike accident patients suffered more moderate maxillofacial injuries compared to the conventional cyclists. However, no significant differences were found in maxillofacial trauma severity (**Chapter 5**). Furthermore, logistic regression analysis revealed that bicycle type was not identified as a significant confounder. The above findings suggest that patient related factors, such as age, sex, mechanism of injury and comorbidity, may have more effect on the presence of maxillofacial trauma than bicycle type. For example, previous research speculated that older and untrained patients may have slower reactions and less control over electric-bikes specifically [42]. These patients could benefit from using head protection, especially to reduce craniocerebral injury. Other authors also state that wearing a helmet can reduce maxillofacial injury in up to 40% of the patients [41].

The deduction is that various clinical considerations should be taken into account when assessing patients suspected of midfacial or mandibular fractures. Although clinical decision aids are potentially useful for risk stratification, patient specific characteristics should also be considered when assessing maxillofacial trauma patients.

Radiological advancements

Full three dimensional imaging with CT and CBCT is considered the gold standard for the diagnostic management of maxillofacial trauma [44–49]. Both modalities enable clinicians to visualize the maxillofacial structures using orthogonal planes in a three-dimensional space, including any bone fragments, which is helpful in surgical decision making and post-operative management [48,49]. Nowadays, conventional or plain radiography is generally obsolete due to superimposition and difficulties with patient positioning. CT is preferred for the diagnosis of maxillofacial trauma patients as the geometry allows for the scanning of multiple body parts in a single acquisition, such as traumatic brain injury and cervical spine injury [50–54]. CBCT and panoramic projections using OPG are also popular as diagnostic tools for these patients, especially because of the lower radiation dose [44,55–58]. However, both imaging methods require the patient to sit in natural head position which is mostly not allowed for emergency department patient. Above all, one should consider that radiation exposure is the main disadvantage of all of each these modalities.

As mentioned in the introduction, various strategies can be used to reduce the radiation dose during each individual CT examination such as reducing the tube-current-time product or milliampere-seconds (mAs) [59]. In the studies described in this thesis, the so-called noise index of the automatic exposure control (AEC) was investigated whereby the tube current was modulated automatically based on the patient's anatomy, shape and size (**Chapters 6 to 9**). Reducing the noise index results in a decrease in radiation exposure but there is also an increase in image noise. Consequently, this confines the ability to fulfil the diagnostic task with a CT examination. During each individual examination, the radiation exposure should be reduced in such a way that it does not compromise diagnostic effectiveness. Regarding maxillofacial trauma, the use of low dose CTs might combine the advantages of a CT and conventional radiography, but it is of specific interest to know to what extent low dose CT images are preferred over conventional radiography. In our experimental cadaver study, we found that reducing the CT radiation dose substantially, even by approximately 70%, leads to preferrable results than conventional radiography in the assessment of midfacial fractures (**Chapter 6**). The main advantage of CT is the possibility of post-processing after data acquisition, [48,60–62] which can be beneficial for anatomical analyses, followed by planning and intraoperative strategies for patients undergoing maxillofacial fracture surgery.

One of the major concerns of radiation dose reduction is a decrease in diagnostic performance due to a decrease in image quality. In this thesis, both CT and CBCT dose-reduction protocols were studied and we found that the objective and subjective assessments were consistent among all the maxillofacial scan protocols (**Chapter 7**). Also, the sensitivity and specificity remained constant after radiation dose reduction. Above all, evidence was provided that the image quality of both low dose CT and CBCT protocols was still good enough for clinical decision making. Considering these outcomes, low dose protocols seem to be clinically usable for both the diagnostic workup and the treatment management of maxillofacial trauma patients. The image assessments in this study were conducted by both radiologists and oral and maxillofacial surgeons. From a clinical perspective, both these professions interpret the radiological images for a different purpose. Whereas radiologists focus on the presence and location of maxillofacial fractures, oral and maxillofacial surgeons primarily focus on the clinical consequences of these fractures and then on decision making by specifically assessing the degree of dislocation and/or related complications that can result in unfavourable functional or aesthetic outcomes. Considering displaced fractures, one would expect that radiation dose does not affect the diagnostic management as any disruption in the anatomical landmarks is clearly visualized in these patients' scans. As presented in this thesis, a CT is also used for the assessment of soft tissue structures such as the optical nerve and extra-ocular muscles [21,63,64]. This is of major importance because, for example, extraocular muscle entrapment and retrobulbar fat herniation may require immediate surgical intervention [28,65,66]. This thesis shows that this should be taken into careful consideration as image noise is known to negatively affect the contrast-to-noise ratio significantly of datasets reconstructed from a soft-tissue kernel. A previous study of the optic nerve and inferior rectus muscle also reported a significant decrease in the contrast-to-noise ratio after an 88.7% to 98.6% radiation dose reduction[67]. The authors also found that the use of adaptive statistical iterative reconstruction (ASIR) and model-based iterative reconstruction (MBIR) significantly improved the contrast-to-noise ratio over datasets that were reconstructed using filtered back projection. Another study by the same author group used these iterative reconstruction algorithms to assess the diagnostic image quality of midfacial fractures [68]. They found that iterative reconstruction algorithms substantially reduced the image noise of the ultra-low dose protocols, but the detection rates could not be improved due to smoothing effects. Considering these findings, radiation dose reduction is feasible for maxillofacial trauma protocols but reconstruction algorithms should be considered to improve the loss-of-noise related image quality.

Furthermore, we provide evidence that both iterative reconstruction algorithms and artificial intelligence algorithms are of great value for maintaining image quality after substantial radiation dose reduction (**Chapter 8**). We found that these algorithms significantly improve the signal-to-noise and contrast-to-noise ratio for bone and soft-tissue reconstructed datasets of maxillofacial trauma patients after substantial radiation dose reduction. The introduction of noise is known to especially decrease the image quality of soft-tissue reconstructed datasets which are used to visualize intra-orbital contents [21,69]. The densities, or Hounsfield units, of these tissues are known to be closely related and, therefore, sufficient low contrast detectability is needed to visualize the associated injury. Considering that both algorithms substantially reduce image noise, they seem to be particularly useful for optimizing soft tissue datasets [70]. Nowadays, iterative reconstruction algorithms are available for all CT vendors and are clinically well integrated into the dataset reconstruction workflow [71]. The main advantage of these algorithms is that they reduce noise and artefacts compared to the originally used filtered back projection [70,72]. The algorithms were proposed to maintain the image quality after radiation dose reduction [73]. However, the disadvantages of these algorithms include the long computational requirements and variations in image appearance that is referred to as 'blotchy' or 'pixelated' [72,73] (**Chapter 8**). Today's iterative reconstruction algorithms use a process of backward and forward projection to suppress noises while maintaining the structure of the image [72,74]. These projections are based on smoothness constraints and cannot exploit more complex features of the image [75]. The introduction of artificial intelligence, or deep learning algorithms, has enabled more complex image feature learning that potentially increases the performance of reconstruction methods further [70,75,76]. In this thesis, we found that a deep learning algorithm is able to improve the signal-to-noise and contrast-to-noise ratio substantially after reconstructing the raw dataset using iterative reconstruction algorithms (**Chapter 8**). The algorithms have the potential to produce a high-quality reconstruction from a low dose CT dataset [75,77–79].

