Novel Assessment Techniques To Diagnose Syndesmotic Instability

Noortje Hagemeijer

Propositions belonging to the thesis

Novel Assessment Techniques To Diagnose Syndesmotic Instability

1 *The 2.0 mm threshold value of arthroscopic distal tibiofibular diastasis may lead to overtreatment of coronal syndesmotic instability.*
– This thesis

2 *Dynamic ultrasound allows to evaluate sagittal translation of the distal tibiofibular joint effectively and reliably.*
– This thesis

3 *Portable ultrasound performs similarly to arthroscopy when diagnosing syndesmotic instability in the sagittal plane.*
– This thesis

4 *Portable ultrasound can reliably detect tibiofibular clear space opening after external rotation stress.*
– This thesis

5 *On weightbearing CT syndesmotic area seems the best and most reliable 2D parameter to detect instability or (mal)reduction of the syndesmosis.*
– This thesis

6 *A healthy contralateral ankle is your best comparison.*
– This thesis

7 *Screw and tightrope reduction techniques do not restore syndesmotic area as compared to the intact contralateral ankle.*
– This thesis

8 *Duurzame zorg is niet geleverde zorg die niet geleverd had hoeven worden.*
– Evelyn Brakema

9 *You may have to fight a battle more than once to win it.*
– Margaret Thatcher

10 *Feminism is for everybody.*
– Bell Hooks

11 *There is nothing so stable as change.*
– Bob Dylan

12 *Enkel het beste.*
– Mees Joachim van Amesfoort

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Noortje Hagemeijer

Colofon

Author *Noortje Hagemeijer*

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Voor *Rien*

Enkel het beste.

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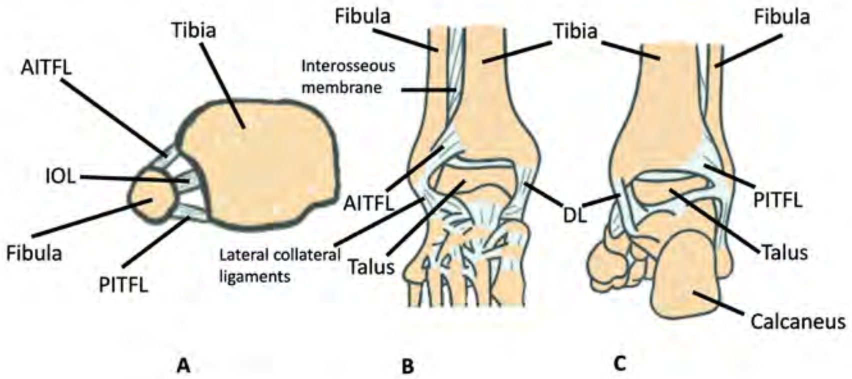
Chapter 1 General Introduction

Anatomy

Normal ankle function is rudimental for our day to day mobility. The ankle consists of the tibiotalar joint, distal tibiofibular (syndesmotic joint) and the talocalcaneal (subtalar joint). Also called the talocrural joint the ankle is formed by the distal epiphyses of the fibula, tibia and talus. In healthy persons the ankle is mainly responsible for plantar flexion and dorsiflexion movements.[66] The distal fibula is called the lateral malleolus and the distal tibia is called a medial malleolus, these malleoli together with the tibial plafond form a mortise which encloses the talar trochlea.[26] The syndesmotic joint is an important stabilizer of the ankle mortise by resisting axial, rotational, and translational motion of the fibula. Medially the mortise is stabilized by the deltoid ligament (DL) which prevents the talus from moving laterally (Figure 1B and C).[30, 78] Laterally, the lateral collateral ligaments are situated including the anterior talofibular ligament (ATFL), calcaneofibular ligament (CFL), and the posterior talofibular ligament (PTFL) (Figure C).[26] The lateral collateral ligamentous complex is not an important stabilizer of the ankle mortise but is an important stabilizer of the ankle and subtalar joints by limiting anterior displacement of the talus and plantar flexion of the foot.[26]

The bony structures of the tibiofibular joint consist of the rounded medial surface of the fibula and the depression on the lateral distal surface of the tibia, also called the incisura fibularis, peroneal groove or syndesmotic notch of the syndesmosis (Figure 1A). The morphology of the fibular incisura varies largely between persons and can be categorized in C shape (56%), 1 shape (25%, and Γ shape (19%).[42] The fibular incisura provides stabilization and allows for tibiofibular adaptation to varying width of the upper articular surface of the talus caused by extreme dorsiflexion and plantarflexion movements.
The ligamentous components of the syndesmosis include; **1.** the anterior inferior tibiofibular ligament (AITFL), **2.** the interosseus tibiofibular ligament (IOL), and **3.** the posterior inferior tibiofibular ligament (Figure 1A, B, and C).[26, 28] The AITFL originates at the anterolateral tubercle (tubercle of Chaput) and extends to the anterior margin of the lateral malleolus (tubercle of Wagstaffe). The PITFL is formed by two components, the superficial and deep component. The superficial component extends from the posterior edge of the lateral malleolus to the posterior tibial tubercle, this component is in parallel with the AITFL.[26] The deep component, i.e. transverse ligament, originates in the proximal area of the malleolar fossa and inserts just posterior of the cartilage of the inferior tibial articular surface. Besides providing tibiofibular stability it also prevents posterior talar translation. The IOL spans at the level of the syndesmosis between the tibia and the fibula and is considered a distal continuation of the interosseous membrane.[26]

Figure 1. Anatomical Illustration of the syndesmotic ligaments and adjacent structures of the Ankle



(A) Axial view the distal tibiofibular joint at 1cm above the tibial plafond; (B) Anterior view; (C) Posterior view.
Abbreviations: AITFL = anterior inferior tibiofibular ligament, IOL = interosseus tibiofibular ligament, PITFL = the posterior inferior tibiofibular ligament, DL = Deltoid ligament.

Injury Mechanism

Understanding the mechanism of ankle injury is important as it will help to improve injury prevention, diagnosis and treatment strategies. Ankle sprains are a common reason for primary care office and emergency department visits with an incidence rate of 2.09 per 100.000 person-years.[72, 75] Often these injuries concern the athletic population as nearly half of all ankle sprains occur during sporting activities.[75] The majority of ankle sprains presented have an inversion mechanism mainly affecting the collateral lateral ligaments with or without involvement of the AITFL.[29]

A relatively small amount of ankle injuries and syndesmotic and/or deltoid injury.[20] The incidence of syndesmotic injury in the general population is reported between 5 and 10% of all ankle sprains.[20, 31] But when investigating the athletic population, isolated syndesmotic injuries occur more frequently with an incidence of about 18%.[2, 8, 25]

Notably, the incidence rates reported do vary widely between sports, ranging from 6% up to even 63%.[9, 14, 43] High risk sports for syndesmotic injury include boot immobilized sports,[22, 23, 77] such as ice-hockey and skiing, as well as collision sports including American football, wrestling, and rugby.[2, 25, 33, 37, 43]

The incidences reported do not only depend on the population but also depend on the definition of the injury and method of diagnosis. Due to a lack of awareness and accessible diagnostic assessment methods it is likely that the incidences reported are an underestimation.[25, 31, 36, 38]

Despite the low incidence as opposed to the more common 'simple' inversion ankle sprain these injuries do entail a longer recovery period with prolonged pain and slower return to sport and therefore should not be missed.[12, 32, 43, 47] About 23% of all ankle fractures may also include injury of the syndesmosis. However, this thesis will mainly focus on isolated syndesmotic injuries, that is defined as a syndesmotic ligamentous injury without a concomitant ankle fracture.[80]

Isolated syndesmotic injuries are commonly caused by an external rotation force with the ankle in dorsiflexion and the foot pronated. The external rotation movement of the ankle causes the talus to rotate in the ankle mortise, pushing the fibula away causing it to rotate externally, move laterally, and translate posteriorly while sequentially tearing the syndesmosis starting with the AITFL and Deltoid ligaments, IOL and finally the PITFL.[56]
Other mechanisms that may cause syndesmotic injury are hyperdorsiflexion of the ankle, inversion, and a combination of inversion and external rotation.[31, 40]

The amount of additional fibular displacement is an important prognostic factor for long term-disability, as an increased amount of fibular displacement leads to a significant increase in mean tibiotalar contact pressure potentially causing articular damage over time.[34] The extend of additional fibular displacement depends on the severity of the injury as well as on trauma mechanism.[6, 44]

Clinical Presentation

Physicians should suspect syndesmotic injuries when there is a suspected trauma injury mechanism, i.e. twisting or rotational moment of the ankle and complains of pain around the anterior syndesmosis. Chronic syndesmotic injury should be considered when complaints, sense of instability and recurrent swelling of the ankle joint, are long-standing.[55] When suspecting syndesmotic injury, based upon clinical presentation, the physician may perform the following clinical tests which may increase suspicion for syndesmotic injury.

