Thesis

RISK FACTORS FOR NONUNIONS IN CONSERVATIVELY TREATED CLAVICULAR FRACTURES.

A Retrospective Study at a Level-I Trauma Centre.

submitted by

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Declaration of Academic Integrity

I hereby confirm that the present diploma thesis is the result of my own independent scholarly work. I also confirm that in all cases, where material from the work of others (in books, articles, essays, dissertations, and on the internet) is acknowledged, quotations and paraphrases are clearly indicated. No material other than that cited in the reference list has been used. I have read and understood the Medical University's regulations and procedures concerning plagiarism.

Graz, 09.11.2023 Christina Kummer m.p.

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Zusammenfassung in Deutsch

Titel: Risikofaktoren für Pseudoarthrosen bei konservativ behandelten Claviculafrakturen. Eine Retrospektive Studie an einem Level-I Traumazentrum.

Autoren: Kummer CH, Smolle MA, Seibert F.

Hintergrund: Bis zu 10% aller Frakturen betreffen die Clavicula. Somit sind diese die häufigste Art von Frakturen des Schultergürtels. Behandlungsmöglichkeiten umfassen konservative Behandlung und rekonstruktive Verfahren. Claviculafrakturen werden oft als gutartige Verletzungen mit einer hohen Heilungsrate und hervorragenden funktionellen Ergebnissen beschrieben. Es können jedoch Komplikationen wie Pseudoarthrosen auftreten. Diese verursachen häufig Beschwerden und können zu Instabilität, persistierenden Schmerzen, veränderter Schultermechanik und Kompression von Nerven und Gefäßen führen. Ein Versagen der konservativen Behandlung von Claviculafrakturen ist bei bis zu 15% aller Patient*innen zu verzeichnen. Diese Arbeit soll die Hypothese prüfen, ob Frakturmerkmale und klinisch erhobene patient*innenbezogene Risikofaktoren einen Einfluss auf Knochenheilung haben und die Wahrscheinlichkeit einer Pseudoarthrose anzeigen können, wenn eine Claviculafraktur konservativ behandelt wird.

Methoden: In dieser retrospektiven Studie werden Patient*innen mit konservativ behandelten Claviculafrakturen untersucht. Zu den analysierten Parametern gehören patient*innenspezifische Variablen, Art der konservativen Behandlung, frakturspezifische Charakteristika und radiologische Merkmale zur Zeitpunktbestimmung der knöchernen Konsolidierung. Statistische Methoden werden eingesetzt, um Zusammenhänge mit Pseudoarthrosen nach Claviculafrakturen aufzuzeigen und Risikofaktoren zu bestimmen.

Ergebnisse: Von den untersuchten Risikofaktoren erreichten die P-Werte für Allergien (0.006), Niereninsuffizienz (0.038) und Verkürzung der Fraktur (0.033) statistische Signifikanz. Die logistische Regressionsanalyse zeigte eine deutliche Assoziation zwischen Clavicula-Pseudoarthrosen und zwei unabhängigen Risikofaktoren: Allergie (OR 3.12; 95% CI 1.34-7.28) und Niereninsuffizienz (OR, 3.34; 95% CI, 1.09-10.21).

Conclusio: Von einer hohen Pseudoarthrose-Rate bei geschlossener Frakturbehandlung wurde in der Literatur berichtet. Diese Studie zeigt, dass Allergien und Niereninsuffizienz signifikante prädiktive Risikofaktoren für Clavicula-Pseudoarthrosen sind. Diese Ergebnisse können zu einer verbesserten Risikoevaluierung von Patient*innen beitragen und die Therapieentscheidung von Claviculafrakturen unterstützen. Als Limitationen sind

eine begrenzte Fallzahl für Parameter wie beispielsweise einige Komorbiditäten, Raucher- und Alkohol-Status zu nennen, wodurch die Interpretation der Ergebnisse erschwert ist.

Abstract in English

Title: Risk Factors for Non-Unions in Conservatively Treated Clavicular Fractures. A Retrospective Study at a Level-I Trauma Centre.

Authors: Kummer CH, Smolle MA, Seibert F.

Background: Fractures of the clavicle are accounting for up to 10% of all fractures and are the most common type of fracture of the pectoral girdle. Treatment strategies include conservative management and surgical options. Clavicular fractures are generally considered benign injuries with excellent healing prognosis and decent functional recovery. However, complications such as nonunion may occur. Usually accompanied by symptoms, nonunions can result in impaired shoulder mechanics, persistent pain, instability, and compression lesions of vascular and nerval structures. Failure of conservative treatment of clavicular fractures has been observed to occur in up to 15% of all patients. The objective of the study relies upon testing the hypothesis that fracture characteristics and patient-related risk factors assessable by the clinician at patient presentation are associated with impaired bone healing and allow to estimate the probability of nonunion if clavicular fracture is treated conservatively.

Methods: Patients with conservatively treated clavicular fractures are examined in this retrospective study. The parameters assessed include patient-specific variables, type of conservative treatment, fracture-specific parameters, and radiological features to determine the time span until bony consolidation has taken place. Statistical Methods are used to show association with nonunions after clavicular fracture and to determine risk factors.

Results: Among all investigated risk factors, p-values for allergy (0.006), renal insufficiency (0.038), and initial shortening (0.033) reached statistical significance.

In logistic regression analysis, we found a significant association between clavicular nonunion and two independent risk factors: allergy (OR 3.12; 95% CI 1.34-7.28) and renal insufficiency (OR, 3.34; 95% CI, 1.09-10.21).

Conclusion: A relatively high non-union rate of closed fracture treatment has been reported. This study discovered allergies and renal insufficiency as significant predictors of nonunion. Clinicians may use this information for improved risk assessment and as a support in the decision-making process regarding treatment approaches (conservatively vs. operatively). Limitations of this study include small prevalence and lack of data in some of

the examined parameters, making it difficult to produce statistically significant and reliable results.

Publications

No publications have been issued or released.

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List of Abbreviations

AC-joint	Acromioclavicular joint
AO	Arbeitsgemeinschaft für Osteosynthesefragen
cm	Centimeter
NSAID	Non-steroidal anti-inflammatory Drugs
OTA	Orthopaedic Trauma Association
SC-joint	Sternoclavicular joint

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Introduction

1.1 Study Objective

This study investigates the treatment outcomes of conservatively treated clavicular fractures, focusing on exploring patient-related risk factors and fracture-specific characteristics and their influence on the development of clavicular nonunion.

To evaluate and assess the results, a retrospective study was conducted, analyzing data from 575 followed-up patients.

The objective of the study is to test the hypothesis that fracture characteristics and patient-related risk factors, assessable by the clinician at patient presentation, have a certain effect on bone healing in conservatively treated clavicular fractures.

Furthermore, the aim is to use the results for improved risk assessment, which can be used to evaluate the risk of developing nonunion in individuals with investigated parameters, while considering the specific fracture type. This study findings are expected to contribute to the decision-making process regarding ideal treatment approaches (conservatively vs. operatively) for patients presenting with clavicular fracture.

The first part of this work provides general background on the clavicle, including its anatomy and function, an overview of fractures, mechanisms of injury and treatment strategies. It also offers insight into current knowledge about nonunions, covering their epidemiology, etiology, symptomatology, and therapeutic options.

In the second part of the paper, our own results are presented, critically comparing them with the existing literature.

1.2 The Clavicle – Development, Anatomy, and Purposes

1.2.1 Development

The clavicle is the first bone of the human body to undergo ossification around the 5th week of embryonal development. (1) With the occurrence of a medial and a lateral primary ossification center in the area of the midshaft, the intramembranous ossification process is started. This marks the clavicle unique as in the sense that it is the only long bone that ossifies directly without cartilaginous precursor. (1,2) Around week 6 of gestation the fusion of the two primary ossification centers has taken place, followed by the development of two cartilaginous growth areas situated at the bone´s acromial and sternal end. (1,2) The lengthy growth emerges from the process of endochondral ossification and mainly takes place at the sternal cartilaginous pole (around 80%), whilst only 20% occur at the acromial cartilaginous pole. (2,3) The beginning closure of the epiphysial plates can be radiographically witnessed around the age of 16 years, whereas the complete consolidation occurs around the age of 20 to 26, implying the cessation of ossification. (4)

1.2.2 Anatomy

1.2.2.1 Anatomical Description of the Clavicular Bone

The clavicle appears as an elongated osseous structure with a sigmoidal-shaped configuration. It is known to be an essential element of the pectoral girdle, connecting the manubrium of the sternum to the shoulder blade. (5) It represents the caudal border of the cervical region. Its course is palpable through the skin that is relatively thin above the clavicle. (6) The mean length of the clavicle measures around 16 cm, with gender-specific discrepancies suggesting considerably less arced and shorter collarbones in female individuals. (7)

There are two ends of the clavicle: The sternal extremity shows a roundish cross-section with an articular surface at the medial end aiming towards the manubrium sterni. Together, these bones form the sternoclavicular joint (SC joint). The lateral end is of a broad and flat appearance and is named the acromial extremity. As a part of the acromioclavicular joint (AC joint), this pole also possesses an articular surface enabling joint interaction with the

scapula´s acromion. (8,9) The central section is called the body or corpus. (8) This part is of slender constitution. Especially the area where the lateral meets the middle third is considered the least robust segment of the collarbone. (9,10) In addition, no further stabilizing support is given by attaching ligaments or muscles, wherefore this region is considered the most susceptible one to clavicular fractures. (10,11)

1.2.2.2 Muscle Attachments

Six muscles have their insertions and origins, respectively, on the clavicle. To allow for a better oversight of which muscles are attached to a particular area of the bone, the clavicle can be split up into two separate segments, as follows:

The lateral third section is curved posteriorly in a convex manner, whilst the medial two-thirds are characterized by an anterior convex curvature (12), together leading to the s-shaped formation of the bone.

The lateral third provides a rigid base for the trapezius muscle inserting posteriorly, as well as for the deltoid muscle, originating from the anterior surface.

At the medial two-thirds of the clavicle, the sternocleidomastoid muscle arises superiorly, and the subclavian muscle is attached inferiorly along the eponymous sulcus. Furthermore, at the anterior surface, the pectoralis major muscle originates. At the posterior side, the sternohyoid muscle can be found. (6,12,13)

The knowledge of these muscle attachments is important for understanding how the displacement of clavicular fracture fragments take place via fragments getting pulled in different directions by forces acting through muscular contraction. (6)

In the case of a midshaft clavicular fracture for instance, the medial fragment typically is drawn upwards and posteriorly due to the muscular traction of the musculus sternocleidomastoideus, while the lateral fragment tends to dislocate downwards by the weight of the upper limb. (14)

1.2.2.3 Relation to Other Anatomical Structures

In very close proximity to the clavicle, crucial vascular and nerve structures are situated. Right behind the double-curved bone, major vessels including the subclavian artery (a.) and the subclavian vein (v.), as well as components of the plexus brachialis (PB) are running their course toward the upper extremity, having emerged from the aortic arch and the base of the neck, respectively. (13,15) Deriving from these structures, further surrounding vessels and nerval structures including the axillary artery, the internal jugular vein as well as the supraclavicular nerves can be found. (10)

1.2.3 Purposes of the Clavicle

There are studies suggesting a completely normal functional outcome of the upper extremity without the presence of the clavicle, e.g., after surgical removal. (13,16) However, the clavicle is undoubtedly serving important purposes, playing a key role in the precise, powerful, and variable usage of the upper limb in the three-dimensional space such as grasping with the hand and overhead work. (15) Together with the scapula, the clavicle is forming the shoulder girdle, thus connecting the upper limb to the axial skeleton. (12)

It is the only bony conjunction between the arm and the trunk. By the effect the clavicle exerts on the glenohumeral joint, the arm is lateralized and positioned adequately. In addition, the clavicle enables an increase in the overall range of motion of the shoulder girdle. (12,17) It serves as a solid osseous base for the six muscles attached to it.

Due to its anatomical relations, the clavicle functions as a protecting shield for the PB and the subclavian a. and v. passing underneath its medial two-thirds-segment to reach the axillary region. (13,15)

Finally, the base of the neck is given an aesthetically pleasant line by the collarbone, thus serving a cosmetic purpose. When the clavicle is surgically removed or is missing due to a rare congenital defect like cleidocranial dysplasia, the shoulder girdle appears shortened as the arm gravitates downward, medially, and forward. (15,18) Therefore, a considerable impairment can arise because of fracture, claviculectomy, and length-reduction of the clavicular bone due to fracture and malunion.

1.2.4 Biomechanics – The Interplay of the Shoulder Girdle Components

As mentioned above, the clavicle is involved in the formation of two articulations – the AC-joint and the SC-joint. In the following paragraph, a further elaboration on the anatomical relations, characteristics, and functional principles regarding these joints is presented. The biomechanical aspects of the joint axes are elucidated. A closer look is taken at the interplay of muscular and ligamentous structures and the shoulder girdle.

1.2.4.1 The Acromioclavicular Joint

At its lateral end, the clavicle forms the AC-joint together with the acromion of the scapula. It constitutes to the topographical highest point of the shoulder and is provided with two articulation surfaces covered with fibrous cartilage. Between these two, an intraarticular disc consisting also of fibrocartilage is located. (8,12)

The AC-joint is supported by two ligaments. The acromioclavicular ligament strengthens the superior area of the articular capsule. The second structure, the coracoclavicular ligament, spreads from the coracoid process to the inferior surface of the clavicle. It is composed of two portions, the conoid, and the trapezoid ligament. They offer restriction of the range of motion of the scapula and the clavicle towards and away from each other. (8)

Biomechanical Aspect – Movements at the AC-Joint

Although the AC-joint possesses plane articular surfaces, it functionally acts as a spheric joint. Thus, the motion between the shoulder blade and the clavicle is possible on three axes resulting in a further increase of the shoulder girdle´s range of motion. (8,13,15) As the clavicle is part of two joints, the movements are always combined with those of the SC-joint. (8)

Vertical Axis: This axis is running from the cranial direction through the center of the acromion caudalward. Movement around this axis allows the uplift of the shoulder blade´s medial edge from the thoracic wall and vice versa. Thereby, the range of motion measures up to a maximum of 50 degrees. (15)

Sagittal Axis: The course of the sagittal axis is described as running through the center of the acromion from the ventral to the dorsal side. Along this axis, the shoulder blade changes its position by sliding forward along, the thoracic cage with its inferior angle,

thereby fulfilling an anterior movement. Simultaneously the socket of the glenohumeral joint experiences a twist upwards which is crucial for the elevation of the upper arm. In the sense of a contrary motion, the scapula can be rotated backward towards the spinal column. (15)

Frontal Axis: During the movement of the scapula along the frontal axis, running from lateral to medial, the inferior angle gets lifted off the thoracic cage. (15)

The movements at the AC-Joint are guided by three muscles: The serratus anterior muscle, the major rhomboid muscles major and minor rhomboid muscle, working in an antagonistic manner. (15) The serratus anterior muscle´s lower part plays a role in the process of scapular protraction (i.e. abduction) meaning the scapula glides in an anterior direction along the chest wall. (15,19) The antagonistic movement, termed scapular retraction (i.e. adduction), is performed, amongst others, by the major and minor rhomboid muscles. (19)

1.2.4.2 The Sternoclavicular Joint

The SC-joint is located at the medial site of the clavicle representing the only articular conjunction that connects the entire upper limb to the torso. Like the AC-joint it owns a fibrous articular capsule. It is composed of the sternal extremity serving as the joint head and the manubrial incision of the sternum serving as the socket. (8,12) A fibrocartilaginous articular discus is balancing out the incongruence between the articular surfaces.

The anterior and posterior sternoclavicular ligaments support the capsule ventrally and dorsally, whereas the interclavicular ligament ties together the sternal ends of the left and right clavicle. Additionally, further stability is provided by the costoclavicular ligament. (8)

Biomechanical Aspects – Movements at the SC-Joint

Like the AC-joint the SC-joint functions as a spheric joint, thus enabling motion around three axes. (8,15)

Anterior-posterior Axis: On this axis, two movements are conducted that proceed from the neutral position of the clavicle. First, there is the elevation that is feasible up to approximately 45 degrees. Second, there is the downwards moving of the clavicle, termed

depression, that reaches a range of approximately 5 degrees. The latter motion is mainly inhibited by the first rib. (15)

Vertical Axis: The anterior and posterior translation of the clavicle is accomplished along the vertical axis. Thereby, a protraction up to 15 degrees and retraction up to 15 degrees from the neutral position is possible. Whereas protraction often occurs in combination with the clavicle ascending or descending, retraction is primarily related to an ascending movement of the clavicle. (15)

Rotational Axis: The clavicle can rotate around its longitudinal axis. The rotation occurs in an anticlockwise manner and is thereby combined with an upward motion and retraction of the clavicle. The range of rotation measures up to 50 degrees. (15)

The movements at the SC-joint are also guided by antagonistic working muscle pairs. On the vertical axis, protraction and retraction are carried out by the middle section of the trapezius muscle as well as the upper and middle parts of the serratus anterior muscle. Elevation and rotation of the clavicle around the anterior-posterior and rotational axis respectively, are accomplished by the contractive effects of the upper part of the trapezius muscle and the minor pectoral muscle. (15)

1.3 Clavicular Fractures

1.3.1 Epidemiology

Besides fractures of the distal radius, fingers, and hip, the clavicle belongs to those bones in the human body that frequently sustain a fracture. (20) Thus, fractures of the clavicle have been reported to contribute to 2.6% to 10% of all skeletal injuries. (11,21–23) Further studies have shown even higher proportions occurring among children and in seriously injured patients with 8% - 15% and 10%, respectively. (24,25) Regarding the pectoral girdle, the fractured clavicle is the most common type of shoulder injury with a frequency of 35% to 44%. (21,23,26)

The anatomical distribution of clavicular fractures in the sense of the Allman classification, a system clinically dividing the collarbone into thirds, displays as follows: the midshaft is affected in 65% to 82% representing the most prevalent type of clavicular fractures. For the remaining distribution, the studies estimated that fractures of the lateral third account

for 10% to 29%, whereas medial end injuries have been shown to constitute 2% to 4.5%, thus considered the most uncommon category of the fractured clavicle. (21–23,25,27,28)

The reported incidence of clavicular fractures ranges internationally from 29 to 64 per 100.000 population per year. (21,22,29) However, as recent studies have reported, the annual occurrence of fractured clavicles seems to steadily increase. (22,30,31) From 2001 to 2012, there was an incidence growth from 35 to 59 per 100.000 population, as a study conducted in Sweden has shown. (31) Another epidemiological study revealed a rise of this injury's incidence in Belgium from 56 per 100.000 population in 2006 to 70 per 100.000 population in the year 2015. (30)

As stated above, clavicular fractures are most frequently diagnosed among the younger population. The patient collective accounting for the most clavicular fractures is represented by young men under the age of 30. (22,23,27,29,32,33) In comparison to female individuals, males are approximately two to three times more likely to sustain a fracture of the collarbone. With advancing age, the incidence is declining in both women and men, although the decline is more considerable among the latter group. (22,27,29) Regarding the contribution of fracture incidence, statistics demonstrate the presence of a bimodal pattern; a peak is observed in younger individuals from their first decade onwards, as well as in patients 65 years of age or older. In this respect, females in their seventh decade of life and above are slightly predominantly affected. (22,27,30,32)
Interestingly, a seasonal as well as weekday fluctuation of the incidence has been described as well; most clavicular fractures seem to occur during the months of summer and on weekends, first and foremost on Sundays. (27,28)

1.3.2 Mechanisms of Injury

In the younger and adolescent patient cohorts, the midshaft fracture is the most common type, with displaced fragments. (21–23) Approximately 50% of cases occur during recreational activities. (34,35) Among them, bicycling and team sports that imply intense body contact and aggressive physical play such as American football, rugby as well as soccer, are ranked highest. (27,29,33–36) Also, a fall from horse in equestrianism seems to be a regular cause of clavicular fractures among the female population. (32,34)

Furthermore, clavicular fractures arise during wrestling and snow sports, especially snowboarding and skiing. (33) Non-sports-related injury mechanisms include pre-eminently involvement in traffic accidents, particularly in car and motorcycle crashes. (22,23,25,27,36)

In contrast, fractures of the medial and lateral clavicular segments, generally rather non-displaced, tend to affect first and foremost elderly individuals. (21,22,28) The number one cause of injury seems to be a fall onto the shoulder from a standing position with minimal force. These types of fractures often occur within the frame of domestic accidents and are often linked to osteoporotic bone structure. (22,27,28,32) However, a direct force applied to the shoulder, either caused by high-energy trauma or low-impact falls, remains the topmost provoking factor for clavicular fractures. (22,29,34)

Even though very rare, some other underlying causes and contributing factors in relation to clavicular fractures have been described. These include, for instance, malignant cancerous diseases of the bone, e.g., osteosarcoma and Ewing sarcoma, and other types of cancer like multiple myeloma. In addition, other cancer entities such as renal cell carcinoma, prostate and lung cancer have been noted to metastasize to the collarbone, eventually leading to pathologic fractures. Besides that, osteogenesis imperfecta constitutes an example of an extremely rare congenital cause for clavicular fractures. Preceding radiotherapy also seems to be a promotional reason for spontaneous fractures due to the weakening of the bone matrix. (10)

1.3.3 Classification Systems

1.3.3.1 Allman Classification

The Allman classification was the first established classification system categorizing clavicular fractures into three general groups based on their frequency of occurrence and anatomical location within the bone. According to the Allman classification, the clavicle is divided into three equally sized parts. Although it is the most widely used classification, it offers a general description only, without providing further helpful information regarding the prediction of outcome and choice of treatment. Group I describes the most common fracture type, involving the middle third. Group II corresponds to fractures at the lateral side, whereas Group III equals medial clavicular fractures – the least frequently occurring type. (37,38)

1.3.3.2 Classification of Lateral Clavicular Fractures by Neer

The Neer classification adds three subgroups to lateral fractures of the clavicle. It considers fragment dislocation and the importance of the coracoclavicular ligament for fracture stability. Later, Rockwood introduced a subdivision of type II (IIa and IIb) by paying attention to the significance of the conoid ligament and its condition as either being ruptured or intact. The final modification of Neer's distal clavicle classification system was made by Craig, who added two more types to the system and additionally proposed an overall more detailed categorization, providing further information regarding diagnosis and recommended treatment options. Of note, this classification extension also considers the involvement of the AC-joint. (39,40)

Even more, the modified classification system provides surgeons with additional information regarding fracture stability. Therefore, it is commonly used in the decision-making process to choose the optimal treatment option for patients presenting with clavicular fractures of the distal segment. As shown in Table 1, fracture types II and V according to the Neer classification are described as unstable fracture patterns, particularly due to the loss of ligamentous support. The best choice of treatment for these fractures remains under debate. In contrast, fracture types I and III are categorized as fractures with acceptable stability. Thus, these types may well be treated conservatively. (40)

Table 1 Modified Neer Classification for distal clavicular fractures according to (40,41)

Modified Neer Classification		
Type		**Fracture Stability**
Type I	Fracture lateral to coracoclavicular ligament Conoid and trapezoid ligament intact, undisplaced fracture	stable
Type IIa	Fracture medial to the coracoclavicular ligament Conoid and trapezoid ligament intact, medial clavicle dislocation	unstable
Type IIb	Fracture lateral or between the conoid and trapezoid ligament Conoid ligament ruptured, medial clavicle dislocation	unstable
Type III	fracture lateral to coracoclavicular ligament with intra-articular involvement Conoid and trapezoid ligament intact, minimal dislocation	stable
Type VI	Epiphyseal separation, Conoid and trapezoid ligament intact, dislocation of medial fragment upwards (seen in pediatric population)	stable
Type V	Comminuted fracture, Conoid and trapezoid ligament attached to small inferior fragment, medial clavicle displacement	unstable

1.3.3.3 Classification of Lateral Clavicular Fractures by Jäger and Breitner

Besides the modified Neer classification, the one by Jäger and Breitner is another classification system that categorizes fractures of the distal end of the clavicle. It is more commonly used in European, especially German-speaking countries. (42) Similar to the Neer classification, the focus is on the precise fracture location – i.e., medial or lateral to the coracoclavicular ligaments - as well as the integrity of the ligamentous structures.