Although noise related outcomes quantify the image noise, they are not directly related to the extent to which fracture visualization is affected. Hence, human observer studies were conducted to quantify the image quality using a confidence rating scale. However, human observers are prone to natural limitations of perception and to observer prediction bias so, Structural Similarity Measurements (SSIM) were conducted to assess the structural image quality and the characteristics of midfacial fractures (**Chapter 9**). Our findings suggest that structural similarity is mostly affected by radiation dose reduction while the effects of iterative reconstructions and deep learning algorithms tend to be small. Also, the deep learning algorithm does not seem to affect the fracture characteristics, unlike radiation dose reduction and iterative reconstruction.

Taking the above into consideration, both iterative reconstruction and deep learning algorithms have the potential to provide image noise optimization without negatively affecting the structural image quality and fracture characteristics on a CT. Although iterative reconstruction algorithms are well incorporated in today's data reconstruction workflow, deep learning algorithms are not. Both algorithms' computational requirements meet the clinical needs but the algorithms should be incorporated into a continuous process of data reconstruction on the CT system. Considering the outcomes described in this thesis, both algorithm types can be used to reduce the radiation dose as low as reasonable possible for each individual patient.

Future perspectives

In the last few decades, CT imaging has emerged as the clinical cornerstone for the diagnostic management of trauma patients in the emergency department. The increased utilization has resulted in more radiation exposure among maxillofacial trauma patients. Consequently, future research should focus on how to reduce unnecessary radiological imaging and minimize each individual's radiation exposure through clinical and radiological considerations.

Nowadays, making decisions regarding the diagnostic management of midfacial and mandibular patients is related to a multitude of factors including the physical examination findings, trauma severity, concomitant injuries and mechanism of injury. These factors can vary widely for different patient populations. Although the clinical decision aids presented in this thesis (**Chapter 4**) allow for better risk stratification of the patients, internal and external validation is required in a new population of patients to assess their clinical reproducibility. More importantly, the clinical decision aids (**Chapter 4a and 4b**) should be used to construct a clinical protocol or flowchart to guide the need for radiological imaging for each individual patient that is suspected of midfacial or mandibular fractures. The diagnostic accuracies presented in this thesis (**Chapter 2, 3 and 4**) provide a priori knowledge on how to standardize the physical examination.

Future research should construct a clinical protocol with a score that allows patients to be classified according to 'high', 'intermediate' or 'low' fracture risk and also to classify the need for active treatment. Subsequently, a treatment recommendation can be assigned to each risk group. For example, one could consider 'refrain from radiological imaging' for 'low' risk patients.

Also, regarding the patients classified into the intermediate risk group, one could refrain from radiological imaging during the emergency department visit and reconsider it during an out-patient clinic follow-up. An outpatient low dose CBCT or OPG could be used if radiological imaging is considered necessary. Although physical examination findings were the primary focus, the diagnostic management of each individual patient also depends on various other factors which were not taken into consideration in the studies described in this thesis. As discussed, conventional and electric bike related accidents were a common mechanism of maxillofacial trauma (**Chapter 5**), emphasizing the need to study this population of patients specifically. Future research should also focus on the possible relationship between patient and trauma related factors (e.g., mechanism of injury, age, comorbidity, trauma severity) and the clinical findings, such as the presence of maxillofacial fractures, and the need for fracture treatment.

Exposure to ionizing radiation is an ongoing topic of concern for patients subjected to radiological imaging. CT proved to be the imaging method of choice for the diagnosis of midfacial and mandibular fractures in the majority of patients (**Chapter 4a**). Thus, future research should focus on how to reduce the radiation exposure further for each individual patient. Although iterative reconstruction techniques are clinically well established for all CT vendors, artificial intelligence or deep learning techniques have introduced a completely new chapter to the optimization of the image quality of CT datasets. However, the exact architecture of these techniques is unknown to date and, therefore, future research should focus on the effects of varying image quality measures. The effects of noise related image quality, structural image quality and fracture characteristics were assessed on human cadaver specimens (**Chapter 6 to 9**). Future studies should incorporate both iterative reconstruction algorithms and deep learning algorithms into the clinical scan protocols for maxillofacial trauma to assess how radiation dose can be reduced to as low as reasonably possible. Furthermore, one could assess how these algorithms maintain or even improve the image quality of the clinical protocols.

In conclusion, three dimensional radiological imaging is the cornerstone for the diagnosis of maxillofacial trauma patients in the emergency department once the need for imaging has been clinically established. Both clinical and radiological considerations should be assessed to avoid unnecessary CT exposure or to reduce the radiation dose. From a clinical perspective, a combination of physical examination findings might act as a clinical decision aid to discern either patients at risk of maxillofacial fractures, or patients that require active treatment. Moreover, the most effective way of minimizing the patient's radiation dose is not conducting radiological imaging at all, which should be considered during each examination. Also, this is the most effective method to reduce health care costs and may have a positive effect on crowding in the emergency department. However, if radiological imaging is required, the full potential of the available technological advances should be applied to minimize radiation exposure while maintaining sufficient image quality. Future research should focus on how both the clinical and radiological considerations can be incorporated into the clinical workflow.

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11

CHAPTER 11

Summary

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Summary

Maxillofacial trauma is a frequent cause for presentation at the emergency department. Activities of daily living, sports, assault and traffic related accidents are the leading mechanisms of injury. Maxillofacial trauma is often divided into midfacial and/or mandibular injury. Each of these regions are known for their characteristic and complex anatomy consequently leading to distinctive physical examination findings.

Maxillofacial fractures are known to present in varying degree of severity ranging from non-dislocated fractures to gross comminution in which patients may be at risk for airway compromise via maxillary prolapse, edema, or hemorrhage. Identification of maxillofacial fractures in an early stage of treatment is essential because of the potential functional and/or aesthetic consequences in case of delayed or lack of treatment. Upon entering the emergency department, each trauma patient suspected for midfacial or mandibular fractures should receive a structured and standardized assessment to determine the need of radiological imaging. However, radiological imaging is associated with exposure to ionizing radiation and health care costs. For that reason, it is of specific interest how physical examination findings may lead to an adequate stratification of patients at risk for midfacial or mandibular fractures to reduce unnecessary imaging. The purpose of this thesis is how clinical and radiological considerations avoid unnecessary CT exposure or to reduce the radiation dose.