Squeeze Test;

Manually squeezing the fibula toward the tibia at the midpoint of the calf. This test is considered positive when pain is felt in the distal area of the syndesmosis is.[31] External-rotation test; is usually performed with the knee held in 90 degrees and the foot held in the neutral position. The test is considered positive when pain is felt over the area of the syndesmosis when applying external rotation stress over the foot.[8] External rotation stress may also be performed with the foot maximally dorsiflexed while weightbearing (fixed) or non-weightbearing.[54, 62]

Cotton Test;

Fixing the tibia while performing lateral force to the foot, the test is considered positive when lateral translation is felt.[17]

Fibula Translation Test;

Also called the shuck test this test simulates fibular translation by pushing the fibula in both the anterior and posterior directions relatively to the tibia. The test is considered positive when pain is felt at the syndesmosis or when larger displacement is felt than the contralateral uninjured side.[56]

Syndesmosis Palpation;

Is considered positive when pain is felt with direct palpation of the syndesmosis area.[65]

Dorsi-Flexion Reduction Test;

to perform a dorsi-flexion reduction test the patient is asked to stand and to actively dorsiflex the ankle simulating normal axial loading. Subsequently the dorsiflex movement is repeated with the examiner applying compressive support manually around the malleoli. A positive test is considered positive if compression increases range of motion of the ankle joint, or if compression leads to a less painful examination.[1, 74]

The Circular Tape Test;

is considered positive if the patient experiences significantly less pain when performing a single leg weightbearing dorsal flexion exorotation test. The tape is put 1,5 cm proximal of the ankle joint line.

The Anterior Drawer Test;

Is primarily used to diagnose lateral ankle stability which is an important differential when evaluating the syndesmosis. This test is not correlated with syndesmotic injury.[5]

The clinical tests are helpful in raising suspicion for syndesmotic injury but not good enough to distinguish a stable syndesmotic injury from (chronic) syndesmotic instability.[5] Therefore final diagnosis should be made upon diagnostic assessment techniques.

Classification

Syndesmotic instability is a condition where there is extensive multiplanar motion of the distal fibula relatively to the distal tibia. When left untreated or mistreated syndesmotic instability can lead to longer recovery period with prolonged pain and slower return to sport and degeneration of the ankle joint over time.[32, 33, 43, 46, 58] There are several classification systems reported in the literature but it should be noted that there still is no consensus on a reliable classification system that includes a diagnostic and treatment algorithm.[69]

A commonly used grading system is the West Point Ankle Grading system which divides the severity of the syndesmotic injury into three grades.[25]

Grade I injuries;

Are considered a stable injury with usually only sprain to the AITFL with or without incomplete injury to the lateral ligaments. Probably a Grade I injury will be provoked by an inversion injury and is clinically mild. Patients will have tenderness at the anterior syndesmosis but the external rotation and squeeze test can be negative. No widening on weightbearing radiographs will be detected. Conservative treatment with a short period of non-weightbearing and immobilization in a boot followed by gradual rehabilitation.

Grade II injuries;

Can be a stable or unstable injury. Generally, in Grade II injuries there is injury to the AITFL and IOL. The clinical tests for detecting syndesmotic injury will be positive but widening of the tibiofibular clear space may not be seen on imaging modalities, or only in case of a provocative stress test. There is no consensus on optimal treatment measures for this category because it remains difficult to differentiate between stable and unstable injuries as accessible diagnostic measurement techniques are still lacking.

Grade III injuries;

Is an unstable injury and involves a complete rupture of the syndesmosis (AITFL, IOL, and the PITFL) and the DL. This causes all clinical tests to be positive and shows mortise widening weightbearing radiographs. Often Grade 3 injuries present in combination with a fracture. Because this injury is unstable it requires surgical stabilization.

In 2016 the ESSKA-AFAS consensus expert panel performed a systematic review to formulate guidelines to classify syndesmotic injuries.[69] They recommended a classification system that distinguishes between stable and unstable acute isolated syndesmotic injury. Unstable injuries should be categorized into latent and frank instability injuries. Stable injuries include sprains to the AITFL with or without involvement of the IOL, here the DL must be intact. Latent unstable injuries are those with injury to the AITFL with or without IOL and DL injury, and frank unstable injury includes rupture of all syndesmotic ligaments and the DL. It is advised to treat stable injury conservatively, and unstable injury surgically. They do acknowledge that it is difficult to distinguish between the stable and the latent unstable group due to a lack of accessible diagnostic assessment method capable to differentiate.

Besides grading the severity of the injury it is also possible to categorize it into acute, subacute, or chronic injury.[69] Variability exists within the literature but generally syndesmotic injury is considered acute when the treatment is performed within 6 weeks after the trauma, subacute when treatment is performed between 6 weeks and 6 months, and chronic when treatment is performed after 6 months. The clinical implications of categorizing the injury based upon the time frame remains unclear but late diagnosis generally leads to less favorable outcomes.[68, 69]

Syndesmotic Assessment Techniques

If clinical symptoms of syndesmotic injury are present, further assessment techniques to evaluate suspect syndesmotic instability should be obtained. True consensus on diagnosing syndesmotic instability is difficult since high level evidence is still lacking. There are, however, several assessment techniques that can aid the physician to get to the correct diagnosis.

Conventional Weightbearing Radiography;

Is a widely accessible technique with little risk to the patient, and often a first step when suspecting ankle injury or fracture. The most common techniques for assessment of instability of the syndesmosis are measurements of the tibiofibular clear space (TFCS), tibiofibular overlap (TFO), and medial clear space (MCS) obtained from the anterior-posterior (AP) view and or Mortise view in the weightbearing position.[38] Nevertheless, weightbearing radiographs may not be accurate enough to adequately detect or exclude syndesmotic instability. Therefore, in recent years other assessment techniques have been suggested.[7, 21, 38, 48]

Portable Ultrasound;

Is an accurate and reliable tool for assessing the quality of the anterior inferior tibiofibular ligament (AITFL) and effectively evaluates the tibiofibular clear space (TFCS) when comparing it to MRI.[2, 41, 50, 51, 70] Portable ultrasound has several advantages over other assessment techniques, as it can be used at the point of care, does not involve related risk, allows for a bilateral dynamic stress exams, and carries low cost.[52] Even though this accessible dynamic assessment technique may have good potential for diagnosing (chronic) syndesmotic instability it is not yet being used as such clinically.

Magnetic Resonance Imaging (MRI);

Is often obtained in patients that are suspected for ligamentous injury. MRI is a very reliable technique to identify ligamentous damage, including that of the syndesmosis.[38] But the lack of physical load or applied stress limits the ability to distinguish unstable from stable syndesmotic injuries.

