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# A finite element analysis on the indication for extracting partially impacted mandibular third molars considering mandibular trauma



Yue Ma<sup>1</sup>, Xin Xu<sup>1,2</sup>, Qingmei Liu<sup>1</sup> and Pengfei Xin<sup>1[\\*](http://orcid.org/0000-0002-1981-7497)</sup>

# **Abstract**

**Background** Patients presenting with partially impacted lower third molars (M3) have a higher likelihood of experiencing angle fractures while simultaneously decreasing the risk of condylar fractures. However, the specific biomechanical mechanism responsible for this occurrence remains unclear. Moreover, there is an ongoing debate regarding whether the removal of M3s might actually increase the risk of condylar fractures. This study aimed to evaluate how the presence of M3s influences mandibular fractures resulting from blows to the symphysis and lateral mandibular body, and to determine the indication for extracting M3s in such cases.

**Methods** Models of the mandible with a partially M3-impacted model (M3I), M3-extracted model (M3E), and M3-absent model (M3A) were generated using a computer. A traumatic blown force of 2000 N was applied to the symphysis and the right body of the mandible. Von Mises and principal stresses were analyzed, and failure indexes were determined. Two cases of mandibular linear fractures were chosen for model verification and interpretation.

**Results** When force was applied to the symphysis, the condylar region exhibited the highest stress levels, while stress in the mandibular angle region was much less regardless of the M3 state. On applying the force to the right mandibular body, stress in the condylar region decreased while stress in the mandibular body increased, especially in the blown regions. Impacted tooth or cavity formation post-M3 extraction led to uneven stress distribution on the blown side of the mandible, increasing the risk of mandibular angle fractures. In cases where M3 was absent or the extraction socket had healed, stress from lateral traumatic blown force was evenly distributed along both the inner and outer oblique lines of the mandible, thereby reducing the risk of mandibular fractures.

**Conclusions** The reduced risk of condylar fractures in patients with partially impacted lower M3s and mandibular angle fractures is mainly due to lateral blows on the mandible, which generate less stress in the condylar region than blows on the mandibular symphysis, rather than being caused by the M3 itself. Extraction of the lower M3 can decrease the risk of mandibular fractures, with a minor influence on condylar fractures.

**Keywords** Angle fracture, Biomechanical simulation, Condylar fracture, Failure indices, Mandibular fracture, Third molars

\*Correspondence: Pengfei Xin lifesaver@alumni.sjtu.edu.cn

<sup>1</sup>Department of Stomatology, Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences, Tongji Shanxi Hospital, Third Hospital of Shanxi Medical University, Taiyuan 030032, China <sup>2</sup>Shanxi Medical University School and Hospital of Stomatology, Taiyuan 030001, China



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# **Background**

Mandibular angle fractures and condyle fractures are among the most common types of mandibular fractures, partly due to the lower bone density and anatomical structures that create vulnerable areas. Clinical studies have indicated that the mandibular third molar (M3) is often situated along angle fracture lines [[1,](#page-9-0) [2](#page-9-1)]. Some researchers have debated whether surgeons should extract impacted M3s in cases of mandibular angle fractures [[3,](#page-9-2) [4\]](#page-9-3). Various clinical studies have suggested that the presence of M3s may increase the incidence of mandibular angle fractures while decreasing the incidence of condylar fractures [\[5](#page-9-4)[–12\]](#page-9-5).

The extraction of M3s is a routine surgical procedure performed by dental surgeons. However, mandibular angle fractures can be rare but serious complications following M3 removal. While iatrogenic mandibular fractures post-M3 removal have been documented in several studies, minimizing this risk is essential [\[13\]](#page-9-6). A thorough understanding of the risks and preventive measures not only plays a crucial role in the M3 extraction procedure but also enhances doctor-patient relationships.