Chapters 2 to 4 focus on the diagnostic accuracy of physical examination finding for midfacial and mandibular fractures. In **Chapter 2**, a systematic review and meta-analysis was conducted with the aim to assess the diagnostic accuracy of physical examination findings and related known clinical decision aids, in comparison to Computed Tomography (CT) and Cone Beam Computed Tomography (CBCT), for the diagnosis of midfacial fractures. A total of 42 distinct physical examination findings were identified. The meta-analysis revealed a high specificity and low sensitivity for most of the individual physical examination findings related to the visual appearance of the patient, nasal, ocular and intra-oral assessments, and findings related to the functional assessment and palpation of the midface. These results indicate that the absence of any physical examination finding can be used to successfully identify patients who do not have a midfacial fracture, whereas the presence of individual findings does not necessarily mean that patients have a midfacial fracture. Our systematic review identified various clinical decision aids and risk scores based on these physical examination findings, however, none of them focused on the identification of any midfacial fracture as outcome. The risk of bias assessment revealed low or unclear quality of the studies. Furthermore, there were high concerns regarding applicability, and therefore the outcomes should be interpreted with caution.

The goal of **Chapter 3** was to construct a five-year retrospective cohort from all emergency department patients with a midfacial or mandibular trauma. All patients who had undergone CT or panoramic orthopantomographic radiography (OPG) of the head and neck region were identified and the diagnostic accuracy was calculated for 19 and 14 physical examination findings for midfacial and mandibular fractures respectively. Overall, specificity was found to be higher than sensitivity. Regarding midfacial fractures, high specificity was found for raccoon eyes, malar eminence flattening, findings that are related to palpation and the nasal ocular and intra-oral assessment. Malar eminence flattening, external nasal deformity, nasal septum hematoma, change of globe position and palpable step-off had ad high positive predictive value and positive likelihood ratio. Regarding mandibular fractures high specificity was found for mouth opening restriction, auditory canal bleeding, intra-oral assessment related findings, palpable step-off, inferior alveolar nerve paresthesia, the angular compression test and chin axial pressure test. Based on the results of this study, relevant findings were identified for the standardized physical examination of each patient suspected for midfacial or mandibular fractures.

In **Chapter 4**, a prospective multicenter observational cohort study (REDUCTION trial) was conducted of all patients admitted to the participating emergency departments with a midfacial or mandibular trauma. In this cohort, each patient received a standardized physical examination consisting of fifteen and fourteen findings for midfacial and mandibular trauma, respectively. Subsequently, in **Chapter 4a**, a clinical decision aid was constructed aiming on identifying patients with a low fracture risk. For midfacial trauma patients, a sensitivity of 89.7% and a specificity of 42.6% was observed for any of the following findings; peri-orbital haematoma, epistaxis, ocular movement limitation, infra-orbital nerve paraesthesia, palpable step-off and tooth mobility or avulsion. For mandibular trauma patients, the clinical decision aid produced a sensitivity of 98.5% and a specificity of 34.6% for any of the following findings; malocclusion, tooth mobility or avulsion and a positive angular compression test, a positive axial chin pressure test and a positive tongue blade test. **Chapter 4b** focusses on a clinical decision aid to discern patients without and with midfacial and mandibular fractures that require treatment.

For midfacial trauma patients, the clinical decision aid consisted of facial depression, epistaxis, ocular movement limitation, palpable step-off, objective malocclusion, and tooth mobility or avulsion. A sensitivity of 97.3% and a specificity of 38.6% was found if any of above the physical examination was present. For mandibular trauma patients, a sensitivity of 100% and a specificity of 39.1% was found for any of the following findings; mouth opening limitations, jaw movement pain, objective malocclusion and tooth mobility or avulsion. We concluded that the clinical decision aids presented in **Chapter 4a and Chapter 4b** allow for stratification of patients low at risk for fractures, or patients with fractures that require treatment.

Chapter 5 specifically focusses on the epidemiological characteristics of bicycle accidents and the aim was to compare the incidence and severity of maxillofacial fractures of conventional bicycle compared to e-bike related accidents. Midfacial fractures were found more frequently in e-bike accidents whilst mandibular fractures were observed more in conventional bicycle accidents. Based on the Maximum Abbreviated Injury Scale (MAIS) and Facial Injury Severity Scale (FISS), the maxillofacial trauma and fracture severity did not differ between both groups even though fractures in the conventional bicycle group were more severe. Based on logistic regression analysis, bicycle type was not significantly associated with an increased risk of midfacial fractures, mandibular fractures, skull fractures, dental injury and severe maxillofacial fractures. These results indicate that other cyclist characteristics, such as age, alcohol and comorbidities, might play an important role in sustaining maxillofacial fractures, especially severe ones.

Chapters 6 to 10 focus on radiation dose reduction of maxillofacial scan protocols and how iterative reconstruction and deep learning algorithms optimize image quality. An experimental cadaver study was conducted with the aim to assess the effects of CT dose reduction on the preference for CT and conventional radiography (CR) for the diagnosis of zygomaticomaxillary fractures (**Chapter 6)**. In this study, zygomaticomaxillary fractures were inflicted on four human cadaver heads and subsequently scanned with CT and CR. Forced random image comparisons were performed by a total of 54 observers and after 70% radiation dose reduction, CT remained the preferred imaging technique.

In **Chapter 7** we describe another human cadaver study with the aim to assess the diagnostic reliability of low dose Computed Tomography and CBCT for the diagnosis of maxillofacial fractures. Blinded randomized objective and subjective image assessments were conducted by radiologists and oral and maxillofacial surgeons. The objective analysis consisted of location determination of fractures in pre-defined anatomical sites of the zygomaticomaxillary complex. Subjective analysis was conducted to assess the sufficiency of the image quality for the diagnosis of fractures and clinical decision making. The results of this study showed that after substantial radiation dose reduction, the objective and subjective assessments were consistent among all the maxillofacial scan protocols. Also, evidence was provided that the image quality of both low dose CT and CBCT protocols was still good enough for clinical decision making.

In **Chapter 8**, the human cadaver data was studied focusing on quantitatively assessing the image quality of CT after substantial radiation dose reduction. Each of these datasets was reconstructed using advanced modeled iterative reconstruction (IR) and the PixelShine™ (PS) deep learning algorithm. Signal to noise and contrast to noise ratios (SNR and CNR) were calculated for all reconstructed datasets by using the image noise measurements. This study demonstrated that radiation dose reduction, raising the IR strength and the use of the PS algorithm were all significantly associated with SNR and CNR as outcomes. Most important, the decrease of SNR and CNR due to radiation dose reduction was substantially improved using the IR and PS algorithms. These algorithms provide potential for the optimization of clinical CT protocols.

Chapter 9 is a feasibility study focusing on the multi-scale structural similarity index metric (MS-SSIM) with the aim to assess the feasibility of this metric to measure the structural image quality and fracture characteristics of midfacial fractures. Small and non-dislocated fracture sites were selected from the datasets that were reconstructed in **Chapter 6 to 8.** After attenuating the osseous anatomy, registration was performed to superimpose the datasets and subsequently measure the structural image quality. Changes to the fracture characteristics were measured by comparing each fracture to the mirrored contralateral anatomy. The results of this study show that structural image quality tends to be affected the most by radiation dose reduction, whereas the effects of IR and PS tend to be small. For the fracture characteristic analyses, the data indicate that reducing the radiation dose and increasing the IR strength negatively affects the MS-SSIM, while the PS algorithm does not tend to affect this measure.