(Weightbearing) Computed Tomography (CT);

CT scans are often obtained in patients with ankle fractures and can reliably evaluate the osseous tibiofibular relationships.[79] However, without a dynamic component,
i.e. physical loading or an applied stress, ankle alignment may not be truly appreciated. To overcome this issue various investigators have developed custom-made loading-frames to improve diagnostic accuracy for various foot and ankle pathologies using a regular CT scan.[3] Over the past decade, technology and software advances have resulted in CT scanners that do allow patients to stand (weightbearing CT-scan) and novel noninvasive 3-dimensional measuring methods.[11, 13, 67] By adding these dynamic capabilities and software advances the CT-scan is indeed a promising technique to distinguish unstable from stable syndesmotic injury.[10, 11, 27]

Ankle Arthroscopy;

Has been considered the gold standard for diagnosing syndesmotic instability. Important benefits of the arthroscopy are that it provides direct visualization of the distal tibiofibular articulation statically and under an applied stress. Thereby, it also allows for immediate treatment of syndesmotic instability, associated fractures, and/or osteochondral lesions when indicated.[18, 56, 63, 64] The important drawback of arthroscopy is that it is an invasive and costly technique with related risk to the patient.[71] Consequently, arthroscopy is available to a select group of patients with either a high level of pre-operative suspicion or patients with a concomitant fracture that independently require surgery. As a result, clear arthroscopic cut-off points that can be used clinically have not yet been established.[21, 44, 45, 48, 76]

Injury Management And Outcomes

Syndesmotic injury management depends on severity and may be categorized into conservative management and surgical management. Generally stable high ankle sprains (Grade I and stable Grade II injuries) should be treated conservatively whereas unstable injuries (unstable Grade II and Grade III injuries) should be treated surgically. Since diagnostic assessment techniques capable of accurately distinguishing between a stable and unstable syndesmotic injury are still lacking it remains difficult to properly investigate optimal treatment methods and patient outcome.

The general principles of conservative treatment management for an ankle sprain entail immediate rest, ice, compression, and elevation (RICE). When a grade I syndesmotic ankle sprain is suspected the patient should be informed that this concerns a severer ankle injury than an inversion ankle injury that entails a longer time to heal and requires a more extensive treatment consisting out of 3 phases.[35, 49, 54] First a short immobilization period of 4-7 day in a non-weightbearing cast or boot is recommended followed by a short period of 4-7 days of partial weightbearing as tolerated. At this time physiotherapy focusing on range of motion and light proprioception may be initiated. This is followed by a period in which full weight bearing is allowed as tolerated and the start of functional exercises. The mean time return to sporting activity is 6-8 weeks after the injury but is variable depending on the severity of the injury. As a comparison, a simple inversion sprain takes about 3 to 4 weeks to return to sporting activities.[73]

Surgical stabilization of the syndesmosis is indicated in case of latent or frank instability. Accurate reduction of the syndesmotic joint is essential for restoring normal ankle mechanics and prevent secondary degenerative damage of the ankle joint over time.[24]
The most commonly used techniques to stabilize the syndesmotic joint are one or two syndesmotic screws and one or two suture button constructs. The preferred method for treating syndesmotic instability surgically remains subject of ongoing debate.[57, 59, 61]

The syndesmotic screw is placed through the fibula into the tibia at the level of the syndesmosis. While placing the screw it is important to ensure to maintain a proper reduction of the tibiofibular joint by using a clamp across the fibula and tibia. Placement of the screw leads to a rigid fixation that prevents any dynamic behavior of the syndesmotic joint allowing the syndesmosis ligaments to heal in a stable environment. After 8-10 weeks the syndesmosis will have healed leaving no function for the screw, which makes that many surgeons decide to remove the screw routinely to restore natural movement of the syndemosis.[19] However, routine removal exposes the patient to related risk and it does not seem the patient may benefit from it as till now no difference in clinical outcome have been reported between routine removal and removal only when indicated.[60] The suture button, similarly, is placed through the fibula and tibia while ensuring proper reduction by holding a clamp. The main difference with the screw is that the suture button is a non-rigid construct allowing more physiological motion of the distal fibula with respect to the tibia. Because it is a dynamic construct routine removal is not performed which makes this procedure cost effective even though a suture button construct is more expensive than a screw.[53] To provide full stability in the coronal and sagittal plane, two suture button devices placed divergent relative to one another has been recommended.[4, 15]

The mean time return to normal activities is generally faster when using a suture button construct with a mean of 14 weeks versus a mean of 19 weeks when using a screw.[16] When treated using a suture button about 79% of all patients will be able to return to full sporting activities only after one year versus 69% when using a screw.[39]

Aims Of This Thesis

The aim of this thesis was to evaluate existing diagnostic methods as well as to develop new dynamic diagnostic assessment techniques with the potential of distinguishing stable from unstable syndesmotic injury. Subtle syndesmotic injury can be difficult to appreciate with clinical maneuvers or with static imaging. Therefore, traditionally, the arthroscope has been the golden standard for diagnosis of syndesmotic instability.

In ***Part I*** we reviewed all literature on arthroscopic evaluation of the syndesmosis to calculate a weighted mean for syndesmotic instability and to assess the quality of the published work. **Chapter 2** summarizes the literature with specific emphasis on the measurable threshold for syndesmotic instability. Arthroscopy has obvious disadvantages because of its invasiveness, relatively high diagnostic costs and arthroscopy does not allow for a contralateral side comparison as internal control.

Therefore, in ***Part II*** we explored new dynamic assessment techniques. In **Chapter 3**, using ultrasound, we aimed to establish a dynamic assessment technique that would be widely available, at low cost, with allowance for bilateral examination, and without related risks. As a first step normal ankle motion was investigated in the sagittal plane as well as the reliability of the test and measurements. In **Chapter 4** the biomechanics of the syndesmosis were evaluated using the sagittal dynamic ultrasound test and arthroscopy in a controlled study setting using cadaveric specimens to see if portable ultrasound performed equally well compared to arthroscopy. In **Chapter 5** the ability of dynamic ultrasound was explored to detect the tibiofibular clear space while providing an external rotation force to the ankle and compared it to fluoroscopy, again in a controlled study setting using cadaveric specimens. In **Chapter 6** the distal tibiofibular articulation was investigated in patients with known syndesmotic instability using weightbearing CT scan.

In ***Part III*** of this thesis, radiographic and functional outcomes after syndesmosis fixation treatment were evaluated. First in **Chapter 7** the reliability of published measurements of the distal tibiofibular articulation for weightbearing CT scan were analyzed as these measurements were not performed on a weightbearing CT scan before. **Chapter 8** compared radiographic outcomes of screw and suture button fixation for syndesmotic instability using weightbearing CT scan for which a group of patients at a minimum of one year after operation were recruited. The functional outcomes of these patients were evaluated using PROMIS questionnaires.