Several finite element models (FEMs) have been utilized to analyze the correlation between mandibular fractures and impacted M3s. For instance, Takada et al. employed micro- computed tomography (CT) and the finite element method to study the relationship between the mandibular angle and M3, highlighting how an impacted M3 alters the stress distribution in the mandibular angle  $[14]$  $[14]$  $[14]$ . Szücs et al. explored the effects of bone removal around an impacted M3 through virtual surgery, noting peak stress at the site of molar removal during contralateral mandibular loading [[15\]](#page-9-8). Additionally, Bezerra et al. examined human mandibles with varying numbers of erupted M3s and concluded that the stress distribution differed based on the presence of M3s in the mandible [\[16](#page-9-9)]. Antic et al. conducted a finite element analysis (FEA) to investigate how the presence and positioning of M3s affect the susceptibility of the mandibular angle and condyle to fractures. The study revealed that in cases of frontal blow, a partially impacted M3 was linked to angle fractures, while the absence of an M3 increased the likelihood of condylar fractures [\[17\]](#page-9-10). Subsequent research conducted by the same authors demonstrated that forces exerted on the mandibular body increased the fragility of the angle, whereas forces directed at the symphysis region heightened the fragility of the condyle, regardless of the presence of an unerupted M3 [\[18](#page-9-11)]. Furthermore, the FEA findings were supported by their clinical investigations, indicating that condylar fractures were significantly influenced by the presence of M3s and the location of the blown force, with only the latter serving as a predictor. Additionally, factors related to the presence of M3s had a more pronounced impact on angle fractures than on condylar fractures [\[19](#page-9-12)]. Kilinc Y et al. evaluated the impact of M3 angulation on mandibular angle fragility, showing that M3 angulation increased the fragility of the mandibular angle [\[20](#page-9-13)]. Liu et al. studied stress distribution in the mandible from blown forces with various M3 orientations, concluding that high blown forces were more likely to cause condylar fractures in the absence of lower M3 [[21\]](#page-10-0). Sancar et al. investigated the stresses caused by trauma to the corpus and angle regions from different blown angles and revealed that the most common area to be fractured was the condyle in trauma to both the corpus and the angle [[22](#page-10-1)].

Fractures in the mandibular angle region can be treated using an intraoral incision for open reduction and internal fixation (ORIF), which minimizes the risks of facial scarring and injury to the facial nerve, thereby resulting in shorter surgical times. In contrast, ORIF for condylar fractures necessitates consideration of these risks, often leading to longer surgical durations. Blows to the symphysis of the mandible can cause unilateral or bilateral condylar fractures, while the presence of partiallyM3 increases the susceptibility of the mandibular angle to fracture. These issues have already been addressed in oral and maxillofacial surgery textbooks.

Meta-analyses indicate that patients with M3 are 2 to 3 times more likely to experience angle fractures while simultaneously reducing the risk of condylar fractures [[23–](#page-10-2)[25\]](#page-10-3). This raises the question: why does the presence of mandibular angle fractures correlate with a decreased risk of condylar fractures in patients with M3? What biomechanical mechanisms underlie this phenomenon? Furthermore, there is ongoing debate regarding the management of condylar fractures, with some researchers arguing against the extraction of lower M3 due to concerns that removing partially impacted M3 may increase the risk of condylar fractures.

To address these questions, this study will evaluate the presence/absence of M3 (before extraction, after extraction, and after complete healing at the extraction site) as an independent variable. The aim was to investigate the biomechanical effects of M3 on mandible fractures resulting from blows to the symphysis and lateral body, and to assess the indication for extracting partially impacted lower M3s.

# **Materials and methods**

#### **Data acquisition**

A three-dimensional (3D) virtual master mandible model was constructed using digital cone-beam computed tomography (CBCT) images from a 30-year-old male patient undergoing orthodontic treatment for impacted lower M3s. Written informed consent was obtained from the patient for the use of his imaging data before been included in the study. The CBCT scan parameters on

the NewTom VGi evo machine were as follows: 400 axial images, axial pitch and thickness of 0.30 mm each, FSV at 110 kV and 4.21 mA, SSV at 110 kV and 2.13 mA, FOV measuring  $15\times12$  cm, exposure time of 3.6 s, and mAs set to 11.41. The original data were then exported and stored in digital imaging and communications in medicine (DICOM) format.

# **FEMs of mandibles**

The data were imported into Mimics Research software (version 21.0, Materialise, Leuven, Belgium) for 3D reconstruction of the mandibular bone and teeth. By adjusting the CBCT grayscale (GV) thresholds and manually editing the masks, the mandibular bone and lower M3 were differentiated. Three different models were built: the partially M3-impacted model (M3I), the M3-extracted model (M3E), and the M3-absent model (M3A). Subsequently, voxel meshes were generated, and material properties were assigned. The GVs were discretized into 10 intervals, each representing a specific material. The elastic modulus (EM) was calculated using the empirical formula [[26,](#page-10-4) [27\]](#page-10-5); as follows:

$$
\rho = 1017 * GV - 13.4 \tag{1}
$$

$$
E = 5925 * \rho - 388.8 \tag{2}
$$

The resulting-colored maps displayed the distribution of the elastic modulus in the mandibular models, which exhibited nonlinear elasticity with an elastic modulus ranging from 2.8 to 30.5 GPa and a Poisson ratio of 0.30. The density and elastic modulus of the finite elements for the mandibular bone and teeth were determined, with dark blue and dark red indicating the lowest and highest values, respectively (Fig. [1A](#page-2-0)).