Although the Neer and the Jäger-Breitner classifications are very similar to each other, slight differences among the particular fracture patterns do exist:

First, Jäger-Breitner type II equals fracture type IIb of the modified Neer classification. Therefore, type II describes a fracture located between the trapezoid and conoid ligaments and is further divided into type IIa (includes the rupture of the conoid ligament) and type IIb (includes the rupture of the trapezoid ligament). In comparison to fracture type IIa, which has been described as an unstable condition accompanied by remarkable dislocation of the medial fracture fragment, type IIb is regarded as a stable fracture simultaneously occurring with a slight fragment dislocation. (42,43)

Another difference between the classification systems is visible when looking at Jäger-Breitner type III. This type is characterized by a fracture located medially in relation to the coracoclavicular ligament. The trapezoid portion as well as the coracoid portion remain intact. Thus, type III according to the Jäger-Breitner classification is similar to Neer type IIa. (42,43)

1.3.3.4 Classification of Lateral Clavicular Fractures by Cho

Other studies criticized the sparse information provided by the modified Neer classification concerning diagnosis and optimal treatment management for fractures of the distal clavicle. (44,45) These studies implied low inter- as well as intraobserver reliability and suggested the need for another approach to classify these types of fractures. (44,45)

Therefore, a novel classification for distal clavicular fractures was introduced in 2018 by Cho et al. (46). In addition to considering the anatomical location of the fracture, and its relation to the coracoclavicular ligament as well as its integrity, this classification incorporates other features like the degree of fragment displacement and fracture stability. Fractures are divided into two groups: Type I fractures may be located anywhere along the clavicle and display no to minimal fragment dislocation (i.e. $\leq$ 5mm). Type II fractures are

characterized by significant dislocation by > 5mm and are further distinguished into four subtypes (A-D). In type IIA, the fracture is located medial to the fully intact coracoclavicular ligament. Type IIB depicts a fracture localization medial to the coracoclavicular ligament with a ruptured conoid portion. Type IIC equals a fracture lateral to the coracoclavicular ligament and the loss of integrity of both parts of the coracoclavicular ligament. This fracture subgroup is not apprehended by the modified Neer classification. Finally, type IID is a comminuted fracture with the coracoclavicular ligament still attached to an inferior fragment. Fractures of type I are considered stable, whereas type II fractures including all subgroups are unstable.

This classification system of lateral clavicular fracture was reported to hold moderate interobserver and significant intraobserver reliability. (46)

1.3.3.5 Robinson Classification

A further classification for fractures of the clavicle is the Robinson classification, in which not only the lateral area, but the entire clavicle is considered. Regarding the fracture patterns, Robinson divides the clavicle into a medial fifth and a lateral fifth. In between these parts is the diaphyseal region. Moreover, four fracture features are taken into account: displacement of fracture fragments, angulation, involvement of the SC- and AC-joint, respectively, and comminution. (Figure 1-3) (22)

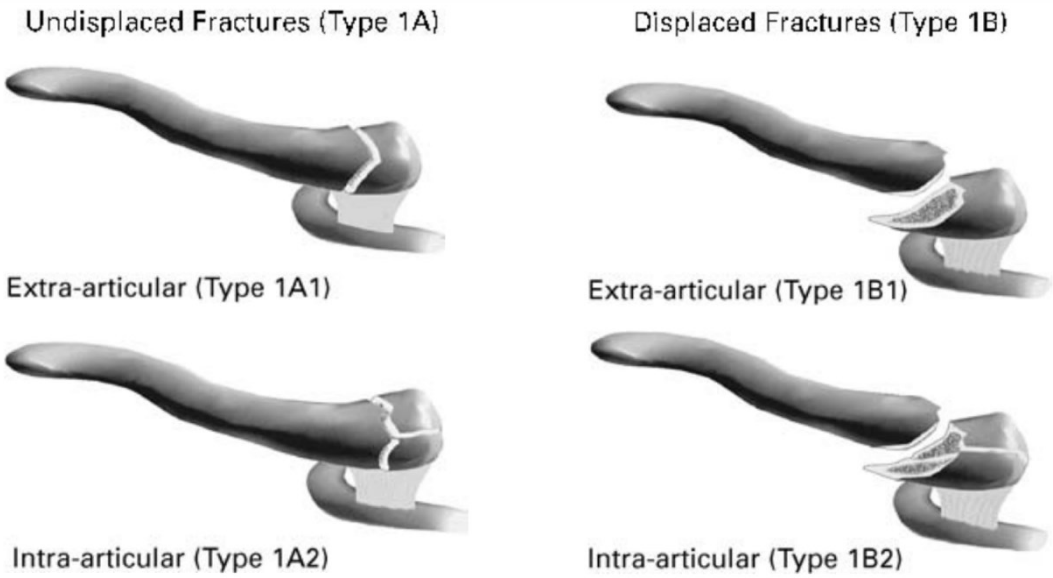

Figure 1: Robinson Classification: Medial clavicular fractures. Robinson CM. Fractures of the clavicle in the adult. J BONE Jt Surg. 1998;80(3).

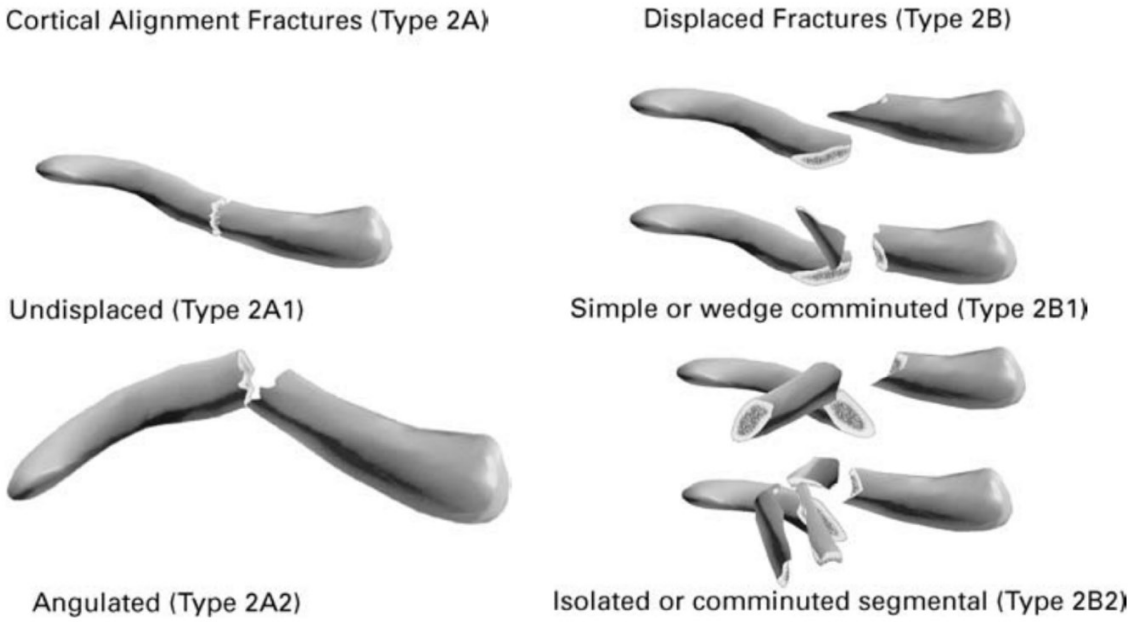

Figure 2: Robinson Classification: Diaphyseal clavicular fractures. Robinson CM. Fractures of the clavicle in the adult. J BONE Jt Surg. 1998;80(3).

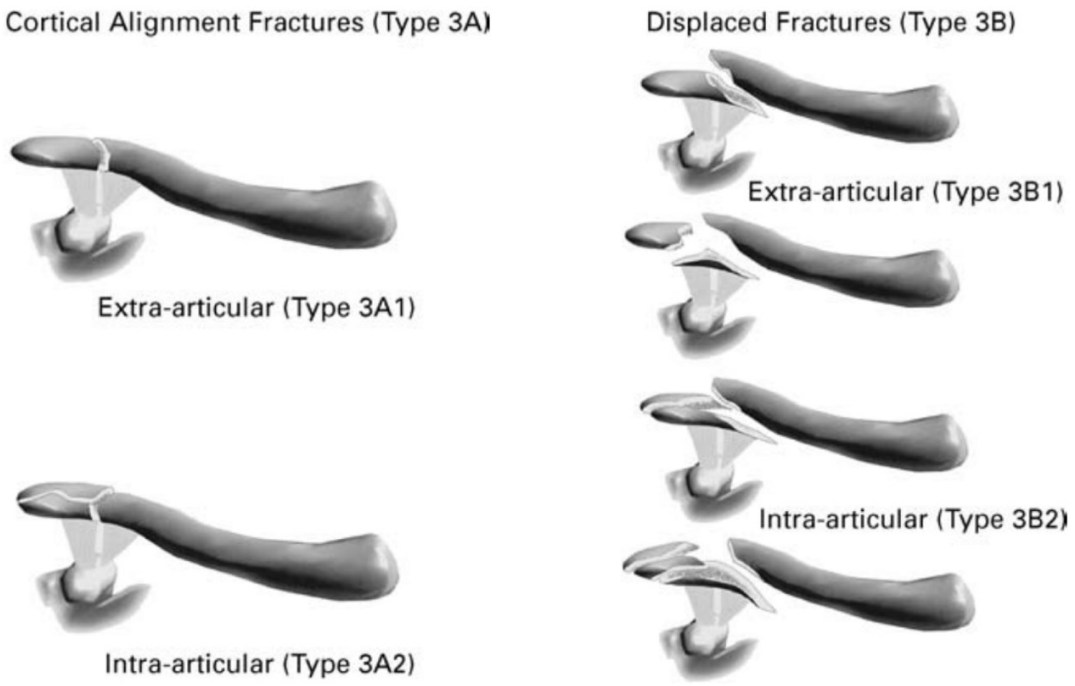

Figure 3: Robinson Classification: Lateral clavicular fractures. Robinson CM. Fractures of the clavicle in the adult. J BONE Jt Surg. 1998;80(3).

1.3.3.6 OTA Classification System

The OTA (short for Orthopaedic Trauma Association) classification system is a standardized method to describe fractures systematically and is widely accepted in clinical practice. Each bone of the human body is assigned a particular number. Fractures are then characterized by their location, degree of dislocation, and injury pattern. Thereby, verbal fracture descriptions are transformed into an alphanumeric code that allows consistent international communication and data exchange for research purposes. (47)
The clavicle is identified by the number 15 according to the OTA classification. Depending on the affected region, the fractures of the clavicle are divided into three main groups with further subdivisions: (48)

Type 1 (= 15.1) represents fractures of the proximal segment end, defined as the medial end of the clavicle including the costoclavicular ligament.
Capital letters are used to mark the morphology of the following subgroups:

A. Extraarticular
B. Partial articular
C. Complete articular fracture

Type 2 (= 15.2) displays fractures of the clavicular diaphysis, known as the extension from the medial located costoclavicular ligament to the attachment of the coracoclavicular ligament.

A. Simple (including spiral, oblique, and transverse fractures; all classified as 15.2.A)
B. Wedge (including spiral wedge, intact bending wedge, and fragmentary wedge fracture)
C. Multifragmentary (including fragmentary spiral, intact segmental, fragmentary segmental fracture)

Finally, type 3 (= 15.3) describes distal fractures. They occur in the segment from the lateral end of the clavicle to a vertical line to the medial border of the coracoid process. Further subdivisions analogous to Type 1, i.e., medial end fractures, are made:

A. Extraarticular
B. Partial articular
C. Complete articular fracture

Additionally, three further subgroups (a-c) exist to define the pattern of fracture in relation to the coracoacromial ligament.

1.3.4 Associated Injuries

Clavicular fractures are often occurring as isolated injuries. However, in case of high-energy trauma, fractures of the clavicle may only be one of several major injuries. Even though associated injuries are rare, it is crucial to stay mindful of them to enable a rapid diagnosis, since some of these medical conditions are potentially life-threatening (49,50): Studies have reported the occurrence of several concomitant injuries to clavicular fractures such as pulmonary effusions, or contusions, pneumothorax, rib fractures, scapula fractures, or even a “floating shoulder”. (i.e. due to a series of osseous and/or ligamentous injuries, the upper limb has lost its attachment to the trunk). (50–52) Other infrequent associated injuries include damage to neurovascular structures such as the brachial plexus and subclavian blood vessels. (49,50,53–59)

1.3.5 Diagnostics

1.3.5.1 Clinical Assessment of Clavicular Fractures

Patient’s History

A thorough patient history including the time and circumstances of the accident should be ascertained, together with the mechanism of injury, since most patients record a direct blow to or fall on the lateral side of the shoulder. Patient's past medical history should be documented, as well as information on individual risk factors like nicotine consumption history, the status of employment, and dominant hand.

Patients should be interrogated concerning the exact location of pain, pathological sensations such as tingling or pricking, or total loss of sensation around the clavicle or the corresponding upper limb. (10,49) Moreover, subjective difficulties in breathing should be evaluated, since pneumothoraces and hemothoraces have been reported as potential associated injuries. (10,24,60)

Physical Examination

First, patients should be visually assessed. During inspection of the shoulder and clavicle, one's gaze should follow the course of the anatomical contour while watching out for conspicuous features such as asymmetry, skin discoloration, deformities, and swelling at the side of the fracture. (10,24,49,60,61) Thereby close attention should be paid to the integrity of the skin. If the skin surrounding the fracture appears blanched, necrosis may ensue due to excessive pressure of a bone fragment under the skin. Furthermore, perforation by sharp fracture fragments may result in an open fracture. (10,24,49,61) Conditions with the skin at risk for opening or already present lacerations are alarming and require urgent intervention. (10) The palpation of the clavicle will expose tenderness and discomfort, crepitus or instability. (10,24,49)

Due to the clavicle´s proximity to the subclavian vessels and the plexus brachialis, a neurovascular examination of the affected upper limb is mandatory. (24,49,60,61) It should cover palpation of the distal pulses of the ulnar and radial artery and testing for intactness of sensory function of the radial, median, ulnar, and axillary nerve. An examination of motoric function should not be missed. (10) Neurological deficits of any kind in the ipsilateral arm may imply an injury of the plexus brachialis. In plexus brachialis lesions, the ulnar nerve is most commonly affected, due to its close relation to the midshaft of the clavicle. (24) The occurrence of considerable or growing hematoma can be indicative of the subclavian artery or vein damage. In such settings, clinical findings include reduced or missing peripheral pulses and differences in blood pressure in the injured upper limb compared to the uninjured side. (49)

Auscultation of the lung and pulse oximetry should be performed on patients complaining of dyspnea to rule out pneumothorax or haemothorax. (24,60) These may arise due to a pulmonary apex injury. (24)

1.3.5.2 Imaging

In the setting of an isolated clavicle injury, radiography with an anterior-posterior (a.p.) of the shoulder girdle and the clavicle in full length (from adjacent AC to SC-joints) should be obtained. (49,61) Usually, this view is sufficient to confirm or rule out a fracture. (60) To evaluate the degree of dislocation and comminution, further X-ray images in the form of a 20-degree or 45-degree cephalic tilt view are necessary. (49,60)

If a pneumothorax, rib fracture, or other musculoskeletal injuries are suspected, an additional p.a. chest radiograph should be obtained. (61)

In polytraumatized patients, a CT scan of the thorax is frequently performed as part of the "polytrauma-CT-scan", and the clavicle can then be further evaluated regarding its pattern, length, and comminution. With recent computer programs, a 3D image of the clavicle may add additional value. (10,24) However, a CT scan is not routinely performed for clavicular fractures. Yet, it plays an important role in the evaluation of delayed fracture healing or nonunion. CT imaging is justified in the acute setting, though, in case severe injuries of inner organs or neurovascular structures are suspected, for example in case of absent distal pulses, fracture dislocation of the SC-joint, or intra- glenoid fracture. (49)

1.4 Management of Clavicular Fractures

1.4.1 Initial Management

As studies have shown an association between nonsteroidal anti-inflammatory drugs (NSAIDs) and increased nonunion as well as infection rates in long bone fractures, their administration is not recommended in clavicular fractures either. (62,63)

However, as soon as patients presenting to the emergency department are diagnosed with a clavicular fracture, they should receive adequate analgesics and a sling for immobilization. This supports the arm and alleviates pain. (10) As previously mentioned, immediate surgical intervention should be sought in case clinical examination reveals skin tenting. Furthermore, Gustillo-Anderson grade II and III open fractures will likewise require fast surgical treatment. Moreover, as open fractures are more prone to infection, antibiotic treatment should be initiated at least for a duration of 24 hours upon arrival at the emergency department. (64)

1.4.2 Treatment of Clavicular Fractures

A multitude of different techniques have been described, thus far for the treatment of clavicular fractures. In broad terms, therapeutic options can be categorized into conservative and operative ones.

The choice of treatment is based on various aspects, including patients' individual activity level, physical constitution, age, and athletic demand. The probably most crucial factors

influencing the decision on which treatment to choose, and thereby reducing the risk for complications, are fracture type and pattern, the anatomical location, degree of displacement as well as initial shortening and accompanying injuries. (65–67)
Still, there is no consensus regarding optimal clavicular fracture management, especially, considering the question of whether to perform surgery or not.

In the past, clavicular fractures were predominately subjected to conservative treatment. Back then, the generally conservative approach demonstrated favorable outcomes with merely minimal rates of nonunion, ranging from 0.1% to 0.8%. On the contrary, in patients treated with primary open reduction, significantly higher nonunion rates occurred. That finding of higher nonunion rates among operatively treated patients resulted in conservative measures regarded as the treatment of choice. (14,68) In the course of time, other studies have been published, presenting opposite results to early studies on clavicular fractures: Increased rates of nonunion rates ranging from 2.2% to 15% following nonoperative fracture treatment, have been reported in more recent studies. (22,69–71) A substantially high association between nonunion and an initial shortening of the clavicle of ≥ 20 mm has been observed. (70) Besides the occurrence of nonunion, several authors described further complications of conservatively treated clavicular fractures. These included persistent pain, neurovascular compromise as a result of excess callus formation, poor functional outcomes, and patient dissatisfaction. These complications were predominantly observed among patients with initially severely displaced midshaft fractures. (14,69,70,72,73) Shoulder mechanics in middle-third fractures treated conservatively appear to be negatively influenced by shortening of the clavicle. Thereby, unsatisfactory results are most commonly seen when shortening of the clavicle exceeds 14 mm in females and 18 mm in males. (72)
Another study demonstrated a correlation between poor functional outcomes after non-operatively treated clavicular fractures and the following parameters: fracture type (especially when comminuted), degree of fragment displacement (≥ 21 mm), and shortening (≥ 5 mm). (66)
These data indicate the need for surgical treatment of clavicular fractures which display certain characteristics such as comminution, significant dislocation, and considerable shortening.

Nevertheless, there is a shared agreement that undisplaced or minimal displaced clavicular fractures, regardless of anatomical location, can be treated conservatively. (32,65,74,75)

Compared to the deficient nonoperative treatment results mentioned earlier, more favorable outcomes following various surgical interventions have been demonstrated. (76–80) Several studies investigated different outcomes after nonoperative vs. operative management of clavicular fractures. They showed better outcomes in function, and lower rates of delayed union as well as nonunion in the surgically treated groups. (73,76,77,79–82) Furthermore, patients with displaced mid-shaft clavicular fractures who underwent surgery were able to return to work earlier compared to conservatively treated individuals. They experienced faster functional recovery. (83,84)
Yet, some authors were unable to report significant clinical or statistical differences between conservatively or operatively treated patients regarding functional scores and patient satisfaction at long-term follow-up. (83,85) Overall, treatment management has progressed over the last decade and shifted towards operative procedures. (31,32,74,86)

As promising as a surgical approach seems, it is substantial to reflect on the potential complications related to surgical interventions and the material used, such as neurovascular compromise, infection, hardware breakage, migration, pain, or bulging of the implant under the skin, and eventually the need for material removal. In case surgery is considered, one should thus take a closer look at the risk-benefit-ratio. The patient should be thoroughly informed about risks and potential side effects as well as the advantages and expected outcomes of the planned operation. (24,65,74,87)

Finally, it is important to bear in mind that the various types of clavicular fractures – medial, diaphyseal, and lateral – display different outcomes and require distinct therapeutic strategies. (65,88)

1.4.3 Conservative Treatment

Indications

As already mentioned, conservative management is usually the standard treatment option for all types of clavicular fractures with no or minimal displacement. However, conservative measures may also be adopted in displaced fractures at a higher risk for deficient functional outcomes, as well as non-compliant patients at risk for complications.