In the general discussion (**Chapter 10**), the results of the studies described in **Chapters 2 to 10** were discussed in a broader perspective and recommendations for future perspectives are given.

Samenvatting

Trauma van het aangezicht is een veelvoorkomende reden voor het bezoeken van de afdeling spoedeisende hulp van een ziekenhuis. De meest voorkomende oorzaken van aangezichtsletsel zijn de algemene dagelijkse levensverrichtingen, sport, geweld en verkeersongevallen. Letsel van het aangezicht wordt veelal onderverdeeld in letsel van het middengezicht en de onderkaak (mandibula). De anatomie van beide regio's is complexen de aanwezigheid van fracturen leiden veelal tot karakteristieke bevindingen bij het lichamelijk onderzoek. Fracturen van het aangezicht variëren in ernst en lopen uiteen van niet verplaatste fracturen tot comminutieve fracturen. Bij de meervoudige fracturen is er een groter risico op een bedreigde ademweg op basis van zwelling, bloeding of verplaatsing van de maxilla of de mandibula.

Het vroegtijdig identificeren van aangezichtsfracturen is van wezenlijk belang voor het inzetten van de juiste behandeling en het voorkomen van functionele en esthetische klachten op de lange termijn. Elke patiënt die naar de spoedeisende hulp verwezen wordt in verband met trauma van het aangezicht dient derhalve gestructureerd en gestandaardiseerd onderzocht te worden om de noodzaak voor aanvullend radiologisch onderzoek zo goed mogelijk in the schatten. Radiologische beeldvorming gaat echter gepaard met kosten en stralingsbelasting. Het is daarom van belang te weten welke bevindingen van het lichamelijk onderzoek voorspellend zijn voor de aanwezigheid van fracturen om hiermee onnodige stralingsbelasting en kosten van röntgenonderzoek te voorkomen.

Hoofdstuk 2 tot en met 4 richten zich op de voorspellende waarde van het lichamelijk onderzoek voor de aanwezigheid van fracturen van het middengezicht of de mandibula. **Hoofdstuk 2** betreft een systematische review en een meta-analyse gericht op de voorspellende waarde van verschillende bevindingen van het lichamelijk onderzoek en de optelsom hiervan in beslisregels. Specifiek werd gekeken naar de diagnostiek van fracturen van het middengezicht welke werden vastgesteld met behulp van computertomografie (CT) of cone-beam computertomografie (CBCT). In totaal werden 42 onafhankelijke bevindingen van het lichamelijk onderzoek geïdentificeerd. De meta-analyse toonde een hoge specificiteit maar lage sensitiviteit voor bevindingen gerelateerd aan de klinische presentatie van de patiënt, bevindingen van het nasaal, oculair en intra-oraal onderzoek, en bevindingen van het functionele onderzoek en palpatie van het middengezicht.

Deze resultaten impliceren dat de afwezigheid van een middengezichtsfractuur voorspeld kan worden als bovengenoemde bevindingen afwezig (negatief) zijn. Anderzijds betekent dit niet altijd dat er een aangezichtsfractuur aanwezig is als de bevindingen wel aanwezig (positief) zijn. Geen van de gevonden beslisregels richtte zich op de diagnostiek van middengezichtsfracturen alleen. De analyse van de studies liet daarnaast zien dat de kwaliteit veelal laag tot onduidelijk was. Tevens was er sprake van een hoog risico voor de toepasbaarheid van de studies en derhalve dient men terughoudend te zijn met directe interpretatie van de uitkomsten.

Hoofdstuk 3 betreft een retrospectief cohort onderzoek van alle patiënten die de afgelopen vijf jaar met een trauma van het middengezicht of de mandibula werden doorverwezen naar de spoedeisende hulp. Alle patiënten die radiologisch onderzoek ondergingen in de vorm van computertomografie van het hoofd-halsgebied of orthopantomografie (OPG) werden geïdentificeerd en de voorspellende waarde van respectievelijk negentien en veertien bevindingen van het lichamelijk onderzoek voor het middengezicht en de mandibula werden berekend. Voor fracturen van het middengezicht werd een hoge specificiteit gevonden voor de aanwezigheid van een brilhematoom, afvlakking van het aangezicht, palpeerbare fracturen en bevindingen gerelateerd aan het nasaal- en intra-oraal onderzoek. Een hoge positief voorspellende waarde en positieve likelihood ratio werd gevonden voor afvlakking van het aangezicht, scheefstand van de neus, septum hematoom, verandering van de positie van de oogbol en palpeerbare fracturen. Voor mandibula fracturen werd een hoge specificiteit gevonden voor mondopeningsbeperking, bloeding uit de externe gehoorgang, intra-oraal gerelateerde bevindingen, palpeerbare fractuur, paresthesie van de nervus alveolaris inferior, de compressietest en de asdruktest. Op basis van de resultaten van dit onderzoek konden bevindingen worden geselecteerd die relevant zijn voor het standaardiseren van het lichamelijk onderzoek van patiënten die verdacht worden van fracturen van het middengezicht of de mandibula.

Hoofdstuk 4 beschrijft een prospectief multicenter observationeel cohort onderzoek (REDUCTION trial) van alle patiënten die naar de spoedeisende hulp van de deelnemende ziekenhuizen verwezen werden in verband met trauma van het middengezicht of de mandibula. Iedere patiënt onderging een gestandaardiseerd lichamelijk onderzoek van het middengezicht en/of de mandibula. Op basis van deze bevindingen werd in **Hoofdstuk 4a** een beslisregel samengesteld die gericht is op het identificeren van patiënten met een laag risico op de aanwezigheid van een fractuur. Voor fracturen van het middengezicht werd een sensitiviteit van 89.7% en een specificiteit van 42.6% gevonden voor de aanwezigheid van één van de volgende bevindingen: periorbitaal hematoom, neusbloeding, stoornissen van de oogvolgbewegingen, paresthesie van de nervus infra-orbitalis, palpabele fractuur en dentale mobiliteit of avulsie. De beslisregel voor mandibula fracturen produceerde een sensitiviteit van 98.5% en een specificiteit van 34.6% voor de aanwezigheid van één van de volgende bevindingen; malocclusie, dentale mobiliteit of avulsie, een positieve compressietest, een positieve asdruktest of een positieve *tongue blade bite* test. **Hoofdstuk 4b** richt zich op een vergelijkbare beslisregel met als doel onderscheid te maken tussen patiënten die wel of geen actieve behandeling behoeven voor fracturen van het middengezicht of de mandibula. De beslisregel voor fracturen van het middengezicht bestaat uit afvlakking van het aangezicht, neusbloeding, stoornissen van de oogvolgbewegingen, palpabele fractuur, malocclusie en mobiele of geavulseerde gebitselementen. Voor de aanwezigheid van een van deze bevindingen werd een sensitiviteit van 97.3% en een specificiteit van 38.6% gevonden. Voor de beslisregel voor mandibula fracturen werd een sensitiviteit van 100% en een specificiteit van 39.1% gevonden bij één van de volgende bevindingen; mondopeningsbeperking, pijnlijke kaakbewegingen, malocclusie en mobiele of geavulseerde gebitselementen. Op basis van de bevindingen van **Hoofdstuk 4a en 4b** concluderen we dat deze beslisregels succesvol in staat zijn om patiënten te stratificeren voor de aanwezigheid van een fractuur en voor het identificeren van patiënten die actieve behandeling van de fracturen behoeven.