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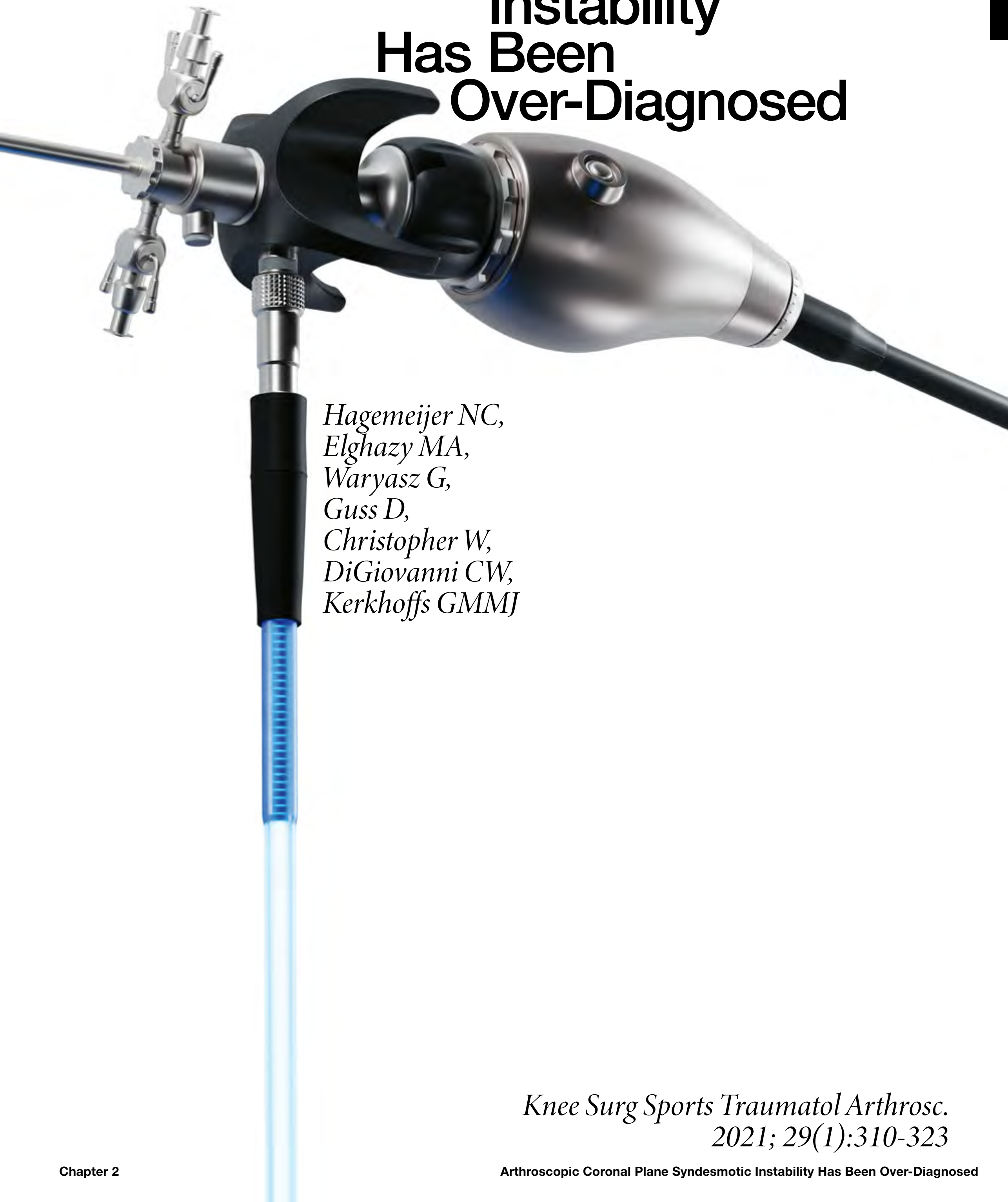
Part I

Arthroscopic Assessment For

Diagnosing Syndesmotic Instability

Chapter 2 Arthroscopic Coronal Plane Syndesmotic Instability Has Been Over-Diagnosed



*Hagemeijer NC,
Elghazy MA,
Waryasz G,
Guss D,
Christopher W,
DiGiovanni CW,
Kerkhoffs GMMJ*

*Knee Surg Sports Traumatol Arthrosc.
2021; 29(1):310-323*

Abstract

Purpose

Ankle Arthroscopy is widely used for diagnosis of syndesmotic instability, especially in subtle cases. To date, no published article has systematically reviewed the literature in aggregate to understand which instability values should be used intraoperatively. The primary aim is to systematically review the amount of tibiofibular displacement that correlates with syndesmotic instability after a high ankle sprain.
A secondary aim is to assess the quality of such research.

Methods

Systematic searches of EMBASE (Ovid) and MEDLINE via PubMed, CINAHL, Web of Science, and Google Scholar were used. Inclusion criteria: studies that arthroscopically evaluated the fibular displacement at various stages of syndesmotic ligament injury. Two reviewers independently extracted data and assessed methodological quality using the Anatomical Quality Assessment (AQUA) Tool and methodological index for non-randomized studies (MINORS).

Results

Eight cadaveric studies and three clinical studies were included for review. All studies reported displacement in the coronal plane, four studies reported in the sagittal plane, and one reported findings in the rotational plane. Four cadaveric studies had a similar experimental set up and the weighted mean associated with instability in the coronal plane could be calculated and was 2.9 mm at the anterior portion of the distal tibiofibular joint and 3.4 mm at the posterior portion. Syndesmotic instability in the sagittal plane is less extensively studied, however available data from a cadaveric study suggests thresholds of 2.2 mm of posterior fibular translation when performing an anterior to posterior hook test and 2.6 mm of anterior fibular translation when performing a posterior to anterior hook test.

Conclusions

The results have concluded that the commonly used 2.0 mm threshold value of distal tibiofibular diastasis may lead to overtreatment of syndesmotic instability, and that using threshold values of 2.9 mm measured at the anterior portion of the incisura and 3.4 mm at the posterior portion may represent better cut off values. Given the ready availability of 3 mm probes among standard arthroscopic instrumentation, at the very least surgeons should use 3 mm in lieu of 2 mm probes intraoperatively.

Introduction

Isolated syndesmotic injuries occur in approximately 18% of all ankle sprains and 10-23% of all ankle fractures [4, 19, 25, 35, 54] and correlate with significantly poorer functional outcomes when left untreated.[14, 42, 44] The ankle draws much of its stability from its mortise structure, and instability of the distal tibiofibular ligamentous complex by definition allows this mortise to widen around the talus. The potentially altered tibiotalar relationship, in turn, can increase joint contact pressures potentiating post-traumatic arthritis.[31, 41, 53] Appropriate diagnosis and surgical repair of syndesmotic instability is therefore crucial towards preserving ankle stability and maximizing long term functional outcomes.[23, 29]

MRI reliably detects syndesmotic injury, but as a static, unstressed modality, it is unable to reliably distinguish between stable and unstable injuries.[22] In contrast, ankle arthroscopy allows direct visualization of the distal tibiofibular articulation, both statically and under an applied stress load.[38, 48] While recent clinical and cadaveric studies have highlighted the role of ankle arthroscopy in diagnosing syndesmotic instability, the amount of fibular motion correlated with instability remains unclear as reported cut off values vary among. Most studies have highlighted a cut off value between 2 to 3 mm, but no published article has systematically reviewed these studies in aggregate to understand which values to use intraoperatively.[7, 10, 30]

The primary aim of this study is to systematically review the published literature exploring the amount of fibular displacement found that correlates with syndesmotic instability after a high ankle sprain. A secondary aim is to assess the quality of such research. The clinical relevance of the present study is that it will provide an instability cut off value based upon a meticulous summary of all the available primary research for diagnosing syndesmotic instability arthroscopically which will be directly usable in the clinic and improve clinical outcome.

Materials And Methods

Search Strategy

Studies from the earliest recorded citations until June 18, 2019 were retrieved from the following electronic databases: EMBASE (Ovid) and MEDLINE via PubMed, CINAHL, Web of Science, and Google Scholar (Table 1). When searching through Google Scholar, only the first 250 results were exported because their search algorithm demonstrated that, despite thousands of results, the relevancy of these results quickly dropped. The search was conducted under the guidance of a clinical librarian.

Eligibility Criteria

All the studies that arthroscopically evaluated fibular displacement in the three planes after different type of ligamentous injuries were considered for inclusion. All randomized controlled trials, controlled non-randomized trials, prospective and retrospective cohort studies and case series were included. Animal studies and review studies were excluded, though the references of related review articles were assessed for any additional eligible studies. No age restrictions were applied.