Types of Conservative Treatment

Historically, several therapeutic devices have been described, including casts, spica casts, splints, and wraps. all with the purpose of immobilization, pain reduction, and maintenance of the fractured clavicle´s alignment, thereby supporting uneventful bone healing. The aim is the recovery and restoration of the shoulder function. (11,14,39,89)

Nowadays, the figure-of-eight bandage and the elbow-to-body slings are the most broadly used types. Several randomized trial studies have been conducted comparing these two non-operative treatment options: A sling was suggested as the primary choice for the conservative management of clavicular fractures, due to earlier relief of pain, less discomfort, and superior overall patient satisfaction compared to the figure-of-eight brace. (90–92) Another advantage of the simple sling is the simple application. (91,92) Furthermore, a comparative study has reported lower malunion rates and better results functional results in mid-shaft clavicular fractures following treatment with a broad-arm sling. (92) When patients were treated with the figure-of-eight brace, they rather complained about severe pain, especially during the first day, as well as discomfort at the axilla with its nearby neurovascular structures. Moreover, the figure-of-eight brace is more complex in application. (90–92) Nevertheless, both reach similar results with regard to cosmetic appearance and function. (90–93) Range of motion usually improves rapidly as soon as bony union has taken place. (91,92) For all these reasons, the sling is favored in the usage of non-operative treatment options compared to the figure-of-eight brace. The former inheres fewer complications and offers more patient comfort, while yielding equivalent outcomes.

Treatment duration of conservative management for the sling as well as the figure-of-eight brace spans a period of 3 to 6 weeks. Upon follow-up, regular radiological assessments and clinical examinations should be performed to ascertain the progress of osseous

consolidation, stability at the fracture site, and function. (10,92,94) Usually patients are able to return to sports after 6 to 8 weeks if they are free of pain upon palpation at the fracture site and range of motion has fully recovered. Contact sports are to be avoided for 8 to 12 weeks, though. (95)

1.4.4 Operative Treatment

Indications

Absolute indications for operative treatment of clavicular fractures include:

- Open fractures
- Fractures with gross displacement and risk of skin perforation
- Damage to neurovascular structures such as subclavian vessels and brachial plexus
- Ipsilateral fracture of scapula neck and clavicle, i.e., “floating shoulder”
- Symptomatic non-union after conservative treatment

(17,92,94,96–98)

Relative indications for surgical interventions involve:

- Shortening of > 15 mm in mid-shaft
- Fractures with displacement
- Comminution
- Polytrauma, multiple injuries
- Fractures of both clavicles
- Unstable Neer type IIA and IIB lateral fractures

(66,69,70,96,99–101)

Surgical Procedures for Clavicular Fractures

Overall, there are various operative techniques and procedures to treat a clavicular fracture. Nowadays, a multitude of anatomically adapted materials are used, including plates, nails, and screws that allow for excellent osteosynthesis of the clavicle. Generally, they result in favorable outcomes regarding bone union and shoulder function. (31,32,73,74,76,77,79–82,86)

Commonly used surgical procedures are open reduction and internal fixation (ORIF) with or without autogenous bone grafting, intramedullary pin fixation with k-wires, or Knowles

pin stabilization, and others more rarely used. Each of these techniques has specific indications and inheres certain advantages and disadvantages, that are mostly linked to patient-specific risk factors and fracture characteristics. (84,102,103)

Operative Treatment of Mid-shaft Clavicular Fractures

Open Reduction and Internal Fixation (ORIF) with Plate and Screws

The operation begins with a skin incision according to the selected surgical approach. When approaching the clavicle anterior-inferiorly, the course of the incision is to be made parallel to the clavicle along its inferior border. (102,104) Should the superior approach be chosen, the incision is to be made superiorly to the fractured clavicle at a length of 8 to 10cm. (104) After the careful release of the soft tissues, the fracture is exposed. Care has to be taken not to excessively release the periosteum from the fracture fragments. Displaced fragments are pulled back into their appropriate anatomical place by using sutures, clamps, and K-wires. After fracture reduction, the plate is positioned on the surface of the clavicle above the fractured area to reconnect the fragments. Screws are used on each side of the fracture to fix the plate to the bone. (105)

ORIF is most commonly used in case of displaced mid-shaft clavicular fractures, and it is regarded as the operative procedure of choice. (74,106) It offers advantages such as an immediate rigid fixation, rotational control of the fracture, as well as cortical compression in case lag screws are used. (106) Furthermore, the fixation with plates and screws enables prompt pain reduction and early restoration of function. (83,84) Yet, some complications may develop following ORIF: need for reoperation and implant removal due to hardware-related problems (e.g., local irritation, and material prominence). Further possible complications include superficial wound infections, deep infections, implant loosening or failure, bony nonunion, refracture after plate removal, as well as iatrogenically caused neurovascular injuries. (80,107–113)

Intramedullary Fixation

Another surgical technique to treat displaced diaphyseal clavicular fractures is stabilization with an intramedullary nail. Hereby, the patient is placed in beach-chair or supine position. The incision measures 1-2 cm and is carried out lateral to the SC-joint at the anterior surface of the clavicle. The portal for the nail is then exposed by gently dissecting the soft tissues until the bone is reached. After fracture reduction with pointed clamps, either

achieved through small stab incisions or percutaneously, the nail is inserted through the entry point. In order to fixate the aligned fracture, the intramedullary nail is then carefully pushed forward into the lateral fracture fragment as distal as possible without perforating the cortex. (104) Different osteosynthesis devices have been described to achieve intramedullary fixation, including elastic stable intramedullary nails, hagie pins, Knowles pins, Rockwood pins, K-wires, and titanium nails. (78,114–117)

The advantages of intramedullary fixation can be seen in the less invasive approach compared to open reduction and internal fixation with better cosmetic and functional outcomes. (118,119) Intramedullary nailing is regarded an alternative treatment option nearly as effective as plating, and may be especially suitable for multiple injured patients or in case of concomitant injuries of the shoulder girdle. (118) Although the indications are nearly the same as for plate and screw fixation, intramedullary fixation may not be recommended in multifragmental and comminuted fractures or severe initial shortening due to the risk for unsatisfactory outcomes. (114)

Disadvantages and complications of intramedullary nailing include the potential occurrence of hardware prominence with subsequent skin irritation and pain, implant breakage, numbness in the area of the surgical scar, wound infections, nail migration, nonunion, and iatrogenic injury of the plexus brachialis. (115,120–123)

External Fixation

Overall, external fixation is very rarely applied in clavicular fractures. It is characterized by placing wires and screws into the unharmed region at both sites of the fracture that are then subsequently connected by rods. Thereby, a rigid construct is created that offers stabilization of the anatomically realigned fractured bone. (10) The advantage of this technique lies in its minimal invasiveness and the maintained excellent blood supply due to only minimal periosteal stripping resulting in efficient and fast bone healing. No second surgical intervention upon general anesthesia is needed since the fixation device can be easily removed. (124,125) Adequate care of the pin-penetrated skin area is necessary to prevent infection. External fixation of clavicular fractures may be applied in instances of open fractures and infected fractures that are unable to unite. (10)

Operative Treatment of Lateral End Fractures

For lateral end fractures with displacement, especially those corresponding to Neer type II, operative treatment is recommended. These types of fractures are considered unstable due to the compromise of the coracoclavicular ligaments, wherefore they are more susceptible to developing nonunion when treated conservatively. (96) Even though for non-surgically managed displaced lateral fractures a nonunion rate of 33% has been reported, functional results are generally acceptable. (126) Thus, a conservative treatment approach of displaced distal clavicular fractures is suggested as an option for elderly and multimorbid patients with low physical or athletic demand.

Several different surgical procedures have been described for the management of displaced lateral third fractures such as coracoclavicular screw fixation, plate or hook-plate fixation, k-wire fixation, stabilization of the coracoclavicular ligaments with suspensory devices (these can also be inserted arthroscopically), as well as a combined construct of the above-mentioned options. (127–134)

Hook plates have been designed for unstable distal fractures with a lateral fracture fragment too small for fixation by conventional plates and screws. The hook at the lateral side of the plate is anatomically shaped to find its position in the subacromial space, while the main portion of the plate is positioned at the superior surface of the clavicle, providing a stable construct to hold the reconstructed fracture in place. Thereby, the hook is positioned without direct contact to the AC-joint. (135) With this technique, decent functional results and high rates of bony union can be reached. (136,137) Nevertheless, the use of hook plates has been described to come along with high complications rates such as hook migration, persistent shoulder pain, AC-joint osteoarthritis, and osteolysis around the hook hole, especially in the subacromial region, consecutive need for a second surgical intervention for plate removal. (135,136,138)

A recent meta-analysis investigated the most suitable surgical procedure for distal clavicular fractures of Neer type IIb. Different operative techniques including hook plate fixation, coracoclavicular stabilization, plate fixation with or without coracoclavicular augmentation, and AC-joint transfixation were analyzed. (138) In this study, hook plate fixation displayed the highest rate of postoperative complications. Even though the functional results were acceptable, outcomes with hook plate fixation were worse than with other procedures investigated. According to this meta-analysis, the most promising clinical

outcomes and low complication rates were seen with an open coracoclavicular stabilization and locking plate fixation. (138) Therefore, they are suggested as today's best choice for Neer type IIb fractures. (138)

In accordance with this, another comparative meta-analysis revealed less favorable functional outcomes in patients treated with hook plates compared to those who underwent conservative treatment, locking plate fixation, tension band wire fixation or combined operative techniques. However, similar results regarding the rate of bony union among all investigated procedures were observed. Eventually, conservatively treated patients displayed a higher rate of nonunion compared to surgically treated cohorts. (139)

Still, the most suitable surgical method for treatment of Neer type II fractures has not been identified yet, considering every procedure carries its advantages as well as disadvantages. Thus, this topic remains a subject of controversy.

Operative Treatment of Medial End Fractures

With an incidence of 2 to 3%, fractures of the medial third are the rarest type of clavicular fractures, usually minimally displaced and therefore treated conservatively. (22,23,140,141) However, in case the fracture is severely displaced, compromises mediastinal structures, or displays any other absolute indications for surgery such as comminution and perforation of the skin, surgical management should be taken into consideration. (32,75,94) Various surgical techniques have been described to treat medial fractures of the clavicle. These include K-wire fixation, the use of hook plates, conventional, pre-shaped as well as inverted plates with or without additional sutures, and elastic intramedullary nailing. (142–150)

Although there is no consensus opinion on the optimal surgical treatment technique concerning medial end fractures, the use of one procedure has fallen out of favor and is therefore not recommended: K-wire fixation is associated with serious complications, especially implant migration. Injuries to the lungs, intrathoracic trachea, and spinal cord due to medial implant migration have been described. (146,151,152)

1.5 Nonunion

1.5.1 Definition

In general, under the term nonunion describes a severe complication that may arise after a fracture, i.e. lack of successful bone healing. Various definitions of "nonunion" exist, yet as of the present day, a universally acknowledged definition of bone nonunion among orthopedic and trauma surgeons is pending. (153) The common notion of nonunion is based on the duration of bone healing. Thus, the term "delayed union" refers to insufficiency in osseous consolidation, i.e. the fracture has not adequately healed after 6 months. (29,94,154) Yet, the healing process is progressing, and the outcome is still uncertain. (94)

A true "nonunion" is considered as the absence of bone healing after 9 months, calculated from the date of injury, and no noticeable progress in the bony union of the fracture fragments for more than three months. (29,94,154)

According to several authors, a clavicular nonunion was precisely characterized as the absence of bony union in the clavicle four months after the initial injury. (155–158)

However, different bones may heal at varying velocities, further complicating a uniformly applicable definition for any affected bone.

Instead of defining a particular period of time, the Danish orthopaedic trauma society prefers to use an alternative definition of nonunion, which offers more adaptability regarding the diverse medical presentations of not united fracture sites. Herien, a nonunion is described as *"a fracture that will not heal without further intervention."*(159) A spontaneous consolidation is not to be expected and a surgical intervention may be highly indicated.

1.5.2 Epidemiology of Nonunion in General

In several publications, the overall rate of nonunion per fracture was mentioned to range between 5% and 10%. (154,160–163) However, this data has encountered skepticism as since not presenting credible data sources; the citations refer to a textbook published in the US in 1999. (159,164)

In contrast to these numbers, a more recent study investigated a population of more than 4 million adults, reporting on a total nonunion risk per fracture of 1,9%. (165) Another epidemiological study assessing tibial, femoral, and humeral fractures in the Spanish population reported an overall nonunion risk of 4%. (166) Additionally, Zura et al. found an overall nonunion rate of 4,9%, when analyzing 18 different bones. (162)

The aspect of age is considered an important factor associated with the probability of nonunion development. In the pediatric and adolescent population, the risk of developing a nonunion appears to be significantly lower than in adults, amounting to 0.21% in patients ≤ 14 years and 0.35% in adolescents up to 19 years. Thus this complication is considered rare among young individuals. (167) In the adult population, the risk of nonunion shows an unimodal distribution; it reaches its peak at the age between 25 and 45 years. After this, a continuous decrease in nonunion rates is observed, reaching its lowest point in the elderly patients > 85 years. (165) In accordance with this data, another study provided further incidence for decreasing nonunion rates with ongoing age. (168) In comparison to females, men appear to have an increased overall risk to develop nonunion. (162,165)
Regarding the anatomical region, nonunion seems to occur most commonly after fractures of the tibia, with an estimated nonunion risk of 5% to 7.6%, followed by femur (13.9%), and the humerus (3%). (162,165)

1.5.3 Epidemiology of Clavicular Nonunion

Also, the clavicle seems to be at higher risk for nonunion. In the study by Mills et al., the overall risk for nonunion after clavicular fracture was 4% to 5% among all age cohorts and therefore higher than reported for other long bones. An outlier regarding nonunion risk was observed especially in patients between 35 to 45 years of age, amounting to 8.1%. (165) Taking into consideration several other studies, the nonunion rates of the fractured clavicle have been reported to range between 0.1% and 15%. (14,22,29,70,76,79,80,141,162,169–179)

Female gender as well as an increasing age have been reported to be an independent risk factor for development of a clavicular nonunion. (22,141) Irrespective of the demographic distribution of clavicular nonunion, as well as in contrast to the data described above,

another study revealed that gender and age, while serving as risk factors in a bivariate analysis, do not emerge as significant independent predictive factors of nonunion in the multivariate regression analysis in regard to diaphyseal clavicular fractures. (180)

However, most clavicular nonunion cases are observed among young and predominantly male patients, since the highest incidence of clavicular fractures is found among this population. (21–23,27,29,33,141,180) These findings can be explained based on the fact that the severity of the injury exerts a certain effect on the process of bone healing. Accordingly, open fractures and high-impact trauma are associated with an increased risk for nonunion. Indeed, the predominance of clavicular fractures within the young adult population is related to traffic accidents with motorcycles or cars as well as sports-related injuries. (22,23,25,27,29,33,34,34–36)

Anatomical Distribution of Clavicular Nonunion

Depending on the anatomical location, different rates of clavicular nonunion have been documented. Particularly in cases with nonoperative treatment, lateral fractures demonstrated considerably higher rates of nonunion compared to mid-shaft clavicular fractures. In 2004, Robinson et al. noted nonunion rates of 11.5% in patients with lateral clavicular fractures, whereas the nonunion rate among mid-shaft fractures accounted to 4.5%. (141)

However, the precise prevalence of lateral clavicular nonunion seems to remain unresolved. According to several publications with smaller case subsets, the nonunion rate for lateral clavicular fractures ranges between 3% and 33%. (22,29,170,181)

This data may imply a potential association, indicating that lateral clavicular fractures are more prone to exhibit challenges in the process of fracture healing compared to mid-shaft fractures.

1.5.4 Classification of Nonunion

A nonunion cannot be seen as a uniform condition. Classifications of nonunion are of significance as they provide a fundamental understanding concerning the pathophysiology of nonunion, an aspect essential for treating physicians in the therapeutic decision-making process. Therefore, each nonunion subtype requires a unique therapeutic approach. (153,159,160)

1.5.4.1 Weber and Cech Classification

According to the Weber and Cech classification of nonunion, the states of bone vitality and biological responsiveness of nonunion can be radiologically categorized into three distinct groups. (153,159,160,182) Established in 1976, the classification is still broadly used today. (182)

1. Hypertrophic Nonunion

The hypertrophic form of a nonunion is characterized by prominent callus formation evident on radiographic imaging. Notably, there is an absence of bridging bone, and therefore fracture ends are not united. The abundant callus formation suggests viable bone as well as a satisfactory blood supply and thus a preserved biological healing potential. However, mechanical stability is not lacking, wherefore osseous consolidation is prevented. (159,160,182)

2. Atrophic Nonunion

In contrast to hypertrophic nonunions, atrophic forms lack callus formation on radiographic imaging. They are considered to have compromised biological healing potential as bone fragments are poorly or non-vascularized. Furthermore, local mechanical stability is disturbed, resulting in hypermobility of fragments at the fracture site. (159,160,182)

3. Oligotrophic Nonunion

Oligotrophic nonunions constitute a combination of hypertrophic and atrophic nonunions. Although callus is radiographically visible, its formation is insufficient or incomplete. However, fracture fragments are viable. It is associated with disturbances in biological aspects as well as in mechanical stability. (159,160,182)

1.5.4.2 NUSS – Nonunion Scoring System

The Nonunion Scoring System – NUSS – is a more complex scoring tool assessing the condition of nonunions. It considers further criteria such as the viability of bone, damage to soft tissue, alignment of fragments, presence of infection, comorbidities, and certain risk factors, etc. Its purpose is to provide a more fundamental guide concerning the complexity

of the presenting nonunion, thereby representing an effective aid tool to categorize nonunion and assist surgeons in the process of treatment-related decision-making. (183)
Based on the obtained scores, which may range from 4 to 100 and correlate with the level of complexity, the nonunion is allocated to one of four groups or protocols, thus providing guidance and recommendations regarding further therapeutic management. This concept is also known as the “ladder strategy”: (182–184)

- Category I: NUSS score of 4 - 25.
  Patients of this category are considered to have an unproblematic nonunion. As the cause of this condition is often solely mechanically related, the main goal of treatment modality is to restore stability. This is achieved by common fixation methods, e.g., plate fixation. (182–184)

- Category II: NUSS score of 26 - 50.
  Nonunions of this category are supposed to require a dual therapy approach, as the underlying mechanisms of nonunion involve both biological as well as mechanical issues. Therapeutic measures include a simple minor fixation and realignment of fracture fragments. Additionally, the reactivation of the biological condition is achieved by using extracorporeal shock wave therapy or biotechnological approaches (e.g. utilization of growth factors, mesenchymal progenitor cells). (182–184)

- Category III: NUSS score of 51 – 75.
  Like nonunions of category II, the problem arises from a combination of mechanical and biological disturbances, however, the degree of complexity extends further. Even more specialized care and an intensified therapeutical regimen are therefore required: the first step in the treatment course is the resection of the nonunion site. The resulting bone defect must be addressed by procedures as bone graft. Biotechnical approaches as the use of cell products and growth factors, are indicated as well. (182–184)

- Category IV: NUSS score of 76 – 100.
  For nonunions meeting the criteria of this category, serious surgical measures such as arthrodesis, prosthesis, or mega prosthesis as well as primary amputation may be considered. (182–184)

1.6 Risk Factors of Nonunion

The probability of nonunion development is generally considered multifactorial and therefore influenced by a multitude of aspects including fracture characteristics, affected bone, patient-related risk factors, comorbidities, initial treatment modality, inadequate fixation of the fracture, as well as medical enrollment. (159,160,162,165,185–187)
These factors may be used to estimate the probability of nonunion development in patients. However, determining which patients will ultimately develop a nonunion remains challenging given the non-specific nature of most risk factors listed below.

1.6.1 Anatomical Location

Concerning the anatomical location, as mentioned above, long bones with reported higher nonunion rates involve the tibia, femur, humerus, and clavicle. (162,165)

1.6.2 Injury- and Fracture Characteristics

Injury- and fracture-related risk factors show a correlation with higher nonunion rates. They include:

- High energy trauma
- Open fracture
- Comminution
- Displacement of fracture fragments
- Multiple fractures
- Contamination or infections
- Extend of soft tissue damage
- Cortical discontinuity
- Bone defects; distance between fragments measuring more than 3 mm
  (22,141,159,162,165,185,187–192)

1.6.3 Patient-Related Risk Factors and Comorbidities

Patient-related risk factors and comorbidities deemed responsible for contributing to the development of nonunion involve:

- Gender
- Age
- High body mass index
- Alcoholism
- Smoking
- Diabetes mellitus
- Vascular diseases
- Vitamin D deficiency
- Renal insufficiency
- Osteoarthritis with rheumatic diseases
- Osteoporosis

(22,141,159,160,162,165,179,185,189,192–198)

1.6.4 Epidemiological Factors

The impact of gender and age on the development of nonunion is discussed controversially. Certain studies have identified the female sex as a risk factor for nonunion, in particular of the clavicle. (22,141,179) Other studies suggest, though, that males are more prone to develop a fracture nonunion in general. (162,165,189)

Divergent results have been reported regarding age as a contributing factor to nonunion development: Robinson et al. reported an increase in clavicular nonunion rate with advancing age (22,141) whereas other authors observed the highest overall risk of nonunion in the middle-aged cohorts, decreasing thereafter. (165,189) Another study supports the latter findings by demonstrating a reduction in the nonunion rate with advanced age. (168) However, the findings above can be most probably explained by the higher occurrence of severe impact injuries in predominantly young male individuals, (199) resulting in a higher risk of fracture nonunion in this population. Eventually, the influence of the age-related risk factor on fracture healing seems to vary across the distinct bones of the human body. Patients' age seems to exhibit a stronger influence on nonunion

development in the clavicle than in other bones. (See also section “Epidemiology of Nonunion in General” and “Epidemiology of Clavicular Nonunions”.)