Hoofdstuk 5 richt zich op de epidemiologie van fiets gerelateerde ongevallen met het doel om de incidentie en de ernst van aangezichtsfracturen met een conventionele fiets te vergelijken met die van ongevallen met een e-bike ofwel een elektrische fiets. Bij e-bike gerelateerde ongevallen werden vaker fracturen van het middengezicht gevonden, terwijl mandibula fracturen vaker werden gezien bij ongevallen met een conventionele fiets. Er werd tussen deze twee groepen geen verschil geobserveerd in ernst van het trauma en de fractuur op basis van de *Maximum Abbreviated Injury Scale* (MAIS) en *Facial Injury Severity Scale* (FISS), hoewel de meer ernstige fracturen vaker werden geobserveerd bij ongevallen met een conventionele fiets. De logistische regressie liet zien dat het type fiets niet significant geassocieerd is met het risico op aangezichtsfracturen, mandibula fracturen, schedel fracturen, dentaal letsel en ernstige aangezichtsfracturen. De resultaten impliceren dat specifieke patiëntkenmerken zoals leeftijd, alcoholgebruik en comorbiditeit mogelijk een belangrijker risico vormen voor aangezichtsfracturen, met name voor ernstige aangezichtsfracturen, dan het type fiets dat werd bereden.

Hoofdstuk 6 tot en met 10 richten zich op stralingsreductie van scanprotocollen voor aangezichtstrauma's en hoe iteratieve reconstructie technieken en *deep learning* algoritmes de beeldkwaliteit kunnen optimaliseren. Eerst werd een experimenteel kadaver onderzoek uitgevoerd met als doel de voorkeur van dosisgereduceerde CT protocollen te vergelijken met conventionele röntgen (CR) voor de diagnostiek van zygomafracturen (**Hoofdstuk 6**). In het onderzoek werden zygomafracturen aangebracht bij humane kadaver preparaten die vervolgens met CT en CR werden gescand. Aan 54 beoordelaars werden beelden van de twee modaliteiten voorgelegd waarbij een verplichte keuze gemaakt diende te worden voor het meest bruikbare beeld. Op basis van deze gedwongen vergelijkingen bleek dat zelfs na een stralingsreductie van 70% de voorkeur voor CT behouden bleef ten opzichte van CR.

Hoofdstuk 7 beschrijft een humane kadaver studie met het doel om de diagnostische accuratesse van CT en CBCT te onderzoeken voor de diagnostiek van aangezichtsfracturen. Hierbij werden geblindeerde objectieve en subjectieve beeldvergelijkingen uitgevoerd door radiologen en kaakchirurgen. De objectieve beoordeling bestond uit het bepalen van aanwezigheid van fracturen in vooraf gedefinieerde anatomische locaties van het zygomaticomaxillaire complex. Bij de subjectieve beoordeling werd de vraag gesteld of de gepresenteerde beeldkwaliteit toereikend was voor de diagnostiek van fracturen en de klinische besluitvorming voor het instellen van de behandeling. Zowel de objectieve als subjectieve beoordelingen bleven consistent, zelfs na een maximale stralingsreductie van 70 procent. De CT en CBCT scanprotocollen met lage stralingsdosis bleken tevens toereikend voor de klinische besluitvorming omtrent de behandeling.

In **Hoofdstuk 8** werden de datasets van de humane kadaver studie gebruikt voor een kwantitatieve analyse van de beeldkwaliteit na een substantiële reductie van de stralingsbelasting. Alle datasets werden gereconstrueerd met behulp van *advanced modeled iterative reconstruction* (IR) en het *PixelShine*^{TM} *(PS) deep learning* algoritme. Eerst werden objectieve metingen, gericht op beeldkwaliteit, uitgevoerd voor alle gereconstrueerde datasets door het meten van de signaal-ruisverhouding en de contrast-ruisverhouding. Het onderzoek laat zien dat stralingsreductie, het gebruik van IR technieken en het toepassen van PS algoritme significant geassocieerd zijn met de ruis gerelateerde beeldkwaliteit. Bovendien was er na stralingsreductie sprake van substantiële verbetering van de signaal-ruisverhouding en contrast-ruisverhouding door het toepassen van beide algoritmes. Het onderzoek liet zien dat deze algoritmes potentieel bieden voor gebruik bij klinische scanprotocollen.

Hoofdstuk 9 betreft een onderzoek naar de uitvoerbaarheid van de *Multi-Scale Structural Similarity Index Metric* (MS-SSIM) voor het meten van de structurele beeldkwaliteit en fractuur karakteristieken van fracturen van het middengezicht. De datasets van **Hoofdstuk 6 tot en met 8** werden gebruikt voor het selecteren van kleine en niet verplaatste fracturen. De structurele beeldkwaliteit werd gemeten door registratie van twee opeenvolgende datasets na het isoleren van de benige anatomie van het middengezicht. De fractuur karakteristieken werden daarentegen gemeten door het vergelijken van iedere individuele fractuur met de gespiegelde contralaterale anatomie. De resultaten lieten zien dat de structurele beeldkwaliteit het meest werd beïnvloed door stralingsreductie terwijl de effecten van IR en PS beperkt waren. De fractuur karakteristieken werden het meest beïnvloed door stralingsreductie en toepassen van IR terwijl de effecten van het PS algoritme minimaal tot geen effect hadden.

Hoofdstuk 10 omvat de discussie van het proefschrift waarbij de resultaten van de onderzoeken zoals deze beschreven werden in **Hoofdstukken 2 tot en met 10** worden bediscussieerd in breder perspectief. Tevens worden aanbevelingen gedaan voor toekomstig onderzoek.

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CHAPTER 12

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Dankwoord

Wat vijf jaar geleden begon als een onschuldige afstudeerscriptie eindigde in dit proefschrift. Het werd een reis waarbij ik de kans kreeg mij coassistentschappen te combineren met wetenschappelijk onderzoek. Daarnaast mocht ik ook nog blijven werken op mijn vertrouwde plek als röntgenlaborant. Al snel werd duidelijk dat het promotieonderzoek een samenwerking werd tussen veel verschillende afdelingen. Ik werd omringd door een gemêleerd gezelschap met collega's van de MKA-chirurgie, spoedeisende hulp, traumachirurgie, radiologie en informatie technologie. Het enthousiasme en de bereidwilligheid was ongekend. Dit proefschrift is een bekroning is op de succesvolle samenwerking tussen deze afdelingen en het doet me goed om de volgende mensen daarvoor te bedanken.