Variables And Target Outcome

The target variables included, **1.** the threshold considered to represent an unstable syndesmosis, **2.** fibular displacement in the coronal, sagittal, and rotational plane in mm or degrees, **3.** associated injuries, **4.** location of the measurement, and **5.** type of stress test. Associated injuries were defined as injuries to the ligamentous structures of the syndesmosis (the anterior inferior tibiofibular ligament (AITFL), the interosseous ligament (IOL), and the posterior inferior tibiofibular ligament (PITFL)), the lateral fibulo-talo-calcaneal ligament complex LFTCL, consisting of the anterior tibiofibular ligament (ATFL), calcaneofibular ligament (CFL), posterior talofibular ligament (PTFL)),[51] the deltoid ligament (DL), and concomitant ankle fractures. Other reported diagnostic tools (radiographs, CT, MRI, or ultrasound) and intra- and inter-rater reliability scores were also recorded.

Reference Standard

In cadaveric studies the ligamentous injury pattern was used as a reference when comparing the amount of fibular displacement across studies. Syndesmotic instability was defined as an injury that was associated with tibiofibular displacement significantly different from the intact state. In In vivo studies, this comparison cannot be made and therefore the threshold considered to represent an unstable syndesmosis and associated injuries was described descriptively for each study.

Study Selection

Two authors (NH and MA) independently screened titles and abstracts, using predetermined inclusion and exclusion criteria with the help of Covidence, https://www.covidence.org/home. Disagreement was resolved by an attempt to reach consensus. In cases where no consensus was reached, a third reviewer (GW) was consulted to resolve the disagreement.

Data Extraction

Data was extracted by one reviewer (NH) and thereafter checked by all co-authors. Extracted data was collected in a predefined format from Microsoft Excel for Mac (version 15.37). Study design, patient or cadaver characteristics, arthroscopic measurement details, diastasis measurements or pre-determined cut off values, related injuries, and other radiographic outcomes were extracted.

Table 1. Search strategy and hits per electronic database

Database	Line		Items found	Unique hits
Pubmed	**#1**	(Arthroscop*[tiab] OR Arthroscopy[mesh]) AND (Syndesmos*[Title/Abstract] OR syndesmotic[Title/Abstract] OR tibiofibular*[Title/Abstract] OR "tibio fibular"[Title/Abstract] OR "high ankle"[Title/Abstract] OR AITFL[Title/Abstract] OR PITFL[Title/Abstract]) AND ("Wounds and injuries"[Mesh:noexp] OR "Sprains and strains"[Mesh] OR Rupture[Mesh:noexp] OR "Joint instability"[Mesh] OR "ankle injuries"[Mesh:noexp] OR Injur*[Title/Abstract] OR sprain*[Title/Abstract] OR instabilit*[Title/Abstract] OR unstable[Title/Abstract] OR rupture*[Title/Abstract] OR disruption*[Title/Abstract] OR tear*[Title/Abstract] OR torn[Title/Abstract])	**126**	**125**
Embase	**#1**	'arthroscopy'/de OR 'ankle arthroscopy'/de	**159**	**54**
	#2	arthroscop*:ab,ti		
	#3	#1 OR #2		
	#4	injury'/de OR 'rupture'/de OR 'ligament rupture'/de OR 'joint instability'/de OR 'sprain'/exp OR 'ligament injury'/de OR 'ankle injury'/de OR 'syndesmotic injury'/de		
	#5	injur*:ab,ti OR sprain*:ab,ti OR instabilit*:ab,ti OR unstable:ab,ti OR rupture*:ab,ti OR disruption*:ab,ti OR tear*:ab,ti OR torn:ab,ti		
	#6	#4 OR #5		
	#7	'syndesmosis'/exp		
	#8	syndesmos*:ab,ti OR syndesmotic:ab,ti OR tibiofibular*:ab,ti OR 'tibio fibular':ab,ti OR 'high ankle':ab,ti OR aitfl:ab,ti OR pitfl:ab,ti		
	#9	#7 OR #8		
	#10	#3 AND #6 AND #9		
CINHAL	**S1**	(MH "Arthroscopy")	**74**	**5**
	S2	TI Arthroscop* OR AB Arthroscop*		
	S3	S1 OR S2		
	S4	TI (Syndesmos* OR syndesmotic OR tibiofibular* OR "tibio fibular" OR "high ankle" OR AITFL OR PITFL) OR AB (Syndesmos* OR syndesmotic OR tibiofibular* OR "tibio fibular" OR "high ankle" OR AITFL OR PITFL)		
	S5	(MH "Ankle Injuries") OR (MH "Ankle Sprain+") OR (MH "Sprains and Strains") OR (MH "Wounds and Injuries") OR (MH "Rupture") OR (MH "Joint Instability")		
	S6	TI (Injur* OR sprain* OR instabilit* OR unstable OR rupture* OR disruption* OR tear* OR torn) OR AB (Injur* OR sprain* OR instabilit* OR unstable OR rupture* OR disruption* OR tear* OR torn)		
	S7	S5 OR S6		
	S8	S3 AND S4 AND S7		
Web of Science	**#1**	TOPIC: (Arthroscop*)	**144**	**52**
	#2	TOPIC: (Syndesmos* OR syndesmotic OR tibiofibular* OR "tibio fibular" OR "high ankle" OR AITFL OR PITFL)		
	#3	TOPIC: (Injur* OR sprain* OR instabilit* OR unstable OR rupture* OR disruption* OR tear* OR torn)		
	#4	#1 AND #2 AND #3 Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=All years		
Google Scholar	**#1**	Arthroscopy | arthroscope | Syndesmoses | syndesmosis | syndesmotic | tibiofibular | "tibio fibular" | "high ankle" | AITFL | PITFL Injury | injuries | sprain | sprains | instability | unstable | rupture | disruption | tear | torn	**500**	**252**
Total			**1.003**	**488**

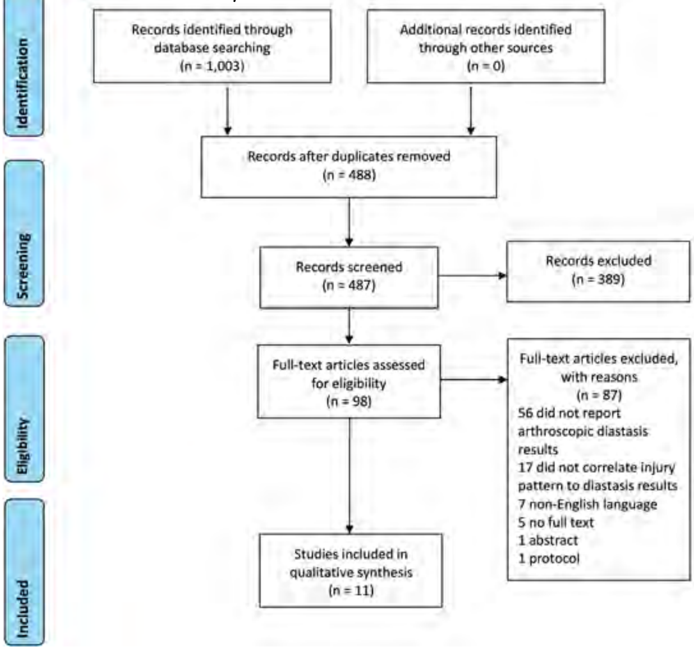
Quality Assessment

28 Methodological quality of the cadaveric studies was assessed using the Anatomical Quality Assessment (AQUA) Tool by two independent reviewers (NC and MA).[18] This tool is designed to help evaluate the performed experiment, i.e. the arthroscopic diagnosis of syndesmotic instability, by addressing five key domains: **1.** whether objectives were clearly defined and appropriate, **2.** whether the study design was appropriate for answering the aims, **3.** whether the methodology was described in sufficient detail to permit replication, **4.** whether the anatomical definitions were accurately defined and described, and **5.** whether the results were accurately calculated and reported. The methodological quality of included studies was assessed using the Methodological Index for Non-Randomized Studies (MINORS) instrument.[46] MINORS is an instrument designed to assess methodological quality of both non-comparative and comparative studies. For this study, only the non-comparative factors of the MINORS instrument were used. Disagreement was resolved by consensus or third-party adjudication (GW).