1.6.5 Medication

Concerning pharmaceutical products, the use of NSAIDs and opioids may have a negative influence on bone consolidation resulting in a significantly elevated risk for nonunion development (162,192,197,200) irrespective of whether the analgesics were administered for a longer time period or just in the acute setting. (201) However, patients using opioids on a regular basis appear to be at an almost twice as high risk for fracture nonunion. (201) Further medications have also been associated with impaired fracture healing. (162,198,201) The strength of their influence also depends on the time period these drugs had been prescribed. (201) Agents associated with a significant increase in fracture nonunion risk upon acute administration include:

- Anticoagulants
- Antibiotics
- Osteoporosis medication (i.e., bisphosphonates)
- Diuretics
- Insulin
- Butalbital
- Anticonvulsants
- Benzodiazepines
- NSAIDs
- Opioids

Among the medications administered over a long period are:

- Anticonvulsants
- Oral contraceptives
- NSAIDs
- Opioids

(162,198,201)

1.6.6 Other Risk Factors

Other biological as well as biomechanical aspects of the fracture have also to be considered to affect the fracture healing. Inadequate vascular perfusion and shear stress due to an unstable fracture site have been recognized as accountable for unsuccessful osseous healing. (154,160) An adequate blood supply is crucial to provide a suitable environment for fracture healing. Subsequently, its impairment contributes to nonunion development. The status of vascularization may be influenced by several variables and biological factors mentioned above i.e., smoking, applied medication, and comorbidities, especially diabetes and peripheral vascular disease. (160)

1.7 Risk Factors of Clavicular Nonunion

The aforementioned risk factors can generally be considered to be of relevance to nonunions of the clavicle as well. Several studies have investigated potential risk factors leading to nonunions in clavicular fractures. In accordance with the general risk variables, the findings of factors associated with clavicular nonunion encompass fracture-specific characteristics as gross initial displacement, shortening ≥ 20 mm in clavicle length, and comminution. Although these features exert a great influence on the nonunion rate regardless of the chosen treatment option, their impact is particularly pronounced in case of conservative fracture management. (22,70,141,174,179,180) Reported rates of clavicular nonunion following nonoperative management range from 2.2% to 15%. (22,69,70,179,180)

Additionally, in a randomized controlled study comparing outcomes after ORIF versus conservative management, the latter has been identified as an independent risk factor for clavicular nonunion in displaced mid-shaft fractures. (79) (See also section “Treatment of Clavicular Fractures” for related information.)

The anatomic site is likewise important as fractures of the distal third are considered to exhibit more challenges in the bone healing process, resulting in a higher rate of nonunions compared to mid-shaft fractures. (22,29,141,170,181) (See also section “Anatomical Distribution of Clavicular Nonunion”.)

Furthermore, intrinsic risk factors significantly associated with clavicular nonunion after a conservative, as well as surgical treatment, have been identified. These include first and foremost the female gender, advanced age and smoking. (80,141,174,179,202,203).

1.8 Diagnostics of Clavicular Nonunion

1.8.1 Medical History, Symptomatology, and Physical Examination

To diagnose a nonunion of the clavicle, the initial step involves obtaining the patient's medical history. Specific inquiries should be directed towards details and the kind of accident that caused the fracture (e.g., high-energy trauma, multiple fractures, etc.), prior surgeries, the patient's comorbidities, risk factors such as smoking, and medications used on a regular basis, with special emphasis on pharmaceutical products known for their negative effect on bone healing such as NSAIDs and opioids. (See also section "Risk Factors of Nonunion".) Furthermore, information concerning the initial treatment of the fracture should be also obtained. (159,160)

In the elderly patient population, a nonunion may be asymptomatic, especially in individuals who do not have high functional demands and who are less physically active. (170,204) However, in case younger and rather active patients develop a nonunion, they often report a variety of symptoms including pain and crepitation at the nonunion site, movement restrictions, and weakness of the arm. Further complaints may be related to aesthetical aspects as fracture deformity can cause a cosmetically unsatisfactory appearance. (68,205–207) Moreover, a nonunion may produce compromises of the underlying neurovascular structures, due to the motion of the ununited bone fragments, or excessive callous formation in the process of the attempted fracture healing. This may lead to neurologic complications including compressive neuropathies of the brachial plexus (with the medial cord most frequently affected) and vascular issues such as compression of the subclavian vein, thrombosis, arterial ischemia, or thoracic outlet syndrome. (68,205–210)

To thoroughly investigate the presence and the extent of symptoms, the physical examination should start with the inspection of the nonunion site, paying attention to visible hints of scars indicative of prior surgeries, signs of infection, soft tissue status, and deformities caused by misaligned fracture fragments. Palpation may reveal pain and level

of instability of fracture. A neurovascular assessment, as well as a functional evaluation, are conducted to complete the clinical examination of suspected clavicular nonunion. Eventually, possible systemic factors increasing the risk for nonunion can be analyzed by laboratory testing, including inflammatory parameters (evaluated leukocyte count, high C-reactive protein levels), and levels of vitamin D, calcium or HbA1c. (159,160)

1.8.2 Imaging

In addition to the clinical criteria, conventional radiographs are required to diagnose and assess nonunions. They are used to determine the status of callus formation – either absent, insufficient, or adequate – as well as the extent of the callous fracture bridging. (211) However, findings on radiographic images are often not sufficient to classify the exact state of bony union, especially in the presence of sclerotic bone tissue and fractures stabilized by osteosynthesis. In such cases, a CT scan can be helpful to determine potential callus formation. Hereby, bone bridging of less than 5% is usually considered indicative of a present nonunion, whereas bone bridging of more than 25% implies a healed bone. (184) Although CT scans are associated with 100% sensitivity, the specificity of 62% in tibial non-union diagnosis is rather low. (212) Therefore, the use of CT scans verify a nonunion entails the risk of overdiagnosis that may lead to unnecessary surgical interventions. (212,213) However, a recent study investigated the accuracy of CT scans to diagnose nonunions of the clavicle. A sensitivity of 100% was found, together with a higher specificity of 81%. The authors of this study suggested that CT scans represent an excellent diagnostic tool to confirm bony unions after diaphyseal fractures of the clavicle. Thus, assessment by CT scans may be beneficial in case bony union of the clavicle is uncertain. (214)

1.9 Treatment of Clavicular Nonunion

1.9.1 Preventive Measures

First, the primary focus should lie on preventing clavicular nonunions by optimizing each of the relevant and modifiable existing risk factors the moment the patient presents with a fractured clavicle in the emergency department. Notably, the cessation of smoking should be crucial in prevention as well as in the process of treatment, given that multiple studies

substantiate smoking as a significant risk factor contributing to disturbances in bone healing and eventually development of nonunion. (80,162,190,195,196,202,203)

The main aims of therapeutical intervention in established nonunions are the amelioration of symptoms such as swelling and pain, as well as the restoration of shoulder function. (159) Depending on the type of nonunion and the achieved NUSS score, different treatment protocols, including stability and/or biological improving measures, may be sought. (See section "Classification of Nonunions")

1.9.2 Surgical Procedures Used in Clavicular Nonunion

In case of symptomatic nonunions of the clavicle, fixation by plate is considered the therapeutical intervention of choice among several authors. Benefits of plate fixation include secure stabilization of the nonunion site and rapid functional restoration of the shoulder. For this procedure, high success rates in terms of bony unions have been reported while complication rates remained low. (206,207,215–219) Based on the specific circumstances of each case (e.g., the presence of a bone defect or marked shortening of bone length), plate fixation can be performed with or without the use of an autologous bone graft. (206,207,215–218,220,221) Resection of bone sclerosis at the fracture ends in combination with plate fixation has been described to lead to a high rate of union. (99,217)

Alternative, less frequently used operative treatment methods encompass vascularized fibular and medial femoral condyle grafts that are mainly applied in cases of recurrent nonunion, or following intramedullary fixation and external fixation. (222–230) While the two latter surgical methods provide a more aesthetically pleasing outcome, their stabilizing ability is inferior compared to plate fixation. (32,97,219) Regarding symptomatic nonunions of the lateral segment of the clavicle, another additional therapeutic intervention may be applied. In case of a small, non-united distal fragment and intactness of the coracoclavicular ligaments, an excision of the lateral clavicle may be performed. However, functional results for following resection of the lateral fragment appear rather poor. Thus, this procedure is usually only justified in case of post-traumatic arthrosis of the AC joint. (32,99,181)

1.9.3 Adjuvant Therapy and Other Methods

The process of bone healing does not solely depend on biomechanical factors such as bone alignment and stabilization of the fracture site. A biologically suitable environment is essential for successful union of osseous fragments, which can be optimized by applying hematologic and biotechnological products boosting osteogenic activity. Several studies have discovered that biological stimulation of bone healing in case of delayed union and nonunion can be induced by, for example, percutaneous injection of bone marrow, growth factor enriched plasma, platelet-rich plasma, or by using bone autografts modified with growth factors, bone-scaffold-building substances, or hyaluronic acid. (231–236) Furthermore, the local application of the recombinant bone morphogenic protein has been suggested to be another possible promoter of osseous regeneration processes. (237,238) Although these findings in the molecular biological field seem promising regarding the management of clavicular nonunion, there is remaining need for further investigation.

Additionally, extracorporeal shock wave therapy has also been reported as a noninvasive and safe treatment option increasing the healing rates of delayed bone unions and nonunions. Through the applied shockwaves, microfractures are induced in the old callous tissue. Hereby, biological stimulants are released which promote the mechanisms of local angiogenesis and subsequently facilitate successful healing of the fracture nonunion. Due to its beneficial effects on biological aspects of bone healing, this treatment modality should be considered prior to surgical intervention. (239–242)

2 Patients and Methods

2.1 Study Design

This retrospective study aimed to investigate the risk factors associated with nonunion of clavicular fractures following conservative treatment. We conducted a single center study at the Department of Orthopaedics and Trauma, Medical University of Graz, Austria. Ethical guidelines of the institution were followed and approval from the ethics committee of the Medical University of Graz was received. (Ethical vote number: 36-003 ex 23/24).

2.2 Study Population

The study included a cohort of patients with clavicular fractures who had been treated conservatively at the Department of Orthopaedics and Trauma, Medical University of Graz, Austria between 01.01.2010 and 15.12.2020. Inclusion criteria involved patients with radiographically confirmed fractures of the clavicle who were subsequently treated conservatively. Patients who received primary or secondary operative treatment were excluded, as were those with a follow-up duration of less than 4 weeks and, or those with unknown outcomes.

2.3 Data Collection

Data was systemically collected from electronic medical records, including fracture characteristics, patient demographics, patient-related risk factors, comorbidities, and clinical outcomes. Fractures were categorized into three groups using the Allman classification system (38), based on conventional radiography anterior-posterior (a.p) images. Each group was further subdivided by factors such as fracture side, types of fragments, degree of dislocation, and initial shortening, among others. Additionally, we documented the type of conservative treatment device chosen (sling, figure-of-eight bandage, or none), as well as the reason for subsequent nonoperative management. Variables of interest, including fracture-specific characteristics, patient-related risk factors, conservative treatment variables, and follow-up, are listed in Table 2.

The follow-up process involved documenting fracture alignment, stability, and callus formation during each appointment, relying on clinical and radiological assessments.

Additionally, the time required for bony union was determined throughout the follow-up period. Any complications and patient complaints were recorded.

Initially, a comprehensive data search yielded 3599 patients. Of these, 967 potential patients could be selected. Out of these, we excluded 227 patients who had undergone surgical treatment, either as primary or secondary intervention (prior to the development of nonunion), along with 160 individuals with follow-up periods of less than 4 weeks. Additionally, five patients with indeterminate outcomes were excluded. Ultimately, our study included 575 patients who had undergone conservative treatment for clavicular fractures.

For the purposes of our study, we adhered to the definitions provided by Simpson et al., Wilkins et al., Manske et al., and O'Neill et al. Clavicular nonunion was precisely characterized as the absence of bony union in the clavicle four months after initial injury. (155–158)

Table 2: Variables of Interest

Fracture specific	**Risk factors at time of fracture**	**Conservative treatment-specific**	**Follow-up**
Date of fracture	Gender	Reason for conservative treatment	Control dates
Location	Size	Type	Radiological assessment
Side	Height	Mobilization	Fracture healing
Fragments	BMI		Date of healing
Fragment dislocation	Allergy		Treatment of Nonunion
Injury mechanism	Anticoagulation		Nonunion treatment type
Polytrauma	Hypertension		
Concomitant injuries	Renal insufficiency		
Shortening	Diabetes mellitus		
	Osteoporosis		
	Rheumatic disease		
	Nicotine		
	Alcohol		
	ASA Score		

2.4 Outcomes

The primary outcomes of this study were fracture and patient-related parameters that contribute to the development of nonunion of clavicular fractures treated conservatively.

2.5 Statistical Analysis

Normally and non-normally distributed continuous variables are provided as means and medians with corresponding standard deviations (SDs) and interquartile ranges (IQRs), respectively. Associations between variables and the development of clavicular nonunion were analyzed with chi-squared tests for binary and categorical variables, as well as t-tests and Mann-Whitney-U-tests for continuous normally and non-normally distributed variables. Logistic regression analysis was performed to determine the odds ratios (OR) of the individual risk factors. OR were provided with corresponding 95% confidence intervals (95% CI). Variables included in the logistic regression model were chosen based on their significance in the univariate analyses, as well as their clinical significance. A p-value of <0.05 was considered statistically significant.

3 Results

3.1 Patient Cohort

3.1.1 Demographics

The study involved a total of 575 patients who had undergone conservative treatment for clavicular fractures. Among these, 211 (36.7%) were females and 364 (63.3%) were males. Therefore, the incidence of clavicular fractures in our collective was 1.73 times higher in males compared to females. (Figure 4)

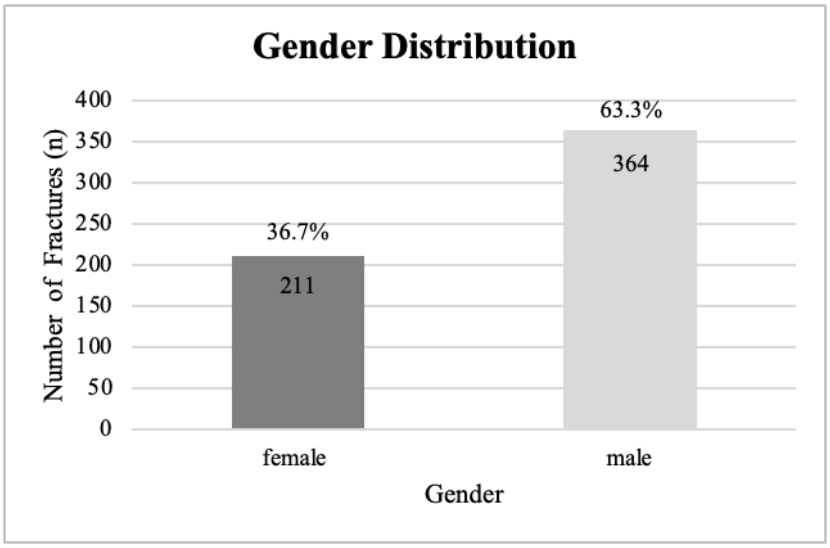

Figure 4: Gender Distribution of Clavicular Fractures. N=575. Females were affected in 211 cases (36.7%) and males in 364 cases (63.3%).

The average age of the included patients was 52.18 years (±20.8), ranging from 12 to 99 years. The mean height amongst the study population was 1.71 m (±0.1), while the mean weight was 71.26 kg (±14.7), and the mean BMI (Body Mass Index) was 24.20 kg/m^2 (±4.2). Additional demographic characteristics of the patient cohort are outlined in Table 3. The normal distribution of age and BMI among the study population suggests that it is representative. (Figure 5 and 6)

Table 3: Demographic Characteristics of Patients Enrolled in the Study.

Demographic Characteristics

	Mean ± Std.Dev.	**Median**	**IQR**
Age (years)	52.2 ± 20.8	50	34 - 70
Size (m)	1.7 ± 0.1	1.7	1.7 – 1.8
Weight (kg)	71.3 ± 14.7	70	60 - 80
BMI (kg/m^2)	24.2 ± 4.2	23.7	21.4 – 26.1

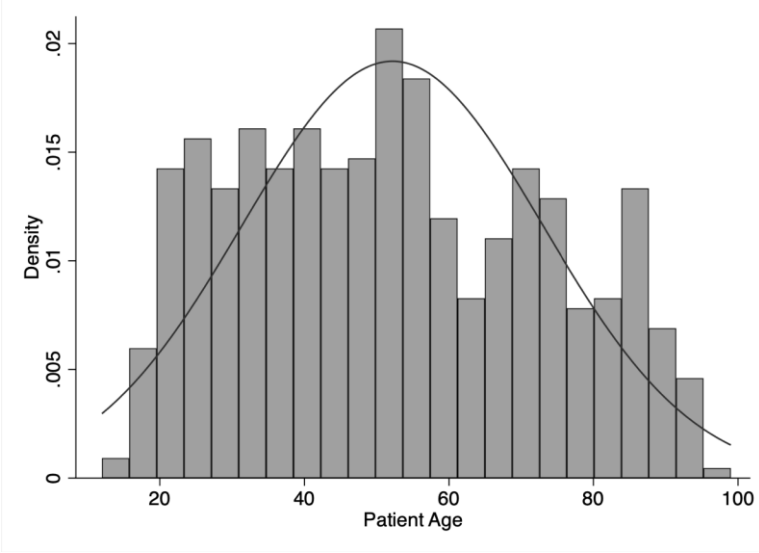

Figure 5: Distribution of Age in the Study Population.

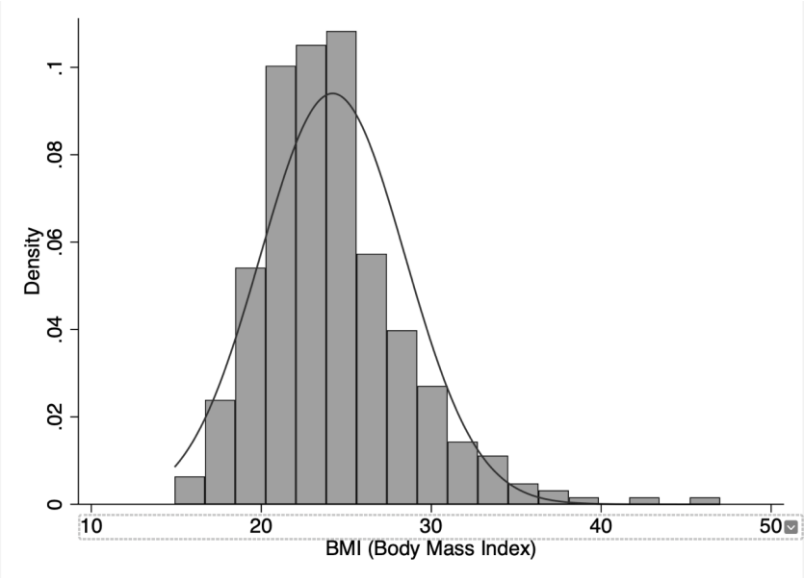

Figure 6: Distribution of BMI (Body Mass Index) in the Study Population.

3.1.2 Fracture-Related Parameters

Fracture Side

Out of all 575 fractures, 292 (50.8%) affected the left clavicle, and 283 (49.2%) the right clavicle. This distribution reveals a relatively balanced occurrence between the two sides, with a slight predominance for the left. (Figure 7)

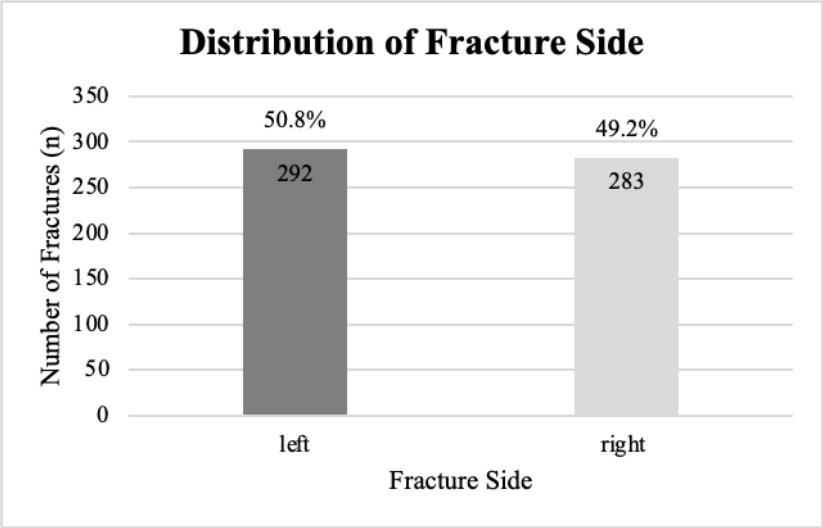

Figure 7: Distribution of Fracture Side. N=575. 292 (50.8%) of fractures occurred in the left clavicle, whereas 283 (49.2%) occurred in the right clavicle.