Geachte prof. dr. F.K.L. Spijkervet, hooggeleerde promotor, beste Fred, U gaf mij als promotor, hoogleraar en afdelingshoofd de kans het proefschrift te schrijven binnen de afdeling MKA-chirurgie van het UMCG. Door uw verschillende functies heeft u een essentiële rol gehad in het waarborgen van de continuïteit van de verschillende onderzoeken. Met name uw holistische visie op het proces van wetenschappelijk onderzoek heb ik enorm gewaardeerd. Tijdens onze jaargesprekken wisten we vaak verrassend snel en effectief een plan te bedenken om de voortgang van de verschillende onderzoeken te garanderen. Naast de inhoudelijke bijdrage had u ook oog voor mij als persoon. Dit heb ik bijzonder gewaardeerd. Tijdens de coronapandemie organiseerde u bijeenkomsten voor de (thuis)onderzoekers om het wetenschappelijk onderzoek op gang te houden. Ik ben u dankbaar voor het platform dat ik heb gekregen om mezelf te mogen ontwikkelen als promovendus om hiermee een bescheiden bijdrage te leveren aan het onderzoek van de afdeling binnen de traumatologie.

Beste dr. B. van Minnen, zeergeleerde copromotor, beste Baucke, een dankwoord voor je rol als eerste begeleider verdient meer dan bijzondere aandacht. Ik kan me nog als de dag van gisteren herinneren hoe we als bleue studenten MBRT werden uitgenodigd met een ambitieus plan voor het schrijven van een scriptie. Je organiseerde dat we als "niet-UMCG'ers" de hulp kregen van meerdere afdelingen binnen het ziekenhuis. Al snel werd duidelijk dat we op een lijn zaten om de scriptie een vervolg te geven en enkele maanden latere lag er een plan voor een proefschrift waarin onze achtergronden perfect samenvloeiden. Het bleek een gouden greep.

Maar al te vaak besef ik me dat ik dit proefschrift niet had kunnen volbrengen zonder jouw bijdrage. Ik had me geen betere begeleider kunnen wensen. Je hebt een ongekend organisatorisch talent en daardoor wisten we veel verschillende afdelingen aan ons onderzoek te binden. Door je constructieve werkhouding en je oneindige enthousiasme verliet ik elke afspraak weer vol goede moed. Bovendien heb je altijd oog gehad voor mijn persoonlijke situatie, wat voor mij voor erg belangrijk is geweest. Ik heb me daardoor tijdens het promotietraject ook al persoon verder kunnen ontwikkelen. Daarnaast kijk ik uiteraard ook met genoegen terug op de gesprekken over ANPR-camera's, verhoormethoden, hoe onze de telefoon aanslaat op zendmasten, de beste uitspraken van Marcel van de Ven en de belangrijkste lessen uit Kamp Van Koningsbrugge. Baucke, ik kijk terug op een fantastische tijd en ben je ontzettend dankbaar voor de tijd die achter ons ligt. Nu het onderzoek een mooi vervolg krijgt hoop ik dat we onze goede samenwerking verder mogen voortzetten.

Beste dr. ing. M.H.J. Doff, zeergeleerde copromotor, beste Michiel, onze band is niet goed te vatten in woorden. Allereerst als collega en begeleider. Als MKA-chirurg heb je naast je werk in de afgelopen jaren een substantiële bijdrage geleverd aan dit proefschrift. Daarvoor ben ik je enorm dankbaar. Je toewijding bereikte een dusdanig niveau dat je met gevaar voor eigen leven besloot de inclusie van onze studie te stimuleren door moedwillig van je vaders mountainbike te vallen. De gedisloceerde zygomaticomaxillaire fractuur die volgde, bleek van belangrijke meerwaarde voor het behalen van onze steekproefomvang. Daarnaast ben ik je natuurlijk ook dankbaar voor je rol als vriend en broeder. We hebben een bizarre hoeveelheid gezamenlijke interesses; orgelmuziek, oldtimer tractoren, boerennijverheid… ik kan nog wel even doorgaan. Bovenal, we hebben een vriendschap waarvan we weten dat deze gezegend is en nog vele jaren zal voortduren!

Veel dank aan prof. dr. A.J.W.P. Rosenberg, prof. dr. J.C. ter Maaten en prof. dr. J.N. Doornberg. Bedankt dat jullie als leescommissie bereid waren het proefschrift te beoordelen.

Beste drs. P. Onclin, beste paranimf, medepromovendus en vriend, beste Pieter, onze vriendschap kan ik niet goed vangen in woorden maar volgens mij ben ik niet de enige. Hoewel we erg verschillend zijn qua karakter, zitten we absoluut op dezelfde golflengte. Onze gesprekken zijn altijd bizar goed en diepgaand. Ik heb veel steun van je ervaren, ook toen ik minder goed in mijn vel zat. Maar bovenal kunnen we altijd heel hard lachen om elkaars sarcastische humor. Ook voor de toekomst hoop ik nog lang betrokken te zijn bij je plannen op professioneel vlak en jullie prachtige gezin.

Beste drs. J.A.M. Schipper, beste paranimf, medepromovendus en vriend, beste Jan Aart, er zijn weinig collega's voor wie ik zo veel respect heb als voor jou. Toen jij de toevlucht naar Groningen zocht hadden we gelijk een klik; verschillend qua karakter maar altijd goede gesprekken. Ik heb als kamergenoot enorm veel steun van je ervaren; sparren over wat praktische zaken, stoom afblazen over de dagelijkse beslommeringen en gratis relatie advies. Jou vragen als paranimf was dan ook geen moeilijke keuze. Of een aanvullende intra-articulaire injectie van de stromale vasculaire fractie bij het spoelen van het kaakgewricht zorgt voor een langdurige afname van pijn en verbetering van de mondopening weet ik niet, maar ik zal PubMeb nauwlettend in de gaten houden.

Beste dr. M. El Moumni, beste Mostafa, als traumachirurg en epidemioloog leverde je een essentiële bijdrage aan dit proefschrift op klinisch en methodologisch vlak. Ik heb altijd veel waardering gehad voor je oprechte en verfrissend kritische houding. Ik ben je bijzonder dankbaar voor de bijdrage aan de statistische uitwerking van onze klinische studies. Je bent als geen ander in staat om de klinische vraag van het onderzoek te vertalen naar de juiste statistiek. Bovenal heb je de belangrijke eigenschap om onderzoekresultaten zo simpel mogelijk te presenteren. Nog meer waardering heb ik misschien wel voor al onze uitstapjes tijdens onze statistiekuurtjes, met onder andere anekdotes uit de kliniek, de bewerkelijkheid van statische toetsen, de betaalbaarheid van de zorg, maar ook waar het nou echt om draait in het leven. Bedankt daarvoor!

Beste dr. P. van Ooijen, beste Peter, je hebt een belangrijke bijdrage geleverd aan het radiologisch technische hoofdstuk van het proefschrift. Hierdoor kwam mijn werkervaring als radiodiagnostisch laborant mooi samen met de MKA-chirurgie. Als spin in het web bracht je mij in contact met de juiste personen waardoor we het onderzoek konden uitvoeren met een alternatieve technische invalshoek. Veel dank voor je bijdrage en inzet!