#### **Boundary and FEA of the models**

The mandibular models, consisting of tetrahedral elements with assigned material properties, were exported from Mimics to Abaqus (version 6.13, Dassault Systèmes-SIMULIA, Vélizy-Villacoublay, France) for further analysis. The superior and posterior part of the bilateral condyles were fixated in all degrees of freedom. Four muscles—masseter  $(8.0 \text{ cm}^2, 376.0 \text{ N})$ , temporalis  $(9.1 \text{ m})$  $\text{cm}^2$ , 427.7 N), lateral pterygoid (0.8  $\text{cm}^2$ , 37.3 N), and medial pterygoid  $(4.4 \text{ cm}^2, 207.6 \text{ N})$  were included in the model, with muscle forces consistent with previous studies [\[26](#page-10-4)]. In this study, the right lower M3 was partially impacted while the left M3 was normally erupted. A traumatic blown force of 2000 N was applied in two positions with a contact area of 1 cm²: the symphysis and the lateral body of the mandible (at the impacted tooth site). The loading, constraints, and muscle support were illustrated graphically (Fig. [1](#page-2-0)B). The von Mises stress, compression and tensile stress were assessed via FEA for each of the three models. This study assessed model failure using the maximum principal stress criterion. Failure is determined when the maximum (or minimum) principal stress surpasses the tensile (or compressive) ultimate strength. The values of tensile strength and compressive

<span id="page-2-0"></span>

**Fig. 1** Graphical representation of the models: (**A**) Density and elastic modulus distributions, and (**B**) Loading, constraints, and muscle support

strength in the osteons direction were 138 MPa and 199.5 MPa, respectively [\[17](#page-9-10)]. The Failure index (FI) is defined as the ratio of principal stress from the finite element model to the material's strength [\[17](#page-9-10)]. This dimensionless coefficient ranges from less than 1 (no failure) to 1 (initiation of failure, like crack formation) to greater than 1 (failure, indicating fracture formation).

#### **Model verification and clinical case interpretation**

The FEA results alongside clinical cases were interpreted. To control for variables, we selected two cases of mandibular linear fractures involving partially impacted lower M3 for model validation and interpretation.

### **Results**

#### **Impact on the condylar area of the mandible**

The von Mises stress contour lines were set at 3000 for visual comparison across the different models (Fig. [2](#page-3-0)). The findings revealed that in the event of a frontal blow, irrespective of the presence of M3s, the areas of high stress concentration in the mandible were primarily situated in the bilateral condylar processes and the neck of the condyle. The stress distribution in the bilateral condylar regions appeared to be symmetrical. Conversely, during a lateral blow, the stress in the condylar region notably decreased compared to that during a frontal

blow, with the maximum stress decreasing by approximately half. Regardless of the presence of an impacted M3, the force-applied side of the condylar process and neck experienced greater stress than does the nonforceapplied side. When comparing the maximum stress values in the condylar region during frontal force, the order from highest to lowest stress was M3I  $(1.334e+04)$  > M3A  $(1.001e+04)$  > M3E (7.905e + 03). Notably, there was no significant difference in stress distribution within the condylar region among the three models, indicating that the presence or absence of M3 minimally affects stress distribution in this region.

# **Impact on the mandibular angle area**

In various force-applied cases, the von Mises stress levels experienced in the mandibular angle area were lower than those experienced in the condylar area. To observe the stress distribution more clearly in the mandibular angle area, von Mises stress contour lines were set at 500. The results demonstrated that during a frontal blow, there was no significant difference in stress magnitude or distribution in the mandibular angle area, for the stress distribution in the mandibular angle area in these three cases was all kept at a relatively large level (Fig. [3](#page-4-0)). The condition of the M3s significantly impacted the distribution of stresses on the mandibular body and angle areas

<span id="page-3-0"></span>

**Fig. 2** Effects of various blows on stress distribution in the mandibular condylar process. Horizontal black arrows indicate frontal blow at the symphysis, oblique black arrows represent lateral blow on the right body of the mandible, with "a" denoting the anterior view of the right condyle and "p" denoting the posterior view of the right condyle

<span id="page-4-0"></span>

Fig. 3 Effects of different blows on stress distribution in the mandibular angle area and along the outer oblique line. Regions of interest, hereinafter, are referring to the regions marked with rectangles or ellipses on the desaturated diagram

in the cases of a lateral blow, for there was a big difference between the three, highlighting the interplay between M3 state and biomechanics.

mandible, thereby providing a certain level of protection to the mandibular angle.