Fracture Location

Mid-shaft fractures were the most common, accounting for 57.7% of cases within the patient cohort. Lateral clavicular fractures were second most common, amounting to 38.1%. The medial clavicle segment was the least affected anatomical location, representing only 4.2% of fractures. (Figure 8)

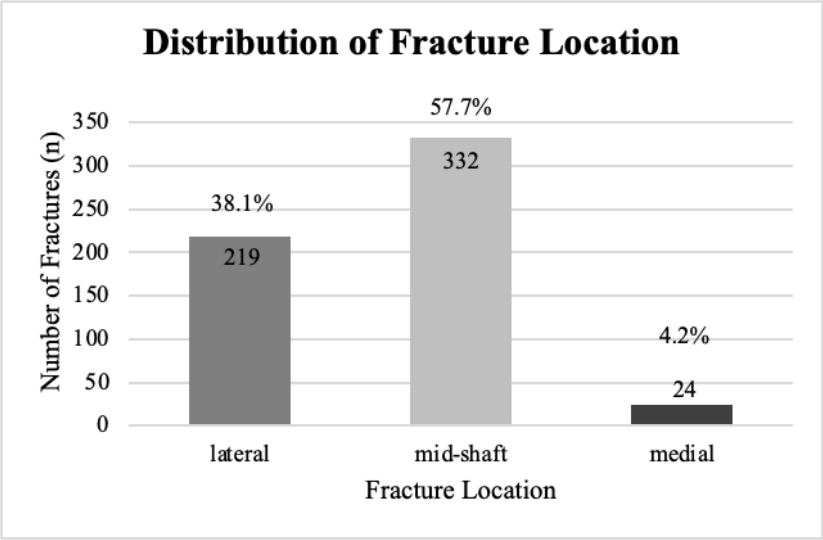

Figure 8: Distribution of Fracture Location. N=575. Mid-shaft fractures comprised 57.7% of all cases, while lateral fractures were present in 38.1% of cases, and medial fractures accounted for 4.2% of cases.

Fracture Pattern

The most common fracture pattern was a simple fracture (63.8%), characterized by a clean bone break without additional fragments. Wedge fractures, which exhibit a triangular-shaped break in the clavicle, accounted for 20.7% of cases. Complex and multifragmental fractures were less frequent, occurring in 15.5% of all cases. (Figure 9)

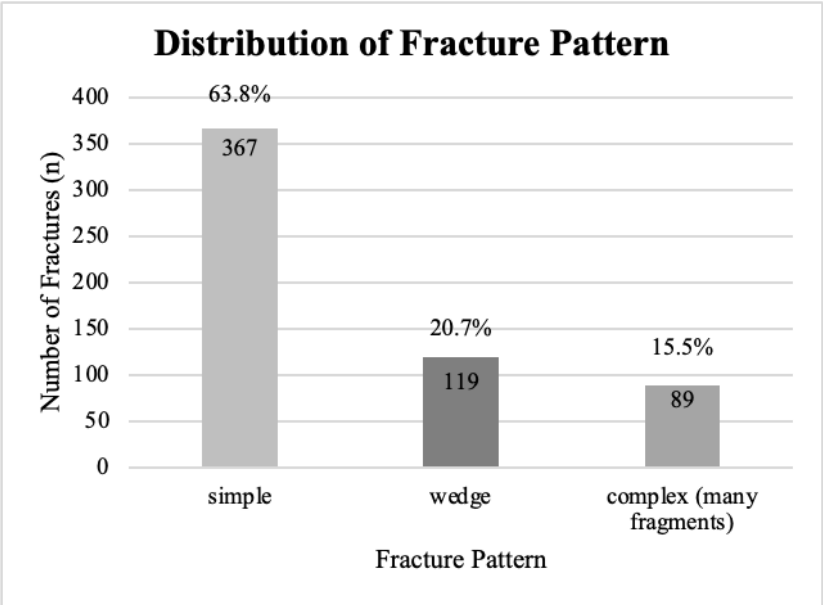

Figure 9: Distribution of Fracture Pattern. N=575. Simple fractures are the most prevalent (63.8%), followed by wedge fractures (20.7%), and complex fractures (15.5%).

Degree of Dislocation

The most common degree of dislocation was by half of the clavicula thickness (24.2%), followed by entire clavicula thickness accounting for 23.7% of the study population. Dislocation by one cortex of the clavicle was observed in 18.6%, whereas dislocation by more than one cortex occurred in 15.5%. Furthermore, 18.1% of all fractures showed no dislocation. (Figure 10)

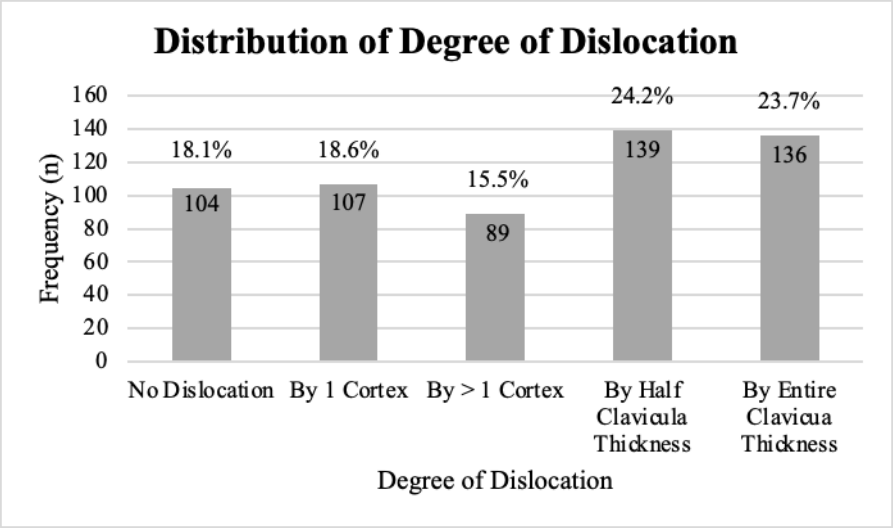

Figure 10: Distribution of Degree of Dislocation. N= 575. Among all clavicular fractures, dislocation by half clavicula thickness was most common at 24.2%, followed by dislocation by the entire clavicula thickness (23.7%).

Shortening in Clavicular Length

Initial shortening of clavicular length was radiographically assessed in 180 patients. Of these, 78.3% exhibited less than 2 cm of bone shortening at initial presentation, while 21.7% showed more than 2 cm shortening in clavicular length. (Figure 11)

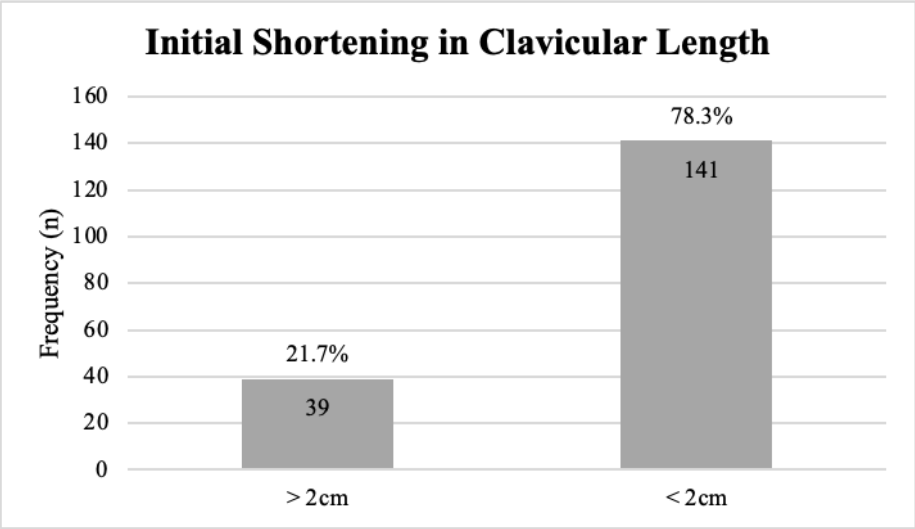

Figure 11: Distribution of Initial Shortening in Clavicular Length. N = 180.

Mechanisms of Injury

When considering the mechanism of injury, the most frequent reasons for clavicular fractures were domestic or low-impact falls (41.5%). These falls included direct falls onto the shoulder from a standing position, falling out of bed, seizure-related falls, or syncopation-induced falls.

The second most prevalent mechanism contributing to clavicular fractures involved various athletic activities, accounting for 36.1% of cases. Among these activities, cycling was the leading sport responsible for clavicular injuries, amounting to 22.5% of all fractures. Other frequent sporting activities included skiing (3.9%), horse riding (2%), as well as team sports characterized by aggressive play and intense body contact, such as football, ice hockey, and American football (3.4%).

Traffic accidents, including car and motorcycle accidents, as well as accidents involving pedestrians, contributed to 20.3% of clavicular fractures. Less frequent causes comprised falls from trees and heights ranging from one to 10 meters. Figure 12 illustrates the distribution of specific sporting activities associated with clavicular fractures, and Table 4 provides a detailed breakdown of the data concerning the various mechanisms of injury.

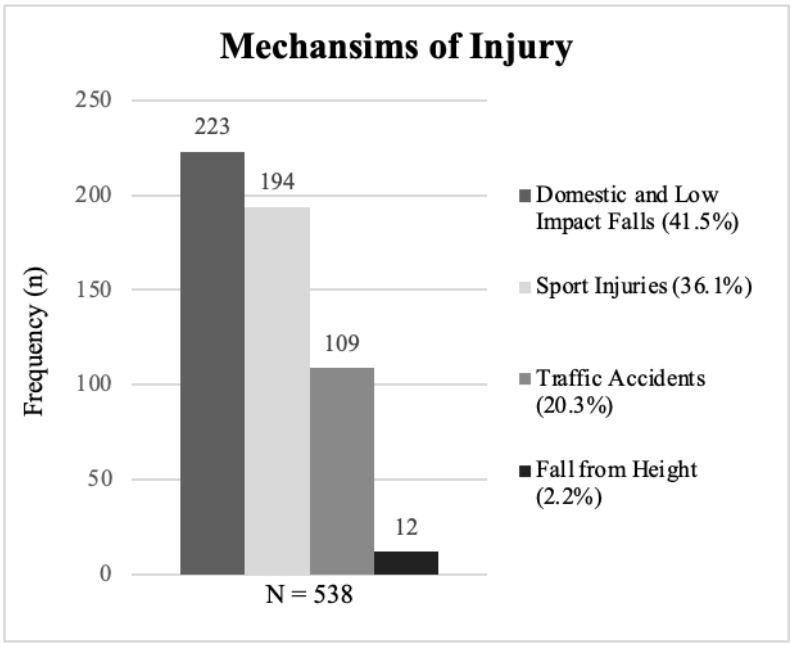

Figure 12: Most Common Mechanisms of Injury Causing Fractures of the Clavicle. N = 538. Domestic and low-impact falls are the primary cause, accounting for 41.5%. Sporting activities were responsible for 36.1% of clavicular fractures. Traffic accidents, including those involving cars, motorcycles, and pedestrians accounted for 20.3%. Fractures resulting from falls from heights occurred in 2.2% of the study population.

Table 4: Frequency of Injury Mechanisms

Mechanism of Injury	**(n)**	**%**
Domestic Falls / Low-Impact Falls	**223**	**41.5**
Sports Activities		
Cycling	121	22.5
Skiing	21	3.9
Football	12	2.2
Horse Riding	11	2.0
Mountain Biking	6	1.1
Ice Hockey	4	0.7
Skating	3	0.6
Hiking	3	0.6
American / Australian Football	2	0.4
Combat Sports	2	0.4
Snowboarding	1	0.2
Running	1	0.2
Kite Surfing	1	0.2
Surfing	1	0.2
Wake Boarding	1	0.2
Sports Injury (unspecified)	4	0.7
Total	**194**	**36.1**
Traffic Accidents		
Car Accident	37	6,9
Motorcycle Accident	50	9.3
Pedestrian Involved in Traffic Accident	22	4.1
Total	**109**	**20.3**
Fall From Height	**12**	**2.2**
Total	**538**	**100**

Polytrauma

Within the cohort of 575 patients, 26 individuals sustained a clavicular fracture as part of polytrauma, contributing to 4.5% of the total patient group. (Figure 13)

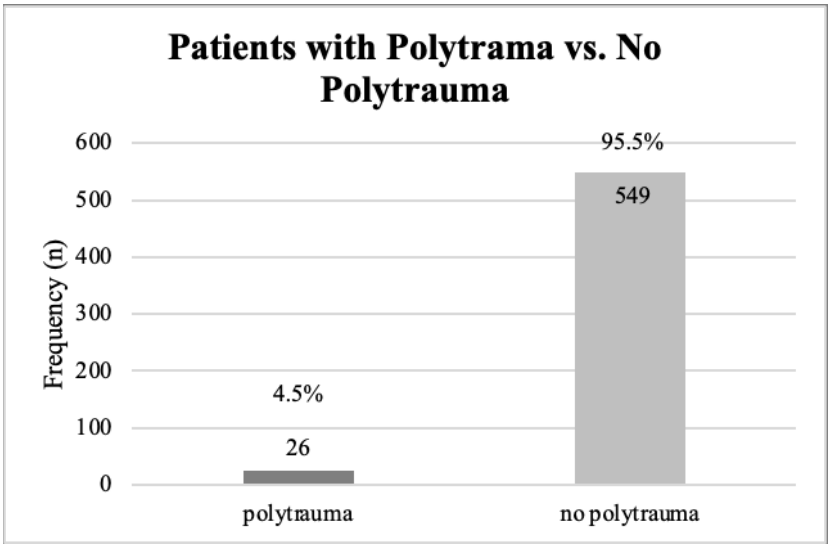

Figure 13: Distribution of Polytrauma Cases among the Study Population. N=575. A total of 26 patients experienced clavicular fractures in the context of polytrauma, representing 4.5% of the entire patient cohort.

Among these, commonly observed concomitant injuries to the upper body region included multiple rib fractures (69.2%), severe head trauma (65.4%), vertebral fractures (50.0%), pulmonary contusion (30.8%), pneumothorax (23.1%) and hemothorax (19.2%). Additionally, three patients sustained concomitant scapular fractures, while two patients also sustained humerus fractures. (Table 5)

Table 5: Frequency of Concomitant Injuries in Polytrauma Patients. Each percentage represents the proportion of polytrauma patients (N=26), meaning that some patients may had multiple injuries.

Concomitant Injuries	Injury Frequency (n) in 26 Patients	Injury Amount (%) in 26 Patients
Serial Rip Fractures	18	69.2
Severe Head Trauma	17	65.4
Vertebral Fractures	13	50.0
Pulmonary Contusion	8	30.8
Fracture of Sternum	6	23.1
Pneumothorax	6	23.1
Hemothorax	5	19.2
Scapula Fracture	3	11.5
Humerus Fracture	2	7.7
(n) total	**78**	

3.1.3 Patient-Related Parameters

Allergy

Information regarding patients' allergies was identified in 409 medical records. Among these, 90 patients had documented allergies, equivalent to 22% of the total patient cohort. (Figure 14)

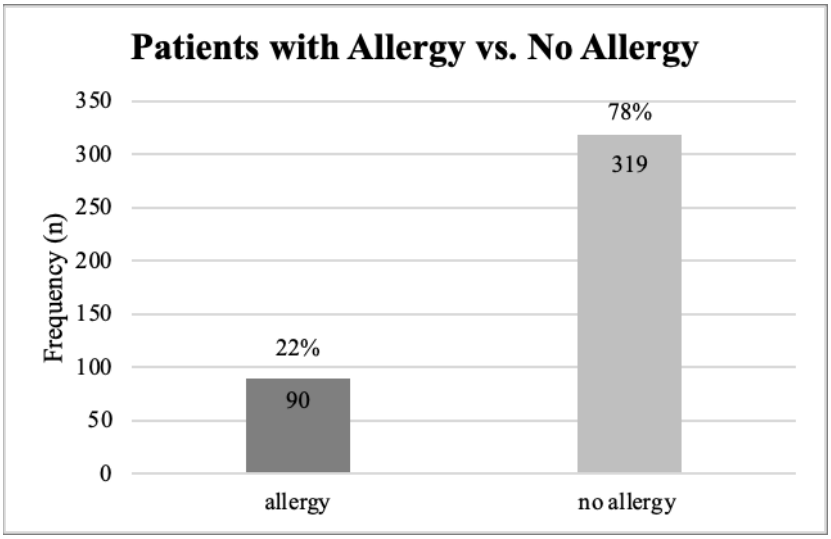

Figure 14: Number of Patients with Allergy vs. no Allergy. N=409. A total of 90 patient had one or several known allergies documented, equivalent to 22% of the investigated patient cohort.

A total of 29 distinct allergy types have been determined that can be categorized into the following 6 groups in descending order of frequency:

1. Pollen/grass/house dust/animal hair/and/or mold (26.7%)
2. Antibiotics (24.4%)
3. Painkillers (17.8%)
4. Hymenoptera and insect venom (12.2%)
5. Contrast agents/iodine (11.1%)
6. Other medication (4.4%)

In the "pollen/grass/house dust/animal hair/and/or mold" group, these allergies occurred either individually or in combination in individual patients. Among the antibiotics group, penicillin was the most common agent on whom an allergy had been reported on, affecting 20.9% of patients. In the painkillers group, NSAIDs including Diclofenac and mefenamic acid were responsible for most allergies (7.8%).

A further subgroup named “others” accounted for 24.4% and encompasses less common allergy types, including nickel, plaster, histamine, fructose, and others. It´s important to note that individual patients within the cohort may have a combination of several types of allergies. The frequency of each allergy is illustrated in Figure 15. The detailed data set including all distinct subtypes regarding categories is presented in Table 6.

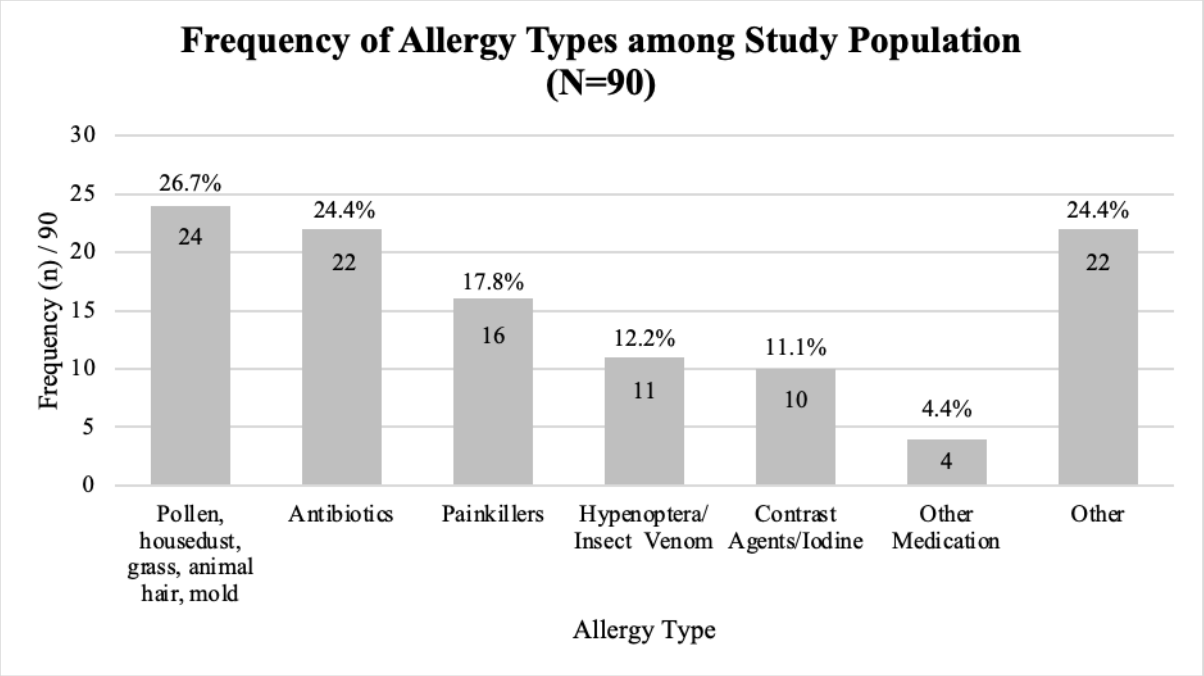

Figure 15: Frequency of Allergy Types among the Study Population. (N=90). A total of 90 medical records provided information about patients’ allergy status and allergy types. Individual patients may have multiple allergies. Pollen, house dust, grass, animal hair, and mold and may occur solely or as a combination in one individual. These allergies were the most common documented (26.7%) followed by antibiotics (24.4%), and painkillers (17.8%).

Table 6: Detailed Frequency of Allergy Types among the Study Population including all Allergy Subtypes. The frequency refers to the occurrence of distinct allergy types in the population with known allergies (N=90). Individual patients may have multiple allergies. Pollen, house dust, grass, animal hair, and mold may occur either solely or as a combination.

Allergy Type	Frequency (n) in 90 patients	Frequency (%) in 90 patients
Pollen, House Dust, Grass, Animal Hair, and/or Mold	**24**	**26.7**
Antibiotics	**Total: 22**	**24.4**
Penicillin	15	16.7
Augmentin	3	3.3
Sulfonamide	1	1.1
Flurochinolone (Zoroxin)	1	1.1
Macrolide (Josalid)	1	1.1
Ampicillin	1	1.1
Painkillers	**Total: 16**	**17.8**
Diclofenac (NSAID)	6	6.7
Mefenamic Acid (NSAID)	1	1.1
Novalgin (Metamizole)	3	3.3
Acetylsalicylic Acid	4	4.4
Opioids	2	2.2
Other Medication	**Total: 4**	**4.4**
ACE-Inhibitor	1	1.1
Enoxaparin	1	1.1
Ezetrol (Ezetimibe)	1	1.1
Pramipexol (Dopamine Agonist)	1	1.1
Contrast Agents and Iodine	**Total: 10**	**12.2**
Contrast Agents	5	5.6
Iodine	3	3.3
Contrast Agent and Iodine	2	2.2

Hypenoptera/ Insect Venom	**11**	**12,2**
Other	**Total: 22**	**24.4**
Nickel	7	7.8
Plaster	4	4.4
Histamine	2	2.2
Lactose	2	2.2
Tetanus serum	1	1.1
Thiomersal	1	1.1
Strawberries	1	1.1
Oranges	1	1.1
Fructose	1	1.1
Fish	1	1.1
Propolis	1	1.1
(n) total	**109**	

Anticoagulation

Data regarding the use of anticoagulation at the time of fracture was identified in medical records of 400 patients. Out of these, 101 patients (25.2%) had been prescribed anticoagulant medication. (Figure 16)

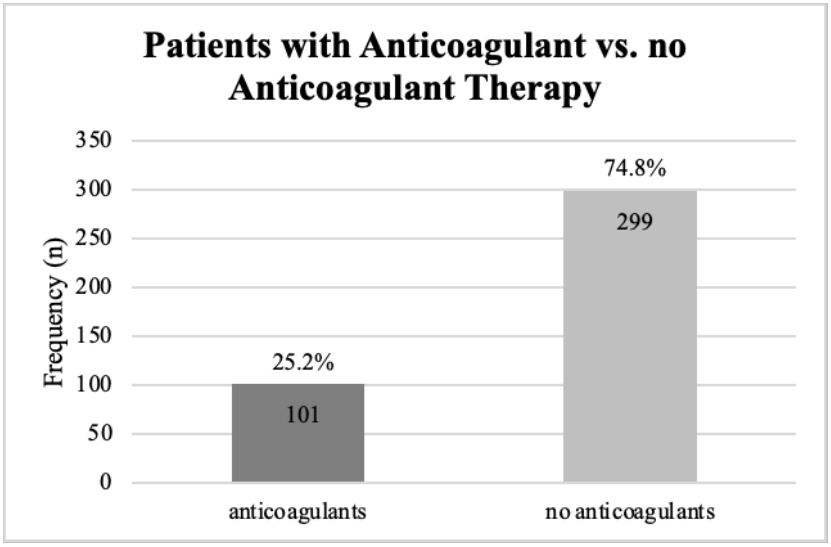

Figure 16: Number of Patients Prescribed Anticoagulants vs. no Anticoagulants. N=400. Anticoagulants had been prescribed for 101 patients, constituting 25.2% of the reviewed medical records.