Beste drs. H.T. Kruitbosch, je bijdrage als data scientist was onmisbaar. Onze eerste meeting kan ik me nog goed herinneren. Binnen een uur hadden we een mooi plan opgesteld voor een tweetal studies, op basis van onze radiologische datasets van de kadavers. Als programmeur kwam je met verfrissende ideeën over het kwantificeren van de beeldkwaliteit op een alternatieve manier. Je bent enthousiast, gedreven en je beschikt over een enorm doorzettingsvermogen. Dankzij de vele uren die je in het project hebt gestoken heeft de radiologische insteek van het proefschrift echt vorm gekregen. Bedankt daarvoor!

Beste dr. K. Delli, beste Konstantina, je bijdrage voor de systematic review was onmisbaar. Ik heb veel waardering voor je kritische houding en constructieve feedback van het manuscript. Hiermee wisten we de systematic review naar een hoger niveau te tillen. Bedankt voor je bijdrage!

Beste drs. G.T. de Vries, beste Gysbert, onze samenwerking was een schot in de roos. Door jou bijdrage hebben we de REDUCTION studie echt naar een hoger niveau kunnen tillen. Je hebt een enorm organisatorisch talent waarmee je de inclusie van patiënten in het Isala ziekenhuis meer dan soepel hebt laten verlopen. Ik ben je daarvoor bijzonder dankbaar! Je passie voor de spoedeisende geneeskunde is enorm aanstekelijk en het verbaast me dan ook niet dat je bent aangenomen voor een fellowship in je vakgebied! Een hele goede tijd gewenst!

Beste drs. R. Verbeek, beste René, ik kan me je enthousiaste reactie nog goed herinneren toen ik je vroeg of jullie vakgroep mee wilde helpen met includeren. De praktische vragen waren snel geregeld en als onderzoeker kon ik daarom veel zaken loslaten. Ik heb veel waardering voor je proactieve houding waardoor problemen op de werkvloer sneller waren opgelost dan ik had kunnen opmerken. Bedankt daarvoor en ik hoop dat we Nij Smellinghe ook in de toekomst wetenschappelijk op de kaart kunnen zetten!

Beste dr. M.F. Boomsma, beste Martijn, je begeleidde mij met het schrijven van mijn masterscriptie geneeskunde en voor het proefschrift bleek dit later de basis voor een vruchtbare samenwerking met het Isala ziekenhuis. Je hebt een belangrijke bijdrage geleverd om deze scriptie te publiceren en als coauteur ben ik je dankbaar voor je altijd constructieve feedback. Ook toen we later besloten twee studenten MBRT te begeleiden leidde dit tot een goed opgezette retrospectieve studie die we later samen publiceerden. Je bijdrage aan het proefschrift was onmisbaar en daarvoor ben ik je enorm dankbaar.

Beste drs. Y.J. Kleinbergen, beste Jurrijn, als MKA-chirurg in het Isala ziekenhuis speelde je een belangrijke rol bij de totstandkoming van onze klinische studie en later in de uitvoering daarvan. Je had verfrissende ideeën over hoe we de REDUCTION studie het beste konden vormgeven. Ook tijdens de inclusie leverde je een belangrijke bijdrage door de arts-assistenten te enthousiasmeren om nieuwe patiënten aan te melden voor de studie. Mede daardoor werden de meeste patiënten van de studie geïncludeerd in het Isala ziekenhuis. Ik heb veel waardering voor je inzet en aanstekelijke enthousiasme. Ik kijk uit naar samenwerking voor een vervolgstudie!

Beste dr. I.H.F. Reininga, beste Inge, we waren het er snel over eens dat we elkaar op een eerder moment in het promotietraject hadden moeten ontmoeten. Al tijdens onze eerste ontmoeting was je enthousiast en had je meerdere ideeën over de vormgeving van de database van onze klinische studie. Ook je rol vanuit het acute zorgnetwerk gaf ons de gelegenheid om extra gegevens toe te voegen aan de database. Er volgde een vruchtbare samenwerking die leidde tot een artikel over aangezichtsfracturen bij e-bike en fiets-gerelateerde ongevallen. Dank!

Beste drs. P.D. van der Zaag, beste Date, met veel enthousiasme ben je begonnen aan je opleiding tandheelkunde en daarna de opleiding tot MKA-chirurg. Ook heb je een mooie doorstart gemaakt met het huidige onderzoek. Door jouw inzet ligt er momenteel een prachtig manuscript bij het tijdschrift die hopelijk geaccepteerd gaat worden. Ik kijk uit naar alle mooie onderzoeken die in het verschiet liggen en hoop op een vruchtbare samenwerking.

Beste drs. B.W.J. Bens, drs. B. Dorgelo, dr. J. Kraeima, drs. H.P.A.M. Poos, dr. D. Postmus en dr. H.E. Westerlaan. Jullie leverden vanuit jullie eigen vakgebied een belangrijke bijdrage aan de manuscripten van dit proefschrift. Veel dank daarvoor!

Alle specialisten, specialisten in opleiding, arts assistenten en coassistenten van de spoedeisende hulp van het UMCG, Isala ziekenhuis en Nij Smellinghe ziekenhuis; dankzij jullie inzet konden alle patiënten van de REDUCTION studie worden geïncludeerd. De database van patiënten met een aangezichtstrauma heeft de basis gevormd voor een aantal studies en zal ook vaak gebruikt gaan worden voor toekomstig onderzoek. Maar al te vaak heb ik me gerealiseerd dat ik het succes van dit proefschrift aan jullie inzet heb te danken. Bedankt voor jullie enthousiaste en betrokken inzet!

Beste Hester Groenewegen, het doel was duidelijk: samen naar de eindstreep. We hebben vaak gefantaseerd over een groot schuurfeest in ‘It Heitelân’ mei in royale foarried Sûkerbôle en Sonnema om onze promotie eens in stijl af te sluiten. Maar helaas, het coronavirus gooide roet in het eten. Dat soort tegenslagen zijn we natuurlijk de baas, te meer na al die afwijzingen van tijdschriften met de reden dat het artikel “niet voldoende in de scope” paste. Maar… “Frysk bloed tsjoch op! Wol no ris brûze en siede” en we gingen vrolijk door. En Hester, dat is precies hoe ik je heb leren kennen. Je bent een echte doorzetter, een fantastische kamergenoot, altijd in voor een goed gesprek maar ook een kleine pauze met je speciale thee. Bedankt daarvoor!

Beste dr. D.E. Wortmann, ofwel zeer geleerde vrouwe, beste Dagmar, in de afrondende fase van ons proefschrift werden we kamergenoten. We hebben het vaak besproken: eigenlijk zijn we heel verschillend, maar dat nam niet weg dat we altijd bizar goede gesprekken hadden. Beiden zijn we er achter gekomen dat het schrijven van een proefschrift je niet komt aanwaaien. Maar hard werken loont en ik hoop dat ik binnenkort met de doctorstitel in je voetsporen mag treden!