Statistical Analysis

For each study, the reported amount of distal tibiofibular displacement, associated injury patterns, and related pathologies were recorded and summarized. Statistical heterogeneity was then determined using the Higgins and Thompson I2 index as well as a chi-squared test to assess for heterogeneity. The I2 was considered to be of low heterogeneity when <0.25, moderate heterogeneity when between 0.25-0.50, and high heterogeneity when >0.50. A fixed model was used when heterogeneity was low or moderate. If the data heterogeneity was high, a formal meta-analysis would not be performed and instead results would be presented in a descriptive manner along with weighted means and SD's when able. In case of unavailable raw data the range of the means would be provided instead. P-values of <0.05 were considered significant. All analyses were performed with Stata 13.0 for Mac (StataCorp LP, College Station, TX, USA).

Figure. 1 PRISMA (preferred reporting items for systematic meta-analyses) flowchart for study inclusion. RCT randomized controlled trial



Results

A total of 1,003 studies were identified (Figure 1). Of these studies, 515 were duplicates and removed prior to the first round of selection. Of those remaining, 389 articles were excluded based upon title and abstract screen and 98 articles were selected for full-text screening. A total of 8 cadaveric studies and three clinical studies were included in this systematic review.[12, 15, 16, 26, 27, 30, 31, 50, 53, 56] Three studies' corresponding authors were contacted by email for additional information but were not ultimately included due to non-response.[40, 49, 52]

Variables And Target Outcome

The threshold that was considered to represent an unstable syndesmosis, amount of displacement, associated injury patterns, and arthroscopy technique details per each study are summarized in Table 2.
All cadaveric studies reported on fibular displacement in the coronal plane. Significant tibiofibular displacement from the intact state ranged from 1.6 – 4.4 mm at the anterior and from 2.4 - 4.4 mm at the posterior third of the incisura.[15, 27, 31, 32, 53] One study provided an instability threshold based upon a cluster analysis, which was 2.6 mm when measuring at the anterior third coronal plane space of the incisura, and 3.4 mm when measuring at the posterior third space.[26] The other two cadaveric studies did not compare tibiofibular displacement to the reference intact state.[12, 27] Due to a high heterogeneity, a formal meta-analysis was not performed and weighted means for syndesmotic instability in the coronal plane were calculated instead for those cadaveric studies who had a similar experimental set up including probe positioning, method of stress application, and the absence of use of an ankle distractor.[15, 27, 31, 32] The weighted mean of syndesmotic instability in the coronal plane with a lateral fibular stress maneuver was 2.9 mm at the anterior portion of the incisura and 3.4 mm at the posterior portion of the incisura. Weighted means of syndesmotic instability and per each injury pattern are provided in Table 3.

All three In vivo studies reported on displacement in the coronal plane. Two of these chose to use the threshold of >2 mm for diagnosing and treating syndesmotic instability.[30, 56]
The other study categorized each injury pattern based upon the diastasis in a self-made grading scheme where they considered <2 mm stable, >2 to <5 mm potentially unstable, and >5 mm unstable.[50]
Three cadaveric studies reported on tibiofibular displacement values in the sagittal plane.[26, 27, 53] One study provided an instability threshold based upon a cluster analysis which was 2.2 mm when pulling anteriorly, and 2.6 mm when pulling posteriorly.[26] Two studies presented their results descriptively.[27, 53]
Only one In vivo study reported on displacement in the sagittal plane, handling a threshold of >2 mm for diagnosing and treating syndesmosis instability.[30]
None of the cadaveric studies reported findings in the rotational plane. One clinical study reported findings in the rotational plane for which they handled a threshold of >2mm.[30]

Feller et al. and Lui et al. reported concomitant radiographic measurements for each injury pattern, which are presented in Table 4.[15, 30]

Two clinical studies reported on in vivo cartilage damage in the setting of syndesmotic instability.[50, 56] Turky et al.[50] reported that over 90% of the patients had additional lesions also including ATFL injuries. All four patients described by Yoshimura et al.[56] had talar lesions on the posteromedial aspect of the talar dome.

There were two cadaveric studies which included an inter-observer agreement analysis as part of their study methodology, which both derived from the same experimental set up, by having two observers assess three specimens independently.[26, 27]
Substantial agreement was found for anterior third coronal plane tibiofibular diastasis and sagittal plane tibiofibular translation. Moderate agreement was found for posterior third coronal plane tibiofibular diastasis.

Quality assessment

All but two studies had a high risk of bias due to a methodology that was not described in sufficient detail to permit replication as per the AQUA tool described above (Table 5). This specifically pertained to a failure to undertake appropriate measures to reduce inter- and intra- observer variability. The only studies included in this review that explicitly analyzed the reliability of the measurements were the studies of Lubberts et al.[26, 27]
The methodological quality of the clinical studies was graded according to the MINORS criteria (Table 6) and the average score was 6.7 out 16 points (41.7% of maximum).

Table 2. Arthroscopic syndesmotic instability measurements per study

Author	Characteristics	Arthroscopic Measurement Details	Coronal Stress (mm)	Sagittal Stress (mm)	Rotational Stress (mm)
Lui et al. 2005 **Country: China** **Design: Prospective Study** **Period: 06/2002 – 12/2003**	nr: 53 Age: 35.4 Sex: NR Cohort: Surgically treated Weber type B or C ankle fractures without radiographic evidence of frank syndesmosis diastasis	Probe: 30° 2.7-mm	Stable injury (<2mm)	Stable injury (<2mm)	Stable injury (<2mm)
		Distractor: NR	**Stressed**	**Stressed**	**Stressed**
		Position: NR	Total: 32	Total: 30	Total 39
		Stress: no stress + LHT + AP directed stress	11 intact	11 intact	11 intact
		Force: NR	2 AITFL	1 AITFL	2 AITFL
			2 AITFL+pIOL	2 AITFL+pIOL	2 AITFL+pIOL
		Instability Definition	10 AITFL+IOL	7 AITFL+IOL	7 AITFL+IOL
		Unstressed	1 AITFL+IOL +pPITFL	2 AITFL+IOL +pPITFL	15 AITFL+IOL+PITFL
		Coronal: >2mm	2 AITFL+IOL+PITFL	3 AITFL+IOL+PITFL	2 AITFL+IOL+#PITFL
		Sagittal: >2mm	4 AITFL+IOL+#PITFL	4 AITFL+IOL+#PITFL	
		Rotational: >2mm			
			Unstable injury (>2mm)	Unstable injury (>2mm)	Stable injury (>2mm)
		Stressed	**Unstressed**	**Unstressed**	**Unstressed**
		Coronal: >2mm	Total: 10	Total: 16	Total: 12
		Sagittal: >2mm	7 AITFL+IOL+PITFL	2 AITFL-IOL	4 AITFL-IOL
		Rotational: >2mm	3 AITFL+IOL+#PITFL	12 AITFL-IOL-PITFL	1 AITFL-IOL-partialPITFL
				2 AITFL+IOL+#PITFL	2 AITFL-IOL-PITFL
			Stressed		5 AITFL-IOL+PITFL#
			Total: 11	**Stressed**	
			1 IOL+PITFL	Total: 7	**Stressed**
			9 AITFL+IOL+PITFL	1 IOL+PITFL	Total: 2
			1 AITFL+IOL+#PITFL	3 AITFL+IOL+PITFL	1 AITFL-IOL-partialPITFL
			1 AITFL+IOL+pPITFL	3 AITFL+IOL+#PITFL	1 AITFL-IOL+PITFL#

Chapter 2
Arthroscopic Coronal Plane Syndesmotic Instability Has Been Over-Diagnosed

Table 2. Cont.