#### **Impact on the M3 region**

The presence or absence of the lower M3 could significantly influence stress distribution in the M3 region following both frontal and lateral blow. While the influence of M3 on the its region might be somewhat masked by the higher stress levels in condylar area during frontal blow, its impact became more pronounced in lateral blow as the overall stress on the mandible decreases (Fig. [4\)](#page-5-0). When the lower M3 was partially impacted, the von Mises stress distribution concentrates in the posterior molar region, resulting in interrupted stress transmission along the inner and outer oblique lines of the mandible. This led to a greater susceptibility to fractures extending from M3 toward the mandibular angle. Following immediate extraction, the extraction socket formed a cavity structure in the mandibular angle area, causing the main stress to shift from the posterior molar region to the socket, making it more prone to fractures extending from the extraction socket towards the mandibular angle. Once the extraction socket was fully healed or when the lower M3 was absent, the cavity structure in the mandibular angle area disappeared, allowing stress to be evenly distributed along the inner and outer oblique lines of the

#### **Evaluation of principal stresses and failure indices**

In the case of a frontal blow, compressive stress was the highest at the point of impact, in the region of the condyle, in the retromolar area, and on the anterior aspect of ramus and coronoid process, bilaterally (Fig. [5\)](#page-6-0). Tensile stress was detected in the angle region, and on the lingual aspect of the symphysis.

In the case of a lateral blow, compressive stresses were the highest at the point of impact, on the ipsilateral angle, on the ipsilateral condylar neck, and on the anteromedial aspect of bilateral condyle. Tensile stress was detected in the retromolar area, and on the lingual side of ipsilateral symphysis.

Failure indices were utilized to assess the probability of fractures occurring in different regions of the mandible. Analysis of principal stress and calculation of FIs suggested that compressive stress was more significant than tensile stress in fracture occurrence (Fig.  $6$ ). In cases of frontal blow, compressive stress was likely to lead to fractures at the symphysis, intracapsular condyle, and mandibular angle including the ascending branch. The order of compressive FIs in the case of frontal blow from highest to lowest stress was M3E (2.453)>M3I (2.252)>M3A (2.004). Conversely, lateral blow might result in fractures in the impacted region, condylar neck, and mandibular

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**Fig. 4** Effects of various blows on stress distribution: Posterior view of the entire mandible regarding frontal blow applied at the symphysis (**A**), lateral blow applied in the mandibular body (**B**), medial view of the lower third molar area regarding frontal blow applied at the symphysis (**C**), and lateral blow applied in the mandibular body (**D**)

angle excluding the ascending branch. The order of compressive FIs in the case of lateral blow from highest to lowest stress was M3I (2.659)>M3E (2.581)>M3A (2.246). The presence of an impacted M3 could disrupt stress distribution, concentrating stress in vulnerable areas like the lower mandibular angle and mental foramen, potentially causing fractures. Following M3 extraction immediately, abnormal stress concentration in the extraction socket and lower posterior mandibular angle increased the risk of fractures. However, once the extraction socket healed or there was no impacted M3, stress distribution became more uniform in the mandible body, reducing the probability of fractures.

# **Model verification and interpretation of clinical cases**

**Case 1** An 18-year-old male sought medical attention after falling and injuring his chin. The CBCT 3D reconstruction (Fig. [7A](#page-8-0)) confirmed fractures at the mandibular symphysis and the neck of the right condyle. The CBCT panoramic reconstruction (Fig. [7B](#page-8-0)) revealed bilateral par-

tially impacted lower M3s, which were similarly classified. Experimental results indicated that when the mandibular symphysis was subjected to blow, both the symphysis and the neck of the condyle experienced greater compressive stress, making them more susceptible to fracture. In this scenario, the impaction status of the lower M3s had a negligible effect on stress in the mandibular angle region, suggesting that the presence of M3 does not reduce the risk of condylar fractures by increasing the likelihood of fractures in the mandibular angle.