Among the patients with positive history of anticoagulants, the drug most commonly prescribed was low-dose aspirin (46.5%), followed by coumarin derivates, e.g., Marcoumar (17.8%), direct oral anticoagulants (14.9%, including Xarelto, Lixiana, Eliquis, and Pradaxa) and clopidogrel (11.9%). Additionally, three out of 101 patients received dual antiplatelet therapy, combining low-dose aspirin with either Plavix or Marcoumar. Two patients were treated with low molecular weight heparin (Enoxaparin [Lovenox]), while another two patients had a documented history of continuous anticoagulation use without documentation of the specific drug prescribed. (Figure 17)

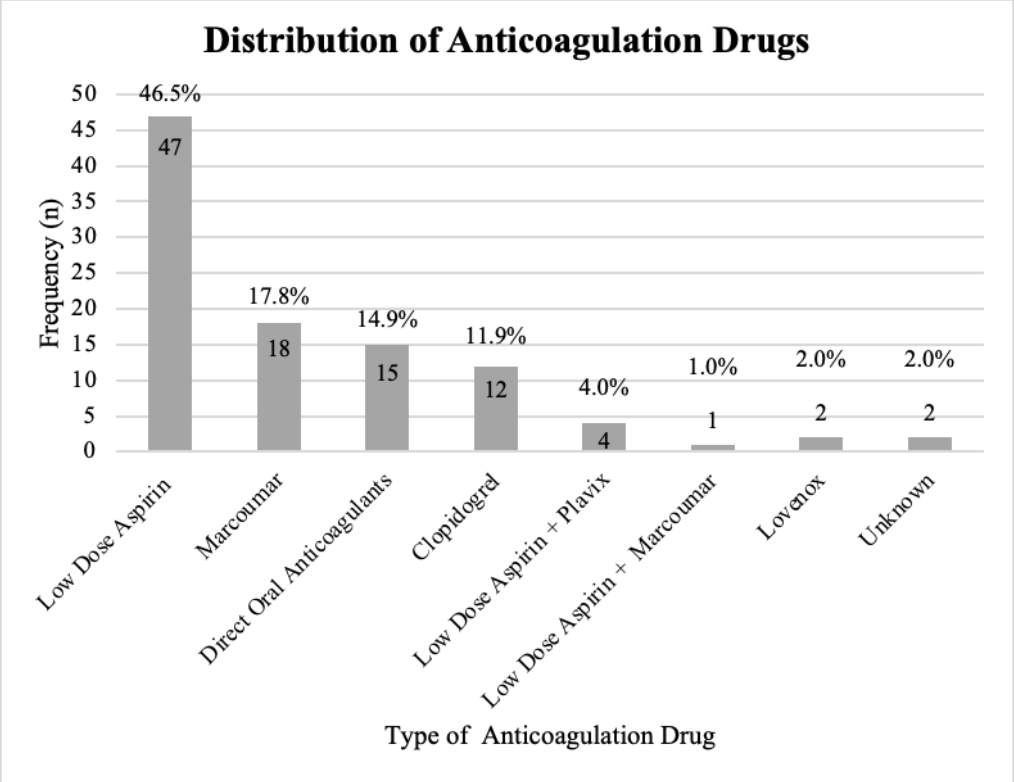

Figure 17: Distribution of Anticoagulation Drugs among the Study population. N=101. Low-dose aspirin is the most commonly used anticoagulant (46.5%). 'Unknown' indicates regular anticoagulation medication use with unspecific drug details.

Hypertension

In 395 patients, information on presence of hypertension was available. Of these, 150 had hypertension, representing 38.0% of the investigated patients. (Figure 18)

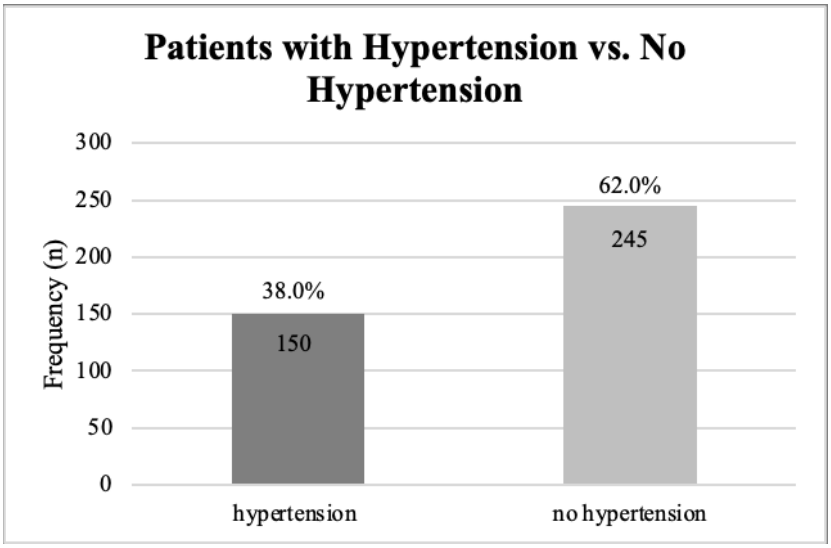

Figure 18: Number of Patients with Hypertension vs. No Hypertension. N=395. Hypertension was identified in 150 patients, amounting for 38.0% of all patients.

Renal Insufficiency

Data on renal insufficiency available in 391 patients. Of these, 38 (9.7%) had renal insufficiency, while the remaining 353 patients (90.3%) had normal kidney function. (Figure 19)

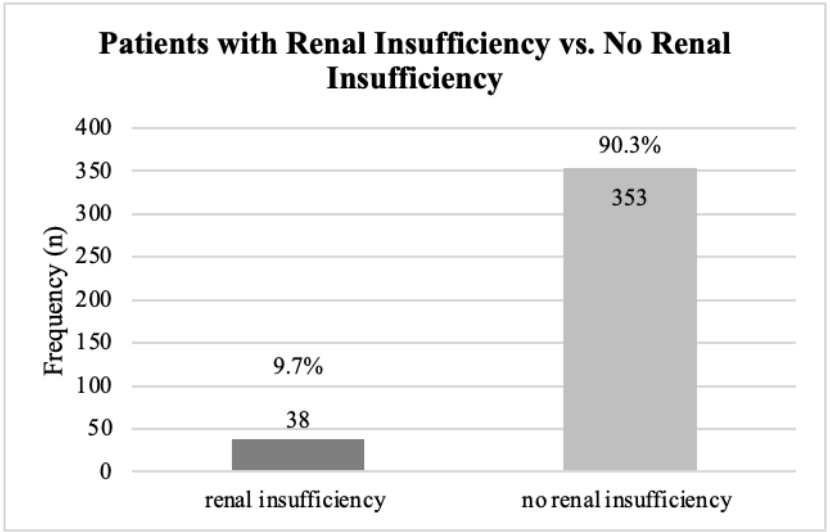

Figure 19: Number of Patients with Renal Insufficiency vs. No Renal Insufficiency. N=391. Out of 391 patients, 38 (9.7%) had confirmed renal insufficiency.

Diabetes Mellitus

Data on presence of diabetes mellitus was ascertainable in 390 patients. Among these, 32 patients (8.2%) had been diagnosed with diabetes. (Figure 20)

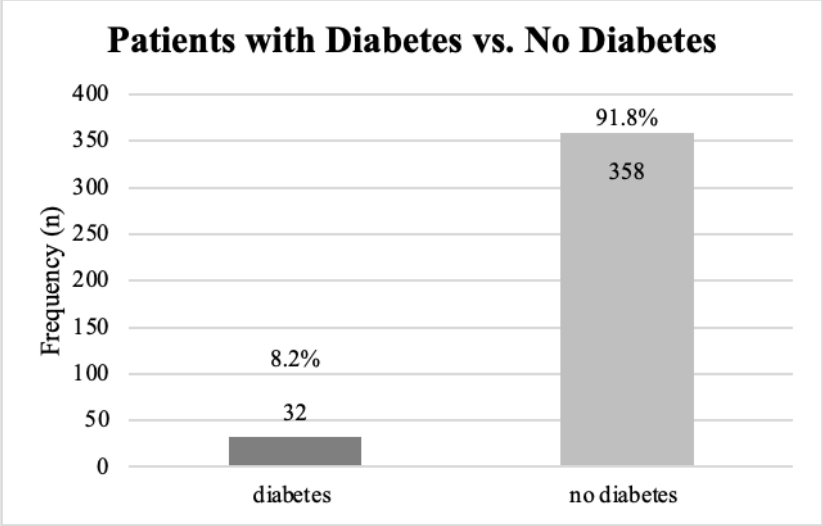

Figure 20: Number of Patients with Diabetes vs. No Diabetes. N=390. The prevalence of diabetes among these patients was 8.2%.

Osteoporosis

Of 391 patients with information on osteoporosis was available, in 28 had a positive history, accounting for 7.2%. (Figure 21)

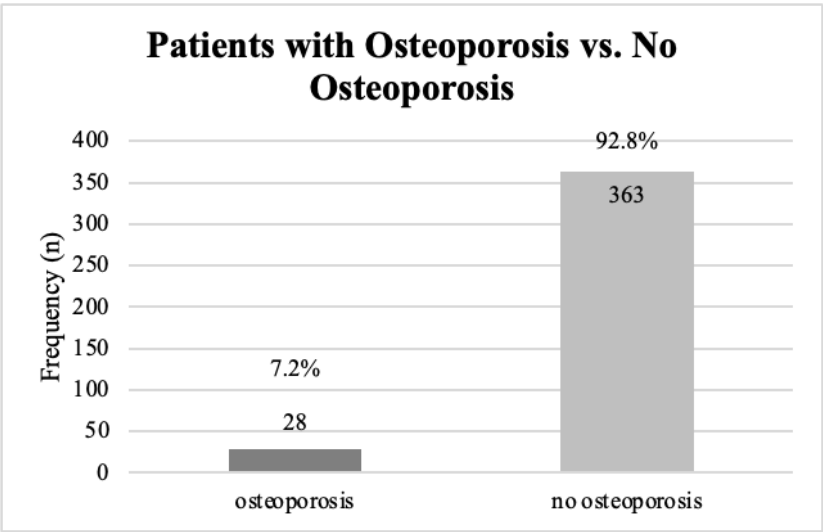

Figure 21: Number of Patients with Osteoporosis vs. No Osteoporosis. N=391. The prevalence rate of osteoporosis was 7.2%. among the patient cohort.

Rheumatic Disease

Out of 393 patients with information available on rheumatic diseases, history was positive in 14 patients (3.6%). (Figure 22)

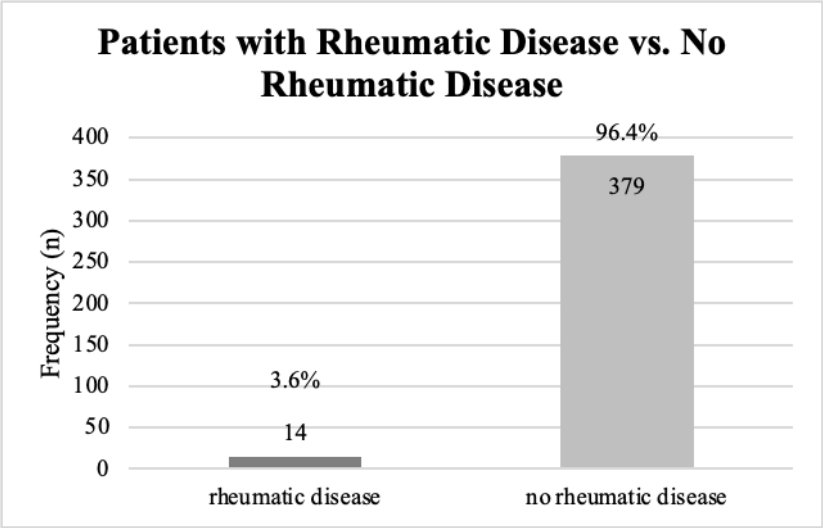

Figure 22: Number of Patients with Rheumatic Disease and Those without. N=393. The prevalence of rheumatic diseases among the study population was 3.6%.

Nicotine Abuse

Information on smoking history was available in 278 patients. Among them, 77 (27.7 %) had a documented history of smoking, while the remaining 72.3% were non-smokers. (Figure 23) Among the cohort of smokers, the mean figure of pack-years was 38.9 (± 37.2).

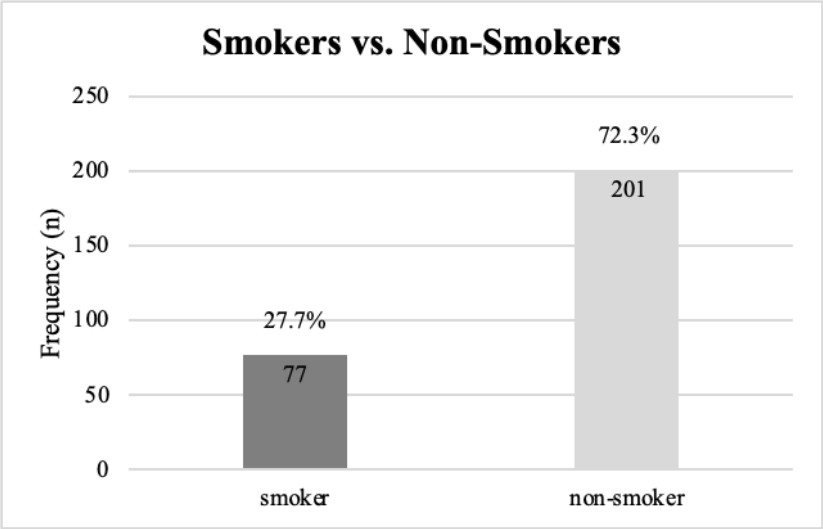

Figure 23: Distribution of Smokers and Non-Smokers. N=278. The data revealed that 27.7% of the study cohort had a history of smoking.

Alcohol Consumption

Among the 257 patients with information on alcohol consumption available, 148 (57.6%) had a positive history, indicating that more than half of the cohort regularly consumes alcohol. (Figure 24)

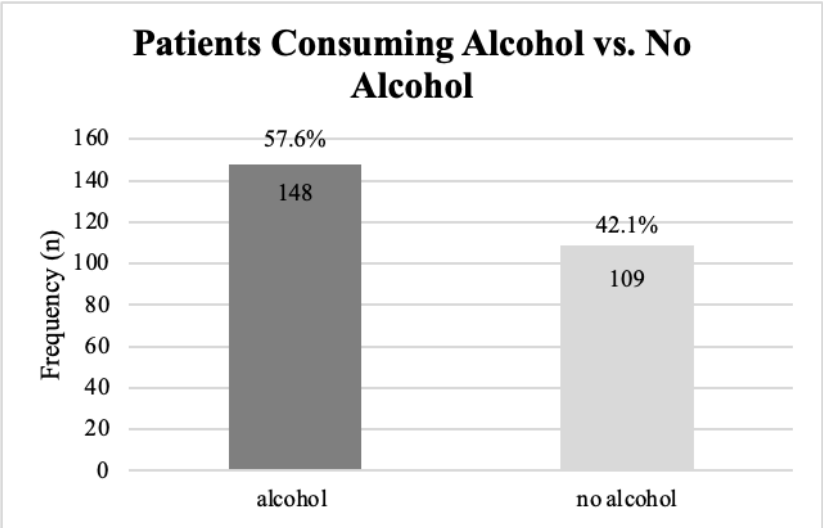

Figure 24: Distribution of Alcohol Consumption. N=257. Alcohol consumption was reported in 57.6% of the total cohort.

ASA Score

The ASA score had been assessed in 245 patients within the study population (although none of the patients had undergone surgery for clavicular fractures). The majority of patients fell into ASA category 2, representing those with mild systemic diseases (40.8%). ASA category 3 (30.2%) was the next most common, while ASA 1 (18.8%) and ASA 4 (6.1%) were least frequent. ASA 0 accounted for 3.7% and only one patient (0.4%) was classified as ASA 5. (Figure 25)

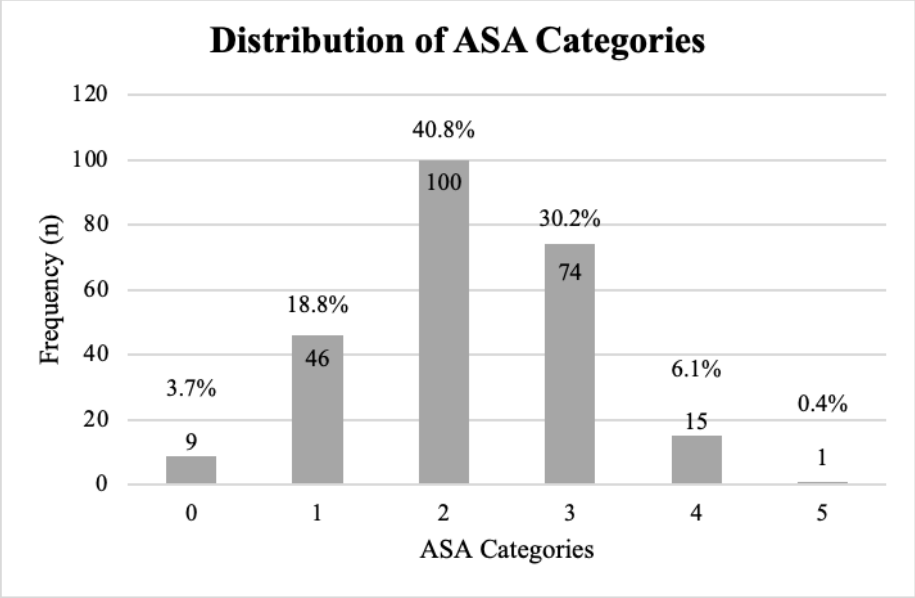

Figure 25: Distribution of ASA Score in the Study Population. N=245. ASA category 2 had the highest representation at 40.8%.

Summary of Patient-Related Risk Factors

Among the patient variables of interest, alcohol consumption had the highest prevalence of 57.6%, followed by hypertension (38.0%). Nicotine abuse was documented in 27.7% of patient, and anticoagulation history was positive in 25.2%. Allergies were reported in 22.0% of patients. Renal insufficiency was found in 9.7% of cases. Diabetes and osteoporosis had a prevalence of 8.2% and 7.2%, respectively. Furthermore, polytrauma was observed in 4.5% of cases. Prevalence of rheumatic diseases was 3.6%. (Figure 26)

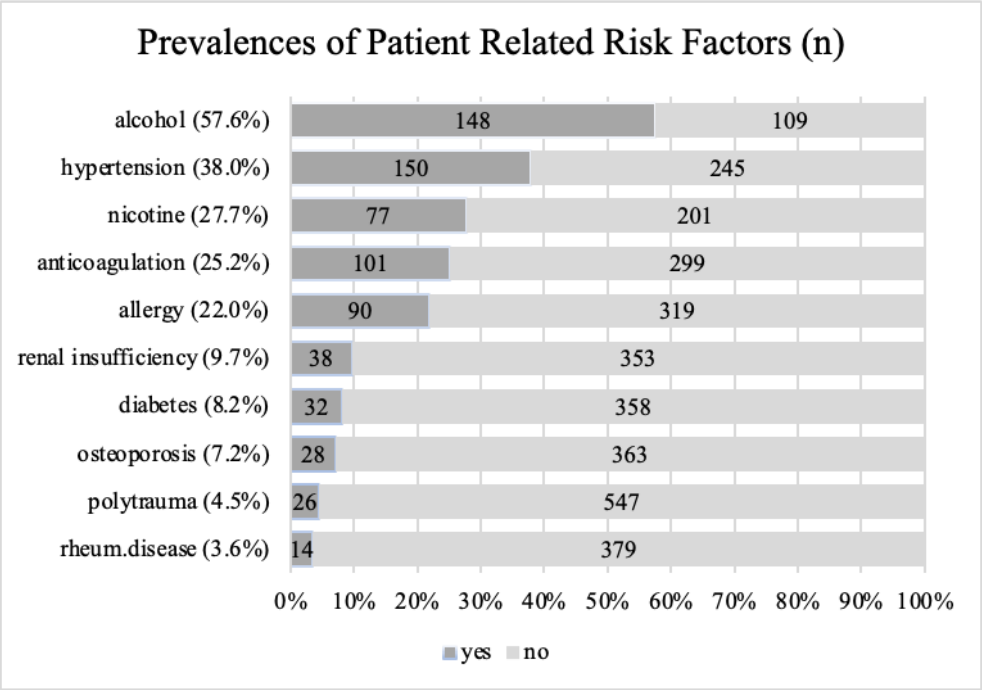

Figure 26: Summary of Patient-Related Risk Factors. This figure displays the prevalence of different parameters. The prevalence rate (%) follows each listed variable in descending order. "Yes" indicates the presence of the respective risk factor, whereas "no" signifies its absence.