Beste drs. B. Gareb, beste Barzi, onder leiding van Baucke en Nico kregen we de kans het onderzoek van de traumatologie van de MKA-chirurgie naar een hoger niveau te tillen. Ik heb je leren kennen als een begaafd onderzoeker met wie ik altijd goed kon sparren over de inhoudelijke zaken van het onderzoek. Bovendien konden we altijd even stoom afblazen onder het genot van een bak koffie. Nu je in de afrondende fase bent van je proefschrift, de opleiding tot epidemioloog en de opleiding tot MKA-chirurg voorzie ik dat er veel mooi onderzoek van jouw hand gaat volgen. Bedankt voor de mooie tijden!

Beste leden van de Terrabyte-bunker, ook bekend als het kennishok, beste Carina, Caroline, Elise, Joyce, Marijke, Marjo en Pieter, jullie vormden het team waarmee het allemaal begon. Ik had me geen warmer bad kunnen voorstellen. Iedereen hielp op zijn eigen manier om mij in de beginfase op gang te helpen (en mijn enthousiasme over trekkers aan te horen). Daarnaast heb ik veel waardering voor de gezellig tijd. Bedankt voor alles!

Beste mw. Kempers, mw. De Vries, mw. Geurts-Jager, beste Lisa, Angelika en Nienke. Bedankt voor alle praktische ondersteuning en vooral de gezellige tijden op de derde verdieping. Ook kon ik bij jullie altijd terecht om even stoom af te blazen. Bedankt daarvoor!

Beste drs. R.N. Hartman, S. van der Duim, beste Richard en Steven, nog altijd kijk ik positief terug op de tijd dat we in 2013 onze scriptie schreven voor de MBRT-opleiding. Met het behalen van het stipendium en het winnen van de Crux wisten de scriptie echt tot een hoger niveau te tillen. Na het afronden van de opleiding gingen we onze eigen wegen: Richard inmiddels als longarts in opleiding en Steven als radiodiagnostisch laborant in Zwitserland. Bedankt voor de fantastische tijd!

Beste Dr. M. de Groot, beste Martijn, je hebt als docent MBRT een bijzondere rol gespeeld in de keuze om te gaan promoveren. Als onbezonnen studenten stapten we je kamer binnen met nogal wat wilde ideeën over de invulling van onze afstudeerscriptie. Hoewel je collega-docenten ietwat terughoudend waren, was jouw reactie onvergetelijk: "klinkt goed, ga maar wat mensen bellen". Al snel zaten we bij Baucke van Minnen aan tafel wat uiteindelijk leidde tot dit proefschrift. Niet alleen heb je mij enthousiast gemaakt voor wetenschappelijk onderzoek, maar je bent ook een rolmodel voor mij door je positief kritische houding en je doortastendheid. Veel dank daarvoor!

Beste collega's van afdeling radiologie van Nij Smellinghe, tijdens mijn hele opleiding geneeskunde mocht ik jullie blijven ondersteunen als röntgenlaborant. Het was de afwisseling die ik nodig had om me steeds weer te realiseren waarvoor ik dit deed: de patiëntenzorg! Jullie onvoorwaardelijke steun om de opleiding af te ronden heb ik enorm gewaardeerd. Ik ga het werk als laborant enorm missen, maar kijk met veel trots terug op de afdeling en wat daar de afgelopen jaren gepresteerd is. Lenie, bedankt dat je me in de afgelopen jaren faciliteerde om ook mijn onderzoek af te kunnen ronden.

Beste collega's van de afdeling chirurgie van het Martini ziekenhuis, beste chirurgen, chirurgen in opleiding, arts-assistenten, de afrondende fase van dit proefschrift mocht ik combineren met mijn eerste stappen als dokter in de kliniek. De afgelopen maanden waren een bijzonder leerzame, maar bovenal gezellige tijd. Bedankt daarvoor en op naar de komende tijd!

Allerliefste familie. Allereerst heit en mem, jullie hebben me altijd onvoorwaardelijk gesteund in alles wat ik deed. Ik kan altijd bij jullie terecht met al mijn vragen en problemen. Ook hebben jullie me geholpen met alle praktische zaken, waaronder meerdere verhuizingen. Lieve Wout en Hilda (en Teije!), ik had me geen betere broer en schoonzus kunnen wensen. Jullie staan altijd voor me klaar en door alles wat er in de afgelopen jaren gebeurd is zijn we enorm naar elkaar toe gegroeid. Ik heb veel waardering voor de mooie en diepgaande gesprekken die we altijd hadden. Bedankt dat jullie als familie altijd voor me klaar staan!

Lieve Margreet, je kwam in de laatste fase van dit proefschrift in mijn leven. Ik kijk uit naar de vele mooie momenten samen en ben trots dat je onderdeel van mijn leven bent geworden.

About the author

Romke Rozema was born on the 20th of June, 1991, in Dokkum, The Netherlands. He grew up in Damwâld and graduated for his pre-vocational secondary education and senior general secondary education in 2007 and 2009, respectively.

In 2009 he started studying Medical Imaging and Radiation Therapy at the Hanze University of Applied Sciences and graduated with distinction in 2013. Subsequently, he started working as a diagnostic radiographer at the department of radiology of the Nij Smellinghe hospital. In 2015, he applied for the Pre-Master Medicine trajectory at the University of Groningen that was successfully finished and followed by the Master of Medicine program. His master thesis was conducted in collaboration with the department of oral and maxillofacial surgery focussing on the diagnostic accuracy of low dose computed tomography for maxillofacial trauma. After finishing his thesis, he applied for the Junior Scientific Masterclass MD/PhD scholarship, which was awarded in 2017. His PhD thesis focussed on the clinical considerations and radiological advancements of maxillofacial trauma patients under supervision of dr. B. van Minnen and prof. dr. F.K.L. Spijkervet. His junior and senior internships were done at the University Medical Center Groningen and Isala hospital. The final internships were followed at the emergency department of the University Medical Center Groningen and department of surgery at the Martini hospital whereafter he received his Master's degree in 2020. Romke will continue his career working at the department of surgery of the Martini hospital.

Besides his professional career, he is interested in agriculture, mechanical engineering, oldtimer tractors, classical organ music, photography, filming and video editing.

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Printing of this thesis was financially supported by the Wetenschapsfonds Medisch Specialisten Isala (WMI), University Medical Center Groningen (UMCG), The Graduate School of Medical Sciences of the University of Groningen (GSMS), Nij Smellinghe hospital, Nederlandse Vereniging voor Mondziekten, Kaak- en Aangezichtschirurgie (NVMKA), Nederlandse Vereniging voor DentoMaxilloFaciale Radiologie (NVDMFR), Nederlandse Vereniging voor Traumachirurgie (NVT), Koninklijke Nederlandse Maatschappij tot bevordering der Tandheelkunde (KNMT), Nederlandse Wetenschappelijke Vereniging van Tandartsen (NWVT), Straumann Group, KLS Martin Group and Noord Negentig.