**Case 2** A 13-year-old male presented with fractures in the left mandibular angle and the region of the right mental foramen after being struck on the left side of the mandible by a heavy object. The CBCT 3D reconstruction (Fig. [7](#page-8-0)C) confirmed these fractures, while the panoramic reconstruction (Fig. [7D](#page-8-0)) indicated bilateral partially impacted lower M3s with negligible bony resistance in dental crown. According to the experimental calculations, lateral blows to the body of the mandible significantly decreased

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**Fig. 5** Principal stress distribution of tensile stresses in the cases of frontal blow (**A**) and lateral blow (**B**), and compressive stresses in the cases of frontal blow (**C**) and lateral blow (**D**)

stress in the condylar region compared to blows to the symphysis, subsequently lowering the risk of condylar fractures. The ipsilateral mandibular angle region experienced higher compressive stress, while the contralateral mental foramen area exhibited increased tensile stress, making them more prone to fracture. In this context, the impaction status of the lower M3s on the impacted side influenced the stress distribution in the mandibular angle region, contributing to fractures in that area.

Thus, the observed reduction in the risk of condylar fractures among patients with partially impacted lower M3s, who also sustain mandibular angle fractures, is not primarily due to M3 itself causing preferential fractures in the mandibular angle. Instead, it arises mainly because such patients typically endure lateral impacts to the mandible, which inherently produce lower stress in the condylar region compared to impacts directed at the mandibular symphysis.

# **Discussion**

In the past decade, clinical articles have predominantly been retrospective studies involving large samples comprising hundreds of patients with mandibular angle and/ or condylar fractures [\[5](#page-9-4), [8](#page-9-14), [28](#page-10-6)[–33](#page-10-7)]. The results and conclusions drawn from these studies are robust and compelling. However, previous retrospective clinical studies utilizing X-rays or CT images, not FEA studies, have not explored the relationship between the direction or position of the applied force and the fracture site. This deficiency exists due to the challenge of obtaining detailed force-related data, such as direction and position, within the confines of a retrospective designed study. Furthermore, there has been a lack of self-controlled studies examining the same patients before tooth extraction, immediately after extraction (empty socket post-M3 removal), and after complete healing (socket filled with new bone formation and calcification). Our study addresses these gaps by considering how different blown forces may lead to varying fracture sites. We conducted

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**Fig. 6** Failure indices of tensile stresses in the cases of frontal blow (**A**) and lateral blow (**B**), and compressive stresses in the cases of frontal blow (**C**) and lateral blow (**D**)

modeling analyses on the same patient in these three states to minimize confounding variables and strive for results that closely mirror reality.

The Winter classification and the Pell and Gregory classifications are commonly used to predict the complexity of M3 removal procedures [[34\]](#page-10-8). A meta-analysis revealed that Class II B impacted M3s, according to the Pell and Gregory classification, are closely associated with mandibular angle fractures, followed by other classes [\[35](#page-10-9)]. The mechanism by which the M3 increases the risk of mandibular angle fractures remains poorly understood, with hypotheses suggesting that M3 weakens the bone at the angle, acts as a wedge splitting the mandibular angle, or disrupts the external oblique ridge in the case of partially impacted M3 [[8,](#page-9-14) [36](#page-10-10)].

Biomechanical analysis offers insights into these hypotheses by visually demonstrating how M3 affects mandibular angle fractures using FEA methods. Stress

concentration in the mandibular angle region occurs due to sudden changes in bone geometry caused by impacted M3s or empty sockets post-extraction. Similarly, stress concentration in the mandibular condylar region results from changes in bone geometry, such as decreased cross-sectional area in the condylar neck region. These irregularities lead to increased stress intensity in the mandibular angle region, increasing the likelihood of fracture. Additionally, fractures in the mandibular condyle or angle region may also arise from nonuniform density or stress distribution across the mandibular bone. The presence of a partially erupted tooth in the angle region weakens the mandible's strength, potentially explaining the impact of partially impacted M3s on mandibular angle fractures. Our models and results elucidate how the removal of M3s can increase the short-term risk of angle fractures, aligning with clinical observations.