Reasons for Pursuing Conservative Treatment

Medical records of 323 patients documented several reasons for choosing conservative treatment. The most common reason for non-operative therapy was a non-displaced fracture (35.6%), followed by fractures with minimal dislocation (22.6%). Clavicular fractures with fragments in an acceptable position accounted for 19.5% of cases in whom surgical therapy was not deemed necessary. In case the fracture displayed noticeable displacement but posed no evident risk of skin perforation, a conservative treatment approach was sometimes likewise chosen (4.0%). Altogether, 14.2% of patients chose conservative therapy by themselves over optional or recommended surgical fracture fixation by the treating physician. Additionally, 3.1% of clavicular fractures were initially managed conservatively to assess whether the fracture would maintain its position during non-operative treatment. All of these patients continued on non-operative treatment until bone healing. In two cases (0.6% of the total), conservative management was the only viable option due to the patients' unsuitability for general anesthesia owing to prevailing

comorbidities. Lastly, one patient (0.3%) received non-operative treatment due to advanced age. (Figure 27)

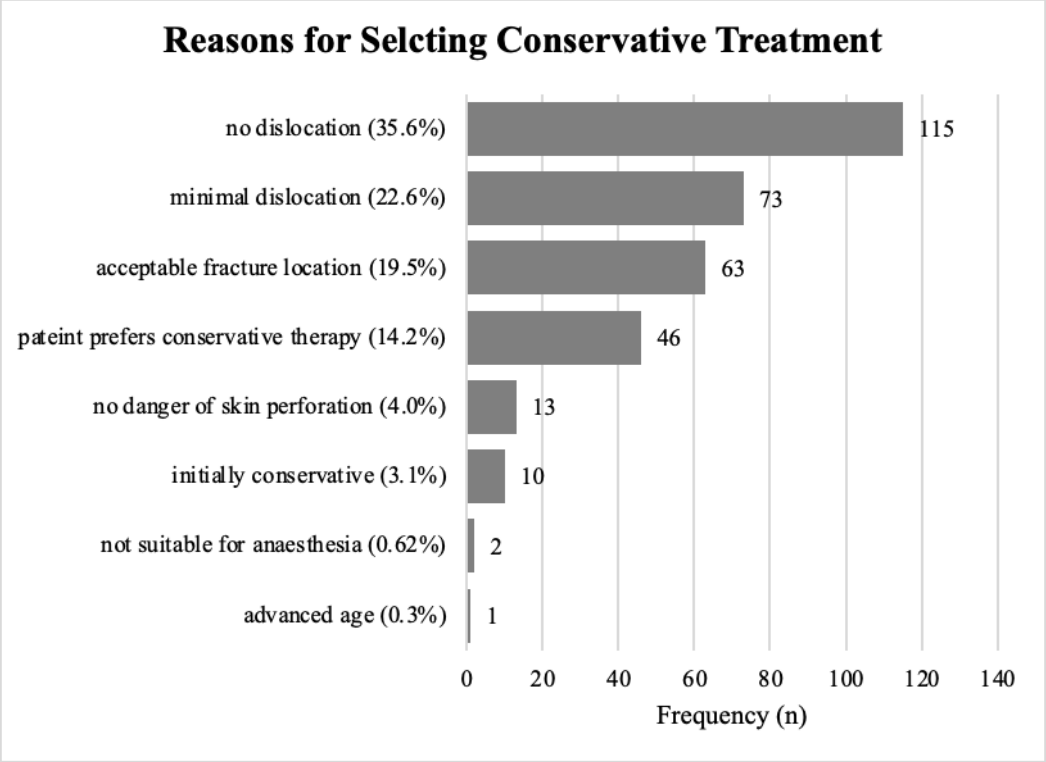

Figure 27: Reasons for Selecting Conservative Treatment of Clavicular Fractures. N=323. Non-displaced fractures were the most common indication for conservative treatment (25.6%). Minimal dislocation and fractures with fragments in an acceptable position were also frequent reasons for opting for non-operative therapy, accounting for 22.6% and 19.5%, respectively.

Conservative Treatment Type

Most patients (57.9%) received treatment with figure-of-eight brace, while 40.1% were treated with a sling (40.1%). Furthermore, nine patients did not receive any treatment device, and two patients alternated between a figure-of-eight brace and a sling throughout the follow-up period. (N=563). (Figure 28)

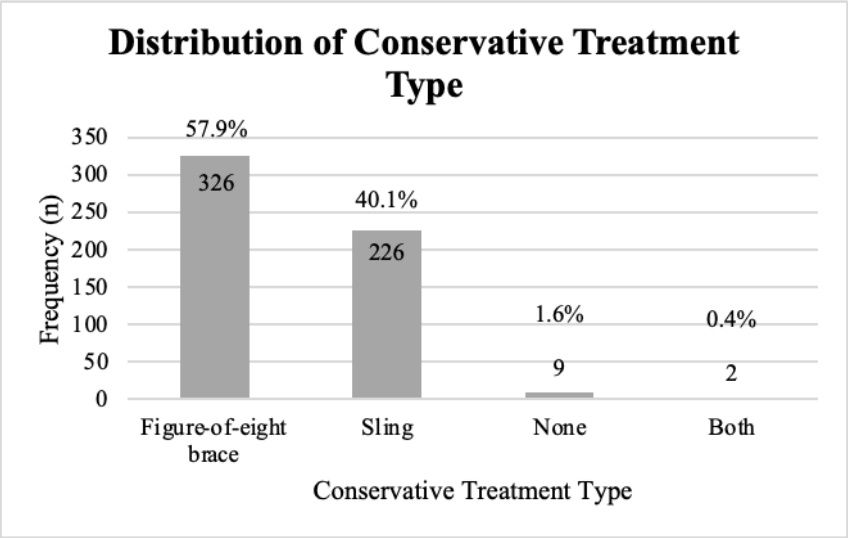

Figure 28: Distribution of Conservative Treatment Type. N=563.

3.4 Description of Follow-Up

Patients had their first follow-up appointment at a median of 7 days (IQR: 6 – 13 days; n=575), followed by a second at a median of 19 days (IQR: 14 – 28 days; n=575). Subsequently, 506 patients attended a third appointment, scheduled at a median of 31 days (IQR: 26 – 42 days), and 337 patients attended a fourth appointment, scheduled at a median of 43 days (IQR: 36 – 56 days) after the date of injury. The most recent follow-up occurred at a median of 49 days (IQR: 38 – 81 days; n=575).

Healing of fractures was observed at a median of 44 days (IQR: 35 – 64 days, n=543).

The most common symptoms among patients who developed a nonunion included mild to moderate pain, pain during movement, tenderness on palpation, and swelling of the affected arm and fingers. Additionally, one patient reported hyperesthesia in the inner side of the upper arm and fingers, corresponding to the median nerve supply region.

3.5 Rates of Clavicular Nonunion

Throughout the present study, we adhered to the definitions provided by Simpson et al., Wilkins et al., Manske et al., and O'Neill et al. to define clavicular nonunions. Clavicular nonunion was defined as the absence of bony union in the clavicle four months after the initial injury. (155–158) Based on this definition, our analysis revealed 32 patients within the entire cohort developing clavicular nonunion, accounting for 5.6% of all cases. (N=575) (Figure 29)

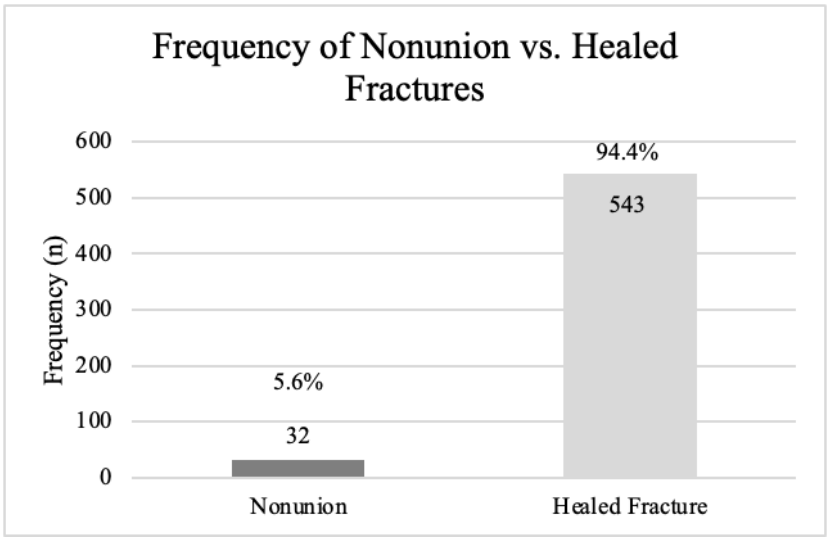

Figure 29 Frequency of Nonunions among the Study Population. N=575. Clavicular nonunion was found in 32 (5.6%) of all cases.

Of these, a total of 16 patients (2.8%) underwent specific treatment: two nonunions underwent extracorporeal shock wave therapy, three patients underwent physiotherapy and 11 patients (1.9%) required surgical treatment. Of those surgically managed, 10 were treated with plate osteosynthesis with or without cancellous bone graft, and one received pin fixation.

The nonunion rate among females was 7.6%, slightly higher than the one observed among males (4.4%). (Figure 30) Furthermore, nonunion rates exceeding 10% were observed in specific patient groups, including those with polytrauma (11.5%), a smoking history (13.0%), allergies (13.3%), and renal insufficiency (15.8%). (Tables 7 - 9)

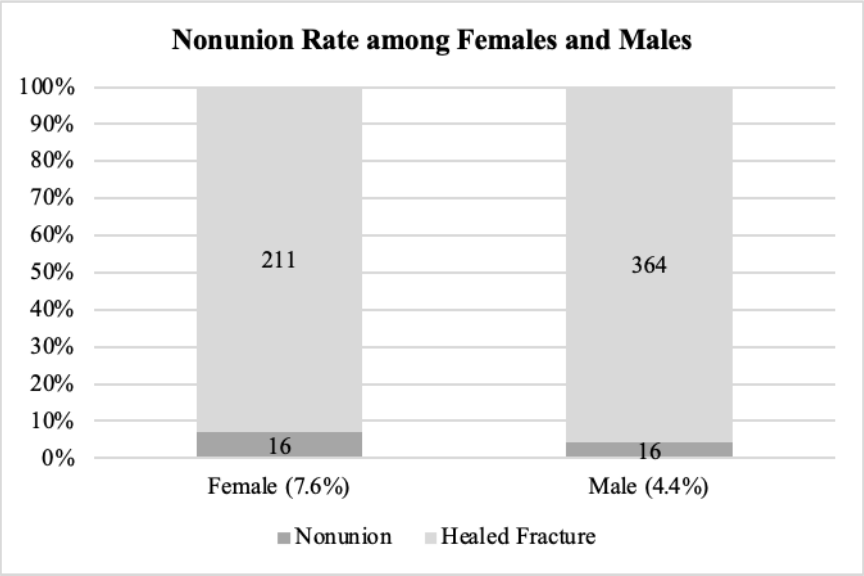

Figure 30: Comparison of Nonunion rates of Females and Males.

Age Distribution

Nonunion rates varied among different age groups. There was a slight increase in patients aged 40 to 49 years, with a rate of 6.7%, and among those aged 60 to 69 years with a rate of 6.4%. The highest rate was observed in the age group of 70 to 79 years, where it reached 10.3%. (Figure 31; Table 7)

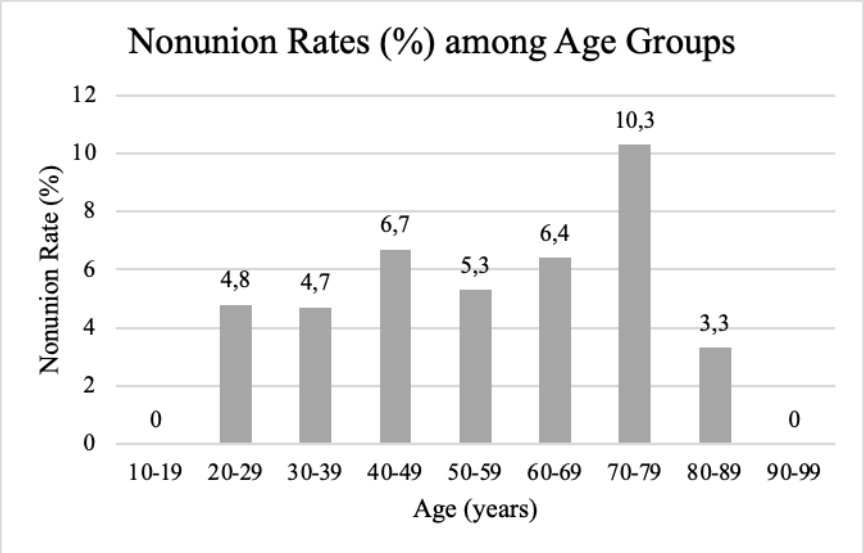

Figure 31: Nonunion Rates (%) among different Age Groups.

Fracture Features and Nonunion

Nonunion occurred most frequently in mid-shaft fractures, where the nonunion rate was 6.0%. The nonunion rate of lateral fractures was lower, at 5.5%. Among medial fractures, no cases of nonunion were observed. (Figure 32; Table 8)

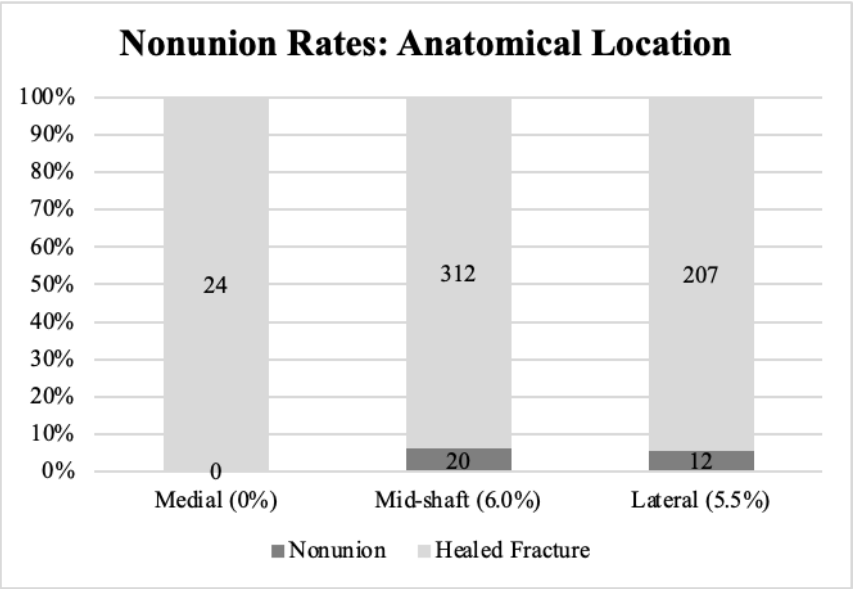

Figure 32: Distribution of Nonunions regarding anatomical location.

Among the investigated fracture patterns, complex fractures with multiple fragments exhibited a slightly higher nonunion rate of 6.7%. Simple fractures were more likely to lead to clavicular nonunion compared to wedge fractures (5.5% vs. 5.0%). (Table 8)

In cases where there was dislocation by more than one clavicular cortex, the nonunion rate was 7.9%– the highest rate in this category. More severe dislocation by half and the entire clavicular thickness led to nonunion almost as frequently (6.5% vs. 6.3%). Conversely, patients with no or minimal fragment dislocation by one cortex had lower rates of nonunion (3.9% and 3.7%). (Table 8)

Additionally, initial shortening of more than 2 cm showed a lower nonunion rate (5.1%) compared to initial shortening of less than 2 cm (6.4%). (Table 8)

In cases where patients were treated with simple sling, a nonunion rate of 6.6% was observed, while the nonunion rate for those treated with figure-of-eight bandage was lower at 4.6%. (Table 8)

Summaries of further demographic characteristics and risk factors of patients with and without clavicular nonunions can be found in Tables 7-10.

Table 7: Demographic Summary of Patients With and Without Clavicular Nonunion.

Characteristic	N (%)	
	Total	**Nonunion**
Patients	575 (100)	32 (5.6)
Patient age at fracture, years (N=575)		
10-19	15 (2.6)	0 (0)
20-29	84 (14.6)	4 (4.8)
30-39	85 (14.8)	4 (4.7)
40-49	89 (15.5)	6 (6.7)
50-59	95 (16.5)	5 (5.3)
60-69	63 (11.0)	4 (6.4)
70-79	68 (11.8)	7 (10.3)
80-89	60 (10.4)	2 (3.3)
90-99	16 (2.8)	0 (0)
Gender (N=575)		
Male	364 (63.3)	16 (4.4)
Female	211 (36.7)	16 (7.6)
BMI (N=352)		
15-19	19 (5.4)	2 (10.5)
20-25	215 (61.1)	20 (9.3)
26-30	86 (24.4)	3 (3.5)
31-35	26 (7.4)	0 (0)
36-40	4 (1.1)	1 (25.0)
>40	2 (0.6)	1 (50.0)

Table 8: Summary of Fracture Features of Patients With and Without Clavicular Nonunion.

Characteristic	N (%)	
	Total	**Nonunion**
Patients	575 (100)	32 (5.6)
Fracture Location (N=575)		
Medial	24 (4.2)	0 (0)
Mid-shaft	332 (57.7)	20 (6.0)
Lateral	219 (38.1)	12 (5.5)
Fracture Pattern (N=575)		
Simple	367 (63.8)	20 (5.5)
Wedge	119 (20.7)	6 (5.0)
Complex (many fragments)	89 (15.5)	6 (6.7)
Fragment Dislocation (N=575)		
None	104 (18.1)	4 (3.9)
By 1 cortex	107 (18.6)	4 (3.7)
By > 1 cortex	89 (15.5)	7 (7.9)
By half clavicular thickness	139 (24.2)	9 (6.5)
By entire clavicular thickness	136 (23.7)	8 (6.3)
Initial shortening (N=180)		
< 2 cm	141 (78.3)	9 (6.4)
> 2 cm	39 (21.7)	2 (5.1)
Polytrauma (N=573)		
yes	26 (4.5)	3 (11.5)
no	547 (95.5)	28 (5.1)
Conservative Type (N=563)		
Sling	226 (40.1)	15 (6.6)
Figure-of-eight brace	326 (57.9)	15 (4.6)
None	9 (1.6)	1 (11.1)
Both	2 (0.4)	0 (0)

Table 9: Summary of Patient-Related Risk Factors among Patients With and Without Clavicular Nonunion.

Risk Factor	N (%)	
	Total	**Nonunion**
Patients	575 (100)	32 (5.6)
Allergy (N=409)		
yes	90 (22.0)	12 (13.3)
no	319 (78.0)	16 (5.0)
Hypertension (N=395)		
yes	150 (38.0)	10 (6.7)
no	245 (62.0)	19 (7.8)
Renal insufficiency (N=391)		
yes	38 (9.7)	6 (15.8)
no	353 (90.3)	23 (6.5)
Diabetes mellitus (N=390)		
yes	32 (8.2)	3 (9.4)
no	358 (91.8)	26 (7.3)
Osteoporosis (N=391)		
yes	28 (7.2)	3 (10.7)
no	363 (92.8)	26 (7.2)
Rheumatic disease (N=393)		
yes	14 (3.6)	1 (7.1)
no	379 (96.4)	28 (7.4)
Anticoagulation (N=400)		
yes	101 (25.2)	7 (6.9)
no	299 (74.8)	21 (7.0)
Nicotine (N=278)		
yes	77 (27.7)	10 (13.0)
no	201 (72.3)	14 (7.0)
Alcohol (N=257)		
yes	148 (57.6)	14 (9.5)
no	109 (42.1)	10 (9.2)

Table 10: Summary of ASA-Score Distribution in Patients With and Without Clavicular Nonunion.

	N (%)	
	Total	**Nonunion**
Patients	575 (100)	32 (5.6)
ASA Score (N=245)		
0	9 (3.7)	1 (11.1)
1	46 (18.8)	3 (6.5)
2	100 (40.8)	8 (8.0)
3	74 (30.2)	7 (9.5)
4	15 (6.1)	2 (13.3)
5	1 (0.4)	0 (0)

3.6 Associations Between Risk Factors and Clavicular Nonunion

The analysis of p-values revealed significant associations between clavicular nonunion and certain risk factors, specifically allergies (p-value=0.006), renal insufficiency (p-value=0.038) and initial shortening (0.033). Although the p-values for the female gender (0.108), polytrauma (0.157), and smoking (0.110) were relatively low, none of these factors reached statistical significance. P-values for all variables investigated are provided in Table 11.

Table 11: Summary of P Values for Investigated Variables

Risk Factor	P Value
Female gender	0.108
Age	0.593
BMI	0.841
Fracture Side	0.237
Fracture Location	0.461
Fracture Pattern	0.835
Fragment Dislocation	0.623
Initial Shortening	**0.033**
Polytrauma	0.157
Allergy	**0.006**
Anticoagulation	0.975
Hypertension	0.687
Renal insufficiency	**0.038**
Diabetes mellitus	0.663
Osteoporosis	0.490
Rheumatic disease	0.973
Nicotine	0.110
Alcohol	0.938
ASA Score	0.965
Cons. Treatment Type	0.631

The univariate and multivariate analysis aimed to determine the odds ratios (ORs) associated with clavicular nonunion and patient-related risk factors. (Table 12 and 13) Two risk factors were independently associated with higher nonunion risk: renal insufficiency (OR, 3.34; 95% CI, 1.09-10.21) and allergy (OR, 3.12; 95% CI, 1.34-7.28). This implies that patients with these conditions are about three times more likely to develop nonunion. However, parameters such as female gender (OR, 1.61; 95% CI, 0.68-3.85) and polytrauma (OR, 2.04; 95% CI, 0.41-10.08) showed potential association with nonunion but showed no significant association with nonunion ($p > 0.05$). Additionally, patient age did not demonstrate a significant association with risk of nonunion. (OR, 0.99; 95% CI, 0.97-1.01). (Table 12)

Table 12: Multivariate Analysis. Summary and Odds Ratios of Patient-Related Risk Factors.