Arthroscopic syndesmotic instability measurements per study

Author	Characteristics	Arthroscopic Measurement Details		Coronal Stress (mm)		Sagittal Stress (mm)		Rotational Stress (mm)	
Yoshimura et al. 2008 **Country: Japan** **Design: Case Report** **Period: 06/2005 – 11/2005**	Nr: 4 Age: 24.5 Sex: 4 males Cohort: Surgically treated Maisonneuve fractures	Probe:	30° 2.7 mm	Stable injury <2 mm		NR		NR	
		Distractor:	yes	none					
		Position:	NR						
		Stress:	ER	Unstable injury >2mm					
		Force:	NR	3 AITFL-IOL					
				1 AITFL-IOL-DL (or medial malleolar fracture)					
		Instability definition							
		Coronal:	>2mm						
		Sagittal:	NR						
		Rotational:	NR						
Watson et al. 2015 **Country: USA** **Design: Cadaveric Study** **Period: NR**	Nr: 7 (C) Age: NR Sex: NR Cohort: Unmatched below knee cadavers	Probe:	“calibrated”	Intact-[AITFL+IOL]-[ATFL+CFL]-PITFL		Intact-[AITFL+IOL]-[ATFL+CFL]-PITFL		Intact-[AITFL+IOL]-[ATFL+CFL]-PITFL	
		Distractor:	no	0lbs:	98N:	PA stress		External rotation stress	
		Position:	center of incisura	0	NR	0 lbs:	22 lbs:	0 lbs:	22 lbs:
		Stress:	LHT+AP+PA+ER	0,4	0	0,2	NR	0	NR
		Force:	Sequential 8.9N Increase in force aplied	2,6	3,8	0,9	1	2,3	2,2
				grossly unstable	grossly unstable	5,2	6,4	4	5
		Instability definition	Descriptive representation of fibular displacement			grossly unstable	grossly unstable	grossly unstable	grossly unstable
						AP stress			
						0 lbs:	22 lbs:		
						0,2	NR		
						1	1,4		
						0,3	0,8		
						grossly unstable	grossly unstable		

Table 2. Cont. Arthroscopic syndesmotic instability measurements per study

Author	Characteristics	Arthroscopic Measurement Details		Coronal Stress (mm)		Sagittal Stress (mm)	Rotational Stress (mm)
Feller et al. 2016 **Country: USA** **Design: Cadaveric Study** **Period: NR**	Nr: 10 (C) Age: 58.3 Sex: 8 males Cohort: unmatched above knee	Probe:	2,2.5,3,4, and 5 mm	Group 1 Intact-AITFL-IOL-PITFL-DL		NR	NR
		Distraction:	no	Anterior	Posterior		
		Position	anterior and posterior of incisura	0.9 [0.1-1.7]	2.7 [2.0-3.3]		
		Stress:	no stress application	3.0 [2.3-3.8]*	3.6 [2.9-4.3]*		
		Force:	none	3.8 [3.1-4.5]*	4.4 [4.0-4.9]*		
				5.0 [NR]*	5.0 [NR]*		
		Instability definition:	Statistically different from intact	5.0 [NR]*	5.0 [NR]*		
				Group 2 Intact-DL-PITFL-IOM-AITFL			
				Anterior	Posterior		
				0.8 [0.4-1.2]	2.2 [1.8-2.5]		
				1.6 [0.7-2.5]*	3.4 [2.6-4.1]*		
				2.0 [0.7-3.3]*	3.9 [3.2-4.6]*		
				2.3 [0.9-3.7]*	4.3 [3.8-4.8]*		
				4.9 [4.7-5.1]*	4.9 [4.7-5.1]*		
Guyton et al. 2017 **Country: USA** **Design: Cadaveric Study** **Period: NR**	Nr: 10 (C) Age: 68.4 Sex: 10 males Cohort: matched below knee	Probe:	2-8.5mm with 0.5mm increments	Intact-AITFL-IOL-PITFL-DL		NR	NR
		Distraction:	yes	1.8 ± 0.3			
		Position:	5mm posterior of anterior margin of incisura	2.4 ± 0.5			
				3.9 ± 0.8*			
		Stress:	no stress application	5.1 ± 1.3*			
		Force:	none	5.8 ± 1.4*			
		Instability definition:	Statistically different from intact				

Table 2. Cont. Arthroscopic syndesmotic instability measurements per study

Author	Characteristics	Arthroscopic Measurement Details		Coronal Stress (mm)		Sagittal Stress (mm)		Rotational Stress (mm)
Lubberts et al.a 2017 **Country: USA** **Design: Cadaveric Study** **Period: NR**	Nr: 14(C) Age: 59 Sex: NR Cohort: Matched above knee	Probes:	ball-tipped with 0.1mm increments	Intact-[AITFL+IOL+PITFL]-DL		Intact-[AITFL+IOL+PITFL]-DL		Notes not to have observed fibular rotation.
		Distraction:	yes versus no	Anterior Unstressed		AP Distraction	AP no Distraction	
		Position:	anterior- and posterior third of incisura	distraction	no distraction	0.6 ± 1.4	0.5 ± 0.7	
		Stress:	no stress +LHT+AP+PA	1.3 ± 2.2	1.4 ± 2.3	2.0 ± 2.8	1.8 ± 2.3	
		Force:	100N	2.1 ± 2.8	2.7 ± 3.6**	2.2 ± 4.6	2.0 ± 3.9	
				2.4 ± 3.4	2.9 ± 4.8**			
		Instability definition:	Descriptive presentation of fibular displacement			PA Distraction	PA no Distraction	
				Anterior Stressed		0.5 ± 0.8	0.4 ± 0.8	
				Distraction	no Distraction	1.8 ± 2.8	1.6 ± 2.9	
				1.4 ± 2.2	1.6 ± 2.4	2.3 ±4.7	2.7 ± 4.7	
				2.4 ± 3.2	2.7 ± 3.6**			
				2.3 ± 3.8	3.3 ± 4.0**			
				Posterior Unstressed				
				Distraction	no Distraction			
				1.5 ± 1.6	1.7 ± 1.6			
				2.3 ± 1.5	2.8 ± 2.2**			
				2.6 ± 2.2	3.0 ± 2.5**			
				Posterior Stressed				
				Distraction	no Distraction			
				1.9 ± 2.0	2.0 ± 1.6**			
				3.1 ± 2.4	3.4 ± 3.2**			
				3.6 ± 3.5	4.0 ± 4.0**			

Table 2. Cont. Arthroscopic syndesmotic instability measurements per study

Author	Characteristics	Arthroscopic Measurement Details		Coronal Stress (mm)		Sagittal Stress (mm)	Rotational Stress (mm)
Massri-Pugin et al.a 2017 **Country: USA** **Design: Cadaveric Study** **Period: NR**	Nr: 14 (C) Age: 59 Sex: 8 males Cohort: unmatched above knee	Probe:	ball-tipped with 0.1mm increments	Group 1 intact-AITFL-IOL-PITFL-DL (n=7)		NR	NR
		Distraction:	no				
		Position:	anterior- and posterior third of incisura	Anterior	Posterior		
		Stress:	LHT	2.0 ± 1.5	2.7 ± 0.9		
		Force:	100N	2.3 ± 1.8	3.3 ± 1.6		
				2.7 ± 2.2	3.5 ± 1.3		
		Instability definition:	Statistically different from intact	3.4 ± 1.8	4.4 ± 1.6*		
				4.7 ± 3.3*	4.8 ± 2.0*		
				Group 2 Intact-PITFL-IOL-AITFL-DL (n=7)			
				Anterior	Posterior		
				1.2 ± 0.6	1.3 ± 0.4		
				1.4 ± 0.9	1.8 ± 0.4		
				1.7 ± 1.1	2.1 ± 0.5		
				2.0 ± 1.4	2.4 ± 0.7*		
				2.0 ± 1.8*	3.2 ± 1.6*		