<span id="page-8-0"></span>

**Fig. 7** CBCT images of Case 1 (**A, B**) and Case 2 (**C, D**)

The findings of this study indicate that the presence of lower M3 may increase the likelihood of mandibular angle fractures, while the extraction of incompletely erupted mandibular M3 can decrease the probability of mandibular angle fractures, consistent with previous research [[28,](#page-10-6) [30](#page-10-11), [37](#page-10-12)]. Fractures in the mandibular angle region are influenced by many factors such as the retromolar space, perimeter of the cross-section just proximal to the second molar, breadth of the ramal cross-section, thickness of the oblique ridge, transgonial angle, location of the ipsilateral mental foramen, and occlusal support [[38–](#page-10-13)[42](#page-10-14)]. Moreover, the results suggest that the presence or absence of lower M3 has a minimal impact on condylar fractures, aligning with the conclusions of some scholars who believe that the direction of force application and lack of occlusal support have a far greater influence on condylar fractures than the presence of M3, to the extent that the presence of impacted M3 can be disregarded [\[18](#page-9-11), [19,](#page-9-12) [22,](#page-10-1) [29](#page-10-15), [39,](#page-10-16) [42](#page-10-14), [43](#page-10-17)].

Currently, there is still insufficient evidence to definitively increase the risk of condylar fracture by prophylactic removal of mandibular M3s. Our research findings suggest that extraction of the lower M3s may temporarily increase the risk of mandibular angle fractures, but in the long term, it may reduce the risk of condylar and angle area fractures. The authors of this paper caution against the view that prophylactic removal of mandibular M3 may increase the risk of condylar fractures [[6,](#page-9-15) [44\]](#page-10-18). Clinical practitioners should prioritize evaluating the potential complications of M3s, such as pericoronitis, odontogenic cysts, and their association with diseases related to the mandibular second molars, rather than considering the increased risk of condylar fractures as a primary concern.

# **Limitations**

There are several limitations that may impact our findings. Firstly, the model utilized in this research does not include certain detailed components like the temporomandibular joint disc, dental pulp, and periodontal ligament, potentially impacting the precision of the analyzing outcomes to a certain degree. Secondly, clinical fractures are more complex than computer simulations suggest, with various types of mandibular fractures reported in both the condyle and angle regions according to the AOCMF classification [[45,](#page-10-19) [46\]](#page-10-20). Our study focuses on analyzing one type of impacted M3 model (Class II B based on the Pell and Gregory classification; and the Vertical impaction per Winter classification) and presents specific findings that may not be generalizable to other scenarios.

# **Conclusion**

A direct blow to the symphysis tends to cause condylar fractures, regardless of the status of M3. When the lateral mandibular body is blown, the condyle in the forceapplied site remains the area of highest stress, but the stress on the condylar area is significantly reduced, while the stress on the mandibular body increases. The reduced risk of condylar fractures in patients with partially impacted lower M3s and mandibular angle fractures is mainly due to lateral blows on the mandible, which generate less stress in the condylar region than blows on the mandibular symphysis, rather than being caused by the M3 itself. The interrupted distribution of stress on the mandibular angle area through the partially impacted M3 leads to uneven stress distribution, making it prone to mandibular angle fractures passing through the M3. When M3 is absent or the socket is fully healed, stress can be evenly distributed through the internal and external oblique lines of the mandible. This reduces the risk of mandibular angle fractures when subjected to lateral blow forces. Therefore, the presence of M3 has a limited influence on the risk of condylar fractures and should not be the primary consideration for extraction.

#### **Abbreviations**



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#### **Author contributions**

Y.M. and X.X. is expected to have made substantial contributions to the acquisition, analysis; Q.L. interpreted the data; P.X. have drafted the work or substantively revised it. All authors read and approved the final manuscript.

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#### **Data availability**

The data that support the findings of this study are available from Shanxi Bethune Hospital, but restrictions apply to the availability of these data, which were used under license for the current study and so are not publicly available. The data are, however, available from the authors upon reasonable request and with the permission of Shanxi Bethune Hospital.

#### **Declarations**

#### **Ethics approval and consent to participate**

The ethical standards of the institutional and/or national research committee and the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards were followed in the whole process involving volunteers. Written informed consent was obtained from the patients for the use of their imaging data before been included in the study. The current research was conducted after the approval of the Ethics Committee of Clinical Research in Shanxi Bethune Hospital (SBQLL-2024-119).

#### **Consent for publication**

Not applicable.

#### **Competing interests**

The authors declare no competing interests.

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