	N (%)			OR (95% CI)	
Risk Factor	**Fractures**	**Healed**	**Nonunion**	**Multivariate**	**P Value**
Age	-	-	-	0.99 (0.97-1.01)	0.593
Female gender	211 (36.7)	195	16	1.61 (0.68-3.85)	0.108
Renal insuff.	38 (9.7)	32	6	3.34 (1.09-10.21)	**0.038**
Allergy	90 (22.0)	88	12	3.12 (1.34-7.28)	**0.006**
Polytrauma	26 (4.5)	23	3	2.04 (0.41-10.08)	0.157
Baseline Odds	-	-	-	0.05 (0.01-0.02)	-
Abbreviations: OR = Odds Ratio; CI = Confidence Interval, Insuff. = Insufficiency					

Table 13: Univariate Analysis: Summary and Odds Ratios of Patient-Related Risk Factors.

	N (%)			OR (95% CI)	
Risk Factor	**Fractures**	**Healed**	**Nonunion**	**Univariate**	**P Value**
Age	-	-	-	1.00 (0.99-1.02)	0.593
Female gender	211 (36.7)	195	16	1.78 (0.87-3.65)	0.108
BMI	-	-	-	0.99 (0.90-1.09)	0.841
Fracture side	-	-	-	1.54 (0.75-3.19)	0.237
Fracture pattern	-	-	-	-	0.835
- Simple	367 (63.8)	347	20	0.92 (0.36-2.35)	-
-Wedge	119 (20.7)	113	6	1.35 (0.53-3.48)	-
-Complex	89 (15.5)	83	6	1	-

Fragment dislocation	-	-	-		0.623
-None	104 (18.1)	100	4	0.97 (0.24-3.99)	-
-By 1 cortex	107 (18.6)	104	4	2.13 (0.60-7.54)	-
-By > 1 cortex	89 (15.5)	82	7	1.73 (0.52-5.78)	-
-By half clavicular thickness	139 (24.2)	130	9	1.25 (0.33-4.79)	-
-By entire clavicular thickness	136 (23.7)	128	8	2.68 (0.57-12.68)	-
Initial shortening	-	-	-	-	**0.033**
< 2cm	141 (78.3)	132	9	1.13 (0.23-5.55)	-
> 2cm	39 (21.7)	37	2	18.5 (0.82-417.15)	-
Renal insuff.	38 (9.7)	32	6	2.69 (1.02-7.09)	**0.038**
Allergy	90 (22.0)	88	12	2.91 (1.32-6.41)	**0.006**
Polytrauma	26 (4.5)	23	3	2.42 (0.68-8.54)	0.157
Nicotine	77 (27.7)	67	10	1.99 (0.84-4.70)	0.110
Anticoagulation	101 (25.2)	94	7	0.96 (0.41-2.39)	0.975
Hypertension	150 (38.0)	140	10	0.85 (0.38-1.88)	0.687
Diabetes Mellitus	32 (8.2)	29	3	1.32 (0.38-4.63)	0.663
Osteoporosis	28 (7.2)	25	3	1.56 (0.44-5.50)	0.490
Rheum. disease	14 (3.6)	13	1	0.96 (0.12-7.64)	0.973
Alcohol	148 (57.6)	134	14	1.03 (0.44-2.42)	0.938
ASA Score	-	-	-	-	0.965
Cons. Type	-	-	-	-	0.631
Simple sling	226 (40.1)	211	15	0.67 (0.14-3.15)	-
Figure-of-8 brace	326 (57.9)	311	15	046 (0.10-2.15)	-
Abbreviations: OR = Odds Ratio; CI = Confidence Interval, Insuff. = Insufficiency					

4 Discussion

4.1 Main Findings

In this retrospective study of conservatively treated clavicular fractures, males had a 1.7 times higher incidence of fractures compared to females. The mean age of conservatively treated patients was 52.1 years (±20.3). Mid-shaft fractures were the most common anatomical type (57.7%), often presenting with a dislocation by half of the clavicular thickness. The most frequent mechanisms of injury included domestic and low-impact falls (41.5%), sports-related injuries (36.1%; with cycling as the leading cause), as well as motorcycle (9.3%) and car accidents (6.9%). Patients with a positive history of polytrauma often experienced concomitant upper-body injuries. In many, these included serial rib fractures (69.2%), severe head trauma (65.4%), vertebral fractures (50.0%), and pulmonary contusion (30.8%). Additionally, pneumothoraces (23.1%), hemothoraces (19.2%), fractures of the sternum (23.1%), and scapula (11.5%) were relatively common concomitant injuries.

The overall nonunion rate of our collective of conservatively treated clavicular fractures was 5.6% (32 of 575 patients), with 1.9% (11 of 575 patients) requiring surgical management. Females had a slightly higher nonunion rate (7.6%) compared to males (4.4%; p-value = 0.108). Among the different age groups, the highest nonunion rate was observed in patients aged 70 to 79 years, reaching 10.3%. Nonunion occurred most frequently in mid-shaft fractures, where the nonunion rate reached 6.0%. In lateral fractures, the nonunion rate was lower, at 5.5%. No cases of nonunion were observed at the medial segment of the clavicle. Fracture-specific characteristics that displayed relatively high nonunion rates included complex fractures with multiple fragments (6.7%), and moderate fragment dislocation by more than one bony cortex (7.9%). Initial shortening of less than 2 cm resulted in a higher nonunion rate (6.4%) compared to initial shortening of more than 2 cm (5.1%).

Slight differences in nonunion rates were observed between two conservative treatment types i.e., simple sling (6.6%) and figure-of-eight bandage (4.6%). Furthermore, nonunion rates exceeded 10% in patient groups with a positive history of smoking, allergies, and renal insufficiency, as well as polytraumatized patients.

Among all investigated risk factors, p-values for allergy (0.006), renal insufficiency (0.038), and initial shortening (0.033) reached statistical significance.

In logistic regression analysis, we found a significant association between clavicular nonunion and two independent risk factors: allergy (OR 3.12; 95% CI 1.34-7.28) and renal insufficiency (OR, 3.34; 95% CI, 1.09-10.21). These findings suggest that patients with these conditions have an approximately three times higher risk of nonunion in comparison to individuals without these conditions. Although initial shortening of > 2 cm, female gender, polytrauma, and smoking showed potential associations, none of these variables achieved statistical significance in predicting nonunion.

4.2 Comparison with Other Studies

Epidemiological Aspects of Clavicular Fractures

Our results are in accordance with previous research indicating that males have a higher likelihood of sustaining clavicular fractures compared to females. However, our study found a gender ratio of 1.7, slightly lower than the ratios of 2 to 3 reported in other studies. (22,23,25,27,35) This difference can be attributed to our focus on conservatively treated fractures only, excluding surgically treated cases. Consequently, the total number of clavicular fractures diagnosed at our institution can be expected to be higher with a greater difference in gender distribution. It is important to note that our study´s scope was conservatively treated clavicular fractures. Therefore, it may not provide a comprehensive epidemiological picture of clavicular fracture ratios and incidences in the general population.

The mean age of patients included in our study was 52 years, being notably higher compared to other studies. In those studies, the mean age ranged from 31 to 48 years. (22,25,27,140) It is worth mentioning that these studies also included younger patients, starting from 13 years onwards (22,25,27), which may have skewed the observed mean age downwards. Additionally, our study excluded all surgically treated cases, which often involved young adults with higher physical demands and a desire to return to work sooner. Moreover, our study was confined to the Department of Orthopaedics and Trauma (Medical University of Graz) focusing primarily on adults, while children and adolescents had been generally treated at the Department of Pediatric and Adolescent Surgery (Medical

University of Graz). All these factors may have contributed to the observed higher mean age of our study collective.

Our findings regarding the anatomical fracture distribution align with previous studies, although we observed a notable shift toward lateral fractures in our study population. Lateral fractures accounted for 38.1% of our study population, surpassing the 10% to 29% range reported in the literature. (21–23,25,27) In contrast, midshaft fractures constituted 57.7% of cases, slightly lower than the 65% - 82% reported by others. (21–23,25,27) This discrepancy may be a result of our higher mean patient age, as lateral clavicular fractures are more common in the elderly population. (21,22) In line with this hypothesis, one study also reported on a higher mean age (51 – 57.5 years) of patients with lateral clavicular fractures compared to those with diaphyseal clavicular fractures (39 - 49 years). (25) Additionally, the incidence of diaphyseal fractures was reported to decrease with ongoing age. (23) The herein observed prevalence of medial clavicular fractures (4.2%) was consistent with literature findings (2% - 4.5%). (21–23,25,27,28)

Overall, we found mechanisms of injuries causing clavicular fractures aligning with literature data: Domestic and low-impact falls have consistently been reported as the most common cause in previous research as well as in our study. (22,27,29) The finding that sportive activities are further leading mechanisms of clavicular injury also aligns with the results of other studies. (21,22,29,34,35) In our study, cycling stands out as one of the most common causes of clavicular fractures as well as in other publications. (22,27,29,34,35) However, the specific percentages of recreational activities causing clavicular fractures can vary. For instance, skiing ranks as the second most common sports-related cause in our study, while in studies from the US, clavicle injuries due to winter sports are less frequent. (33,34) These discrepancies suggest geographical and regional differences among the populations studied. Moreover, our findings are in line with the literature, which also identifies traffic accidents as a significant cause of clavicular fractures. (22,23,25,27)

In the polytrauma patient cohort, common upper body injuries accompanying clavicular fractures included serial rib fractures, severe head trauma, vertebral fractures, scapular fractures as well as thoracic injuries (e.g., pulmonary contusion, fracture of the sternum, pneumothorax, and hemothorax). The data of this study generally correspond with the

findings of other studies investigating patients (with or without sustained polytrauma) with clavicular fractures, reporting on common concomitant injuries of clavicular fractures. (25,27,50,52,243) It is worth noting that our findings as well as other studies suggest that the clavicle serves as a kind of *"gatekeeper"* of the thorax (especially in polytrauma patients), so in case a clavicular fracture is diagnosed, it often indicates the presence of severe thoracic injuries. (243)

Nonunion Rates

Different definitions of clavicular nonunion exist, particularly regarding the time criterion: Typically, a nonunion is defined as unsuccessful bone healing, which varies among authors, occurring between four to nine months after the initial injury. (14,79,154–158,244–246) This variability in definitions makes a cross-study comparison challenging. In this study, we adhered to the definition of clavicular nonunion as the absence of bony union four months after the fracture date. (155–158) The overall observed nonunion rate of 5.6% aligns with previous research, reporting rates ranging from 4% to 7.5%. (22,29,140,157,165,179,246)

The Role of Gender in Clavicular Nonunion

While males generally appear to exhibit a higher risk of nonunion in various anatomical locations (162,165,247), this trend does not seem to be true for clavicular nonunion particularly. Previous research has discovered a higher incidence of clavicular nonunion among females. (140,246), a trend our study aligns with. However, the association between gender and clavicular nonunion has been investigated in several studies, yielding mixed results:

In contrast to the findings above, Liu et al. reported on the highest incidence of clavicular nonunion among young males. (71) They suggested that this finding may be attributed to clavicular fractures being most common among this population. Furthermore, the authors reasoned that high-impact trauma was related to an increased risk for nonunion. (71) Indeed, predominately male, and young patients are involved in traffic or sports-related accidents. (22,23,25,27,33–35)

Additionally, a study by Ban et al. documented a higher occurrence of clavicular nonunion among males with a ratio of 2.7:1. However, this ratio was lower than the gender-based

ratio for clavicular fractures, implying a potentially higher risk of clavicular nonunion among female individuals. (179)

However, female gender has been identified as a relevant and independent risk factor for predicting clavicular nonunion by Robinson et al.in the context of fractures of clavicular mid-shaft. (246) Supporting these findings, Zura et al. revealed male gender as an independent, protective factor for nonunion in clavicular fractures (OR, 0.61; 95% CI, 0.50-0.74), hereby indicating female gender as a risk factor for nonunion. (162) Interesting data was published by another study focusing on factors for nonunion after mid-shaft fractures. Although female gender was revealed as a significant predictive risk factor in bivariate analysis, this significance was lost upon multivariate analysis. (71) However, in other studies, no significant association was found between gender and the development of clavicular nonunion. (79,80,244) Additionally, the study conducted by Robinson et al. revealed no significant association between female gender and nonunions of the lateral clavicle. (246) In our study, female gender showed a potential association with nonunion but did not reach statistical significance. This could be due to random variation among the study cohort, or potential interaction with other parameters that were not attainable from medical records. To establish statistical significance, more data may be needed. At this point, we cannot explain the higher prevalence of nonunion among females. In comparison with existing literature, the relevance of female gender as a risk factor remains uncertain. Further exploration may involve separat investigation of risk factors e.g., for each anatomical location and to gain more insight into whether gender plays a consistent role across all locations.

Influence of Patient Age

Patient age seems to be associated with the development of clavicular nonunion. However, different studies have produced conflicting outcomes. A Scottish study documented notably increased rates of clavicular nonunion among middle-aged patients (35 to 44 years) compared to all the other age groups investigated (8.1% vs. 4.5%). (165) These findings are comparable to our study, as we discovered lower nonunion rates in the age groups 20 to 29 years (4.8%) and 30 to 39 years (4.7%) compared to the middle-aged cohort (40 to 49 years) with a nonunion rate of 6.7%. Additionally, we observed another increase in the nonunion rate among patients aged from 70 to 79 years (10.3%), with a further incline in older age groups. Our data suggests a bimodal distribution pattern of nonunions with

regards to age. However, the relatively small number of nonunions per age cohort (ranging from 0 to 7) has to be taken into consideration when interpreting the results. In contrast to these findings, another study reported the highest number of clavicular nonunion among relatively young patients, predominately males, compared to the elderly population. (71) Supporting this observation, Zura et al. discovered decreasing rates of nonunion with advancing age when studying various fractures, not particularly those involving clavicle. (168) In opposition to these observations, Robinson et al. identified advancing age as an independent risk factor for nonunion in conservatively treated lateral as well as diaphyseal clavicular fractures. (246) However, other studies only partly agree or disagree with these results: For instance, in a study focusing on diaphyseal fractures, age was revealed as a risk factor for nonunion in bivariate analysis, but not in multivariate regression analysis. (71) Furthermore, in a study by Nowak et al., age was identified as a significant risk factor for developing various clavicular fracture-associated sequelae, such as pain and paresthesia, but not nonunion. (140) Our results align with these previous findings, as we did not observe statistical significance for age as a risk factor within our study population.

However, comparing these studies can be challenging, as some of them also included children or focused solely on a specific anatomical location of clavicular fractures. (71,140,246) This variability may have distorted results obtained. Therefore, investigating age as a risk factor separately for each anatomical location may provide a more in-depth understanding of its role in the development of clavicular nonunion.

Fracture Specific Characteristics

Anatomically, fractures of the lateral clavicular segment are known to exhibit higher nonunion rates compared to diaphyseal fractures. (22,29,157,170,181,246) However, our findings do not align with these observations: Within our study population, we observed slightly higher nonunion rates among diaphyseal fractures (6.0%) , while lateral fractures exhibited a nonunion rate of 5.5%. However, the nonunion rates we observed range within the reported rates of diaphyseal nonunions (4.5% to 6%) (157,246), and lateral nonunions (3% to 33%) (22,29,157,170,181,246). Random variation within the study population may be a reason for the observed discrepancies. In our study, fracture location did not reach statistical significance with regards to nonunion risk.

Initial shortening of the clavicle has been suggested as a risk factor for nonunion in previous studies. Hill et al. reported on a significantly higher association between initial shortening of ≥ 2 cm and nonunion. (70) Additionally, Liu et al. identified statistical significance for shortening in the bivariate analysis, but not in multivariate analysis though. (71) However, when considering other studies, initial shortening is more strongly associated with poor functional and cosmetic results, but not with clavicular nonunion. (66,72,140)

In our study, initial clavicular shortening was significantly associated with nonunion, but did not maintain significance in multivariate regression analysis. As we only included patients who presented with initial shortening in statistical analysis, but not those with non-shortening our result regarding shortening may be questionable.

Further significant risk factors regarding fracture features found in the literature include fragment displacement and comminution. Both of them have been reported to be strongly associated with poor functional outcomes. (66) Moreover, they were identified as independent predictive risk factors for clavicular nonunion in several studies. (71,140,174,179,246) Conversely, in one of these studies, a comminuted fracture was reported as a risk factor for clavicular fracture-associated sequelae, but not for nonunion. (140) Another study reported on comminution as a predictive risk factor for mid-shaft nonunions, but not for lateral nonunion. (246) In our study, neither displacement nor comminution reached statistical significance. These discrepancies may arise due to differences in criteria for the degree of fragment dislocation used in various studies. For instance, Nowak et al. determined the degree of displacement in relation to clavicular thickness (<0.5; 0.5-1.5; 1.5-2.5) (140), whereas our study used a different definition (none, one bone cortex, ≥ one bone cortex, half clavicular width, and entire clavicular width). Furthermore, variations in radiographic techniques and how displacement was measured in other studies may have contributed to the observed discrepancies. Nowak et al. used additional tilted 45° views to determine the degree of displacement (140), while in our study, mainly anterior-posterior radiographic images were analyzed. Furthermore, Robinson et al. and Liu et al. assessed fracture displacement differently in their analyses, focusing on its presence or absence. (71,246) Although we observed the highest nonunion rate in complex fractures, indicating a potential association between comminution and nonunion, this parameter did not show statistical significance in our study cohort. The

different methodical and measurement approaches used in several studies, including ours, may affect comparability. However, we cannot explain the lack of significance regarding comminution as a risk factor for clavicular nonunion in our study.

Patient-Related Risk Factors

Two risk factors that emerged with statistical significance in both bivariate and multivariate regression analysis included allergies and renal insufficiency, indicating a three times higher risk of developing nonunion in patients exhibiting these conditions. When comparing our findings to those of Zura et al., some can be observed, though. The authors identified the factor allergy as a preventive factor for nonunion in general as well as for clavicular nonunions. However, in consensus with our findings, renal insufficiency was associated with significantly increased overall nonunion risk. (162) However, the existing literature for allergies as well as renal insufficiency in relation to nonunion is limited. Further research in this field may be necessary to comprehensively explore the role of allergies and renal insufficiency in nonunion – not solely for clavicular fractures but in general.

Various other patient-related risk factors for nonunion have been studied in the literature. Commonly mentioned factors associated with a high risk of nonunion include osteoporosis, diabetes, the use of non-steroidal anti-inflammatory drugs, high body mass index, smoking, and alcoholism. (62,63,162,179,185,187,189,192,194–196,198,200) However, it is worth noting that most of the studies examining the influence of comorbidities and medication use focused on nonunion in a general orthopedic-traumatological context or other long bones, rather than specifically addressing clavicular fractures. Smoking has been extensively examined as a potential risk factor for nonunion (185,187,193–196,198), and it has also been specifically associated with clavicular nonunion. (71,174,179,202,203) Although smoking appeared to be associated with a higher risk of nonunion in our study, we did not observe a statistically significant difference. This could be attributable to the fact that not all patients had available information in their medical records regarding their smoking status, resulting in insufficient data to establish a potential statistical significance for nicotine abuse within our study population.

None of the other investigated risk factors achieved statistical significance, primarily due to the limited prevalence and available data on patient comorbidities within our study

population. The reliability of these findings thus may be questionable and has to be interpreted with caution.

4.3 Clinical Relevance and Recommendations

Our study's findings may be useful during the evaluation of patients with clavicular fractures. Clinicians should consider assessing the presence of allergies and renal insufficiency since this study has shown that these factors are associated with an elevated risk for clavicular nonunion. Furthermore, smoking has been consistently reported as a predictive significant risk factor for developing nonunion. (71,162,174,179,185,187,193–196,198,202,203) Aligning with these findings, our study also indicates an association between smoking and clavicular nonunion. Therefore, smoking cessation should be recommended to patients affected by clavicular fractures to positively influence the healing process (apart from several other positive side effects non-smoking exerts). However, the cause of nonunion development appears to be multifactorial, with various factors interacting in complex ways, making it difficult to predict whether a nonunion will develop under conservative treatment or not.

Besides these individual patient-related risk factors, fracture type and pattern are also important to consider when deciding on the correct treatment strategy. Patients with comminuted or severely displaced fractures should be evaluated for potential operative intervention to reduce the probability of nonunion, as these factors are associated with clavicular nonunion. (71,140,174,179,246) This knowledge can support clinicians in consulting patients concerning the treatment approach for clavicular fractures. For instance, a patient at high risk of developing nonunion may undergo surgical reconstruction to achieve bone union, while patients without risk factors and acceptable positioning of fracture fragments typically receive conservative treatment as the first choice.

4.4 Strengths and Limitations

The strengths of this study include a large and representative patient cohort as well as comprehensive data collection, which enhances the reliability of our findings. Limitations of the study encompass the retrospective study design, as data on comorbidities and certain patient-related risk factors were not uniformly available within our study population. The

small prevalence and lack of data in some of the examined parameters make it difficult to produce statistically significant and reliable results for e.g., diabetes, smoking status, and alcohol abuse. Our findings suggest that a prospective study should be conducted in which all patients with clavicular fractures are comprehensively assessed regarding their medical history, medication, and nicotine as well as alcohol abuse upon presentation to the emergency room. A prospective study could also provide further insight into the role of gender in the context of clavicular nonunion. Additionally, risk factors could be analyzed separately for medial, lateral, and midshaft clavicular fractures and nonunion.

4.5 Conclusion

Overall, our study provides novel data regarding patient-related risk factors for nonunions in conservatively treated clavicular fractures. Allergies and renal insufficiency were discovered as significant predictors for nonunion, with patients presenting with these conditions being at a three times higher risk of developing nonunion. Clinicians may use this information for improved risk assessment and as a support in the decision-making process regarding treatment approaches (conservatively vs. operatively). However, it is worth mentioning that the lack of significance of the other potential risk factors examined in our study may be attributable to the limited availability within medical records. Future studies are necessary to eventually discover significant associations between other parameters and clavicular nonunion. Additionally, further research may strengthen the role of allergies and renal insufficiency as predictive risk factors for clavicular nonunion and provide a deeper understanding of these associations.

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