Table 2. Cont. Arthroscopic syndesmotic instability measurements per study

Author	Characteristics	Arthroscopic Measurement Details		Coronal Stress (mm)		Sagittal Stress (mm)		Rotational Stress (mm)
Lubberts et al.a **Country: USA** **Design: Cadaveric Study** **Period: NR**	Nr: 22(C) Age: 55 Sex: NR Cohort: Matched above knee	Probes:	ball-tipped with 0.1mm increments					
		Distraction:	yes & no	Intact(22C)-AITFL(7C)-IOL(7C)-PITFL(14C)		Intact(22C)-AITFL(7C)-IOL(7C)-PITFL(14C)		
		Position:	anterior- and posterior third of incisura	Anterior	Posterior	AP	PA	
		Stress:	no stress +LHT+AP+PA	0.2 (0.0-0.3)	0.2 (0.1-0.4)	0.2 (0.1-0.5)	0.5 (0.1-0.8)	
		Force:	100N	0.2 (0.2-0.5)	0.4 (0.1-0.4)	0.2 (0.0-0.3)	0.4 (0.2-1.6)	
				0.3 (0.0-1.0)	0.1 (0.7-1.1)	0.4 (0.1-1.0)	1.0 (0.5-1.8)	
		Instability Definition	Cluster analysis to assign each injury setting into stable and unstable groups	0.5 (0.2-0.7)	0.5 (0.2-1.0)	1.8 (0.9-3.0)	1.2 (0.6-1.5)	
				DL(8C)-AITFL(8C)-IOL(8C)- PITFL(22C)		DL(8C)-AITFL(8C)-IOL(8C)- PITFL(22C)		
				Anterior	Posterior	AP	PA	
				0.2 (0.1-0.2)	0.3 (0.2-0.6)	0.4 (0.3-0.8)	0.7 (0.3-1.3)	
				0.2 (01-0.2)	0.3 (0.1-0.4)	0.2 (0.1-0.3)	1.0 (0.3-15)	
				0.4 (0.1-1.1)	0.3 (0.1-0.6)	0.8 (0.5-1.4)	1.4 (0.8-1.9)	
				0.3 (0.2-0.9)	0.7 (0.3-1.3)	1.3 (0.6-2.0)	2.2 (1.3-3.5)	
				PITFL(7C)-IOL(7C)		PITFL(7C)-IOL(7C)		
				Anterior	Posterior	AP	PA	
				0.1 (0.1-0.2)	0.1 (0.0-0.3)	0.3 (0.0-0.8)	0.4 (0.2-0.6)	
				0.2 (0.0-0.4)	0.4 (0.0-0.5)	0.6 (0.2-1.4)	0.5 (0.2-1.0)	
Massri-Pugin et al.a 2018 **Country: USA** **Design: Cadaveric Study** **Period: NR**	Nr: 8(C) Age: 48 Sex: 8 males Cohort: Unmatched above knee	Same as Massri-Pugin et al 2017		Intact-DL-AITFL-IOL-PITFL		NR		NR
				Anterior	Posterior			
				1.4 ± 0.7	2.2 ± 0.5			
				1.6 ± 0.8	2.4 ± 0.4			
				2.1 ± 1.3	2.9 ± 0.9			
				2.5 ± 1.8*	3.0 ± 0.9*			
				2.8 ± 1.8)*	3.3 ± 1.0*			

Author	Characteristics	Arthroscopic Measurement Details		Coronal Stress (mm)	Sagittal Stress (mm)	Rotational Stress (mm)
Turky et al. 2018 **Country: Oman** **Design: Retrospective Study** **Period: Dec 2014 – Jul 2016**	Nr: 78 Age: 32 Sex: 54 males Cohort: Patients with chronic ankle pain or instability symptoms	Probe:	2-5 mm probes	Grade 1 (Stable injury), <2mm	NR	NR
		Distractor:	yes	Anterior / Posterior		
		Position:	anterior and posterior	Intact 30 / 30		
		Stress:	pushing fibula away from tibia with probe	pAITFL 0 / 14		
				pPITFL 4 / 0		
		Force:	NR			
		Instability definition		Grade 2 (potentially unstable injury), >2 to ≤4mm		
		Unstressed grade 0	grade 1 / grade 2			
		Coronal: ≤2mm;	>2 to ≤4mm; >5mm	Anterior / Posterior		
		Sagittal: NR	NR / NR	pAITFL 14 / 0		
		Rotational: NR	NR / NR	pPITFL 0 / 4		
				AITFL+PITFL 22 / 21		
		Stressed grade 0	grade 1 / grade 2			
		Coronal: ≤2mm;	>2 to <5mm; ≥5mm	Grade 3 (unstable injury), >5mm		
		Sagittal: NR	NR / NR	Anterior / Posterior		
		Rotational: NR	NR / NR	AITFL+PITFL 8 / 9		
D'Hooghe et al. 2019 **Country: Qatar** **Design: Cadaveric** **Period: NR**	Nr: 16(C) Age: 58-74 Sex: NR Cohort: Unspecified fleshly frozen cadaver ankles	Probe:	4mm shaver	Intact-AITFL-IOL-PITFL	NR	NR
		Distractor:	no	>4mm		
		Position:	1cm proximal to distal tibiofibular joint	128 ± 8.6N		
		Stress:	pushing 4mm shaver into the tibiofibular joint	105 ± 4.7N*		
				58 ± 6.9N*		
		Force:	required force to push the shaver into the tibiofibular joint measured with dynamometer	54 ± 6.5N*		
		Instability definition:	NR			

Table 3. Weighted means of the arthroscopic diastasis measurements in the coronal plane

Number Of Transected Ligaments	Anterior Incisura (range of means) (mm)	Posterior Incisura (range of means) (mm)
Intact	1.4 (0.8-2)	2.1 (1.3-3.3)
One ligament	2.0 (1.4-3)	2.6 (1.6-3.6)
Two ligaments	2.4 (1.7-3.8)	3.3 (2.1-4.4)
Three ligaments	3.0 (2-5)	3.7 (2.4-5)
Syndesmotic instability value*	2.85 (1.6-4.7)	3.4 (2.4-4.4)

*The syndesmotic instability weighted mean value was calculated using the tibiofibular displacement values from those injury patterns that showed a significant difference from the intact state

Table 4. Fluoroscopic syndesmotic instability measurements per study

Author	Cohort And methods	Measurements		
		TFO (mm)	TFCS (mm)	MCS (mm)
Lui et al. 2005 **Country: China** **Design: Prospective Study** **Period: 06/2002 – 12/2003**	Nr: 53 Age: 35.4 Sex: NR Cohort: Surgically treated Weber type B or C ankle fractures without radiographic evidence of frank syndesmosis diastasis	NR	Injury patterns which did not show widening: 11 intact 2 AITFL 2 AITFL + IOLpartial 9 AITFL + IOL 1 IOL + PITFL 2 AITFL + IOL + pPITFL 4 AITFL + IOL + PITFL 5 AITFL + IOL + PITFL# Injury patterns which did show widening: 14 AITFL + IOL + PITFL 3 AITFL + IOL + PITFL#	NR
Feller et al. 2016 **Country: USA** **Design: Cadaveric Study** **Period: NR**	Nr: 10 (C) Age: 58.3 Sex: 8 males Cohort: unmatched above knee	Group 1 Intact-AITFL -IOL-PITFL-DL 4.9 (4.3-5.6) 4.4 (3.63-5.7) 2.8 (2.4-3.2)* 1.5 (0.1-2.9)* <0 (NR) Group 2 Intact-DL -PITFL-IOM-AITFL 4.7 (3.5-5.9) 3.8 (3.0-4.6) 3.0 (2.0-4.0)* 2.2 (1.6-2.7)* <0 (NR)	Group 1 - Intact-AITFL -IOL-PITFL-DL 4.7 (3.5-5.9) 5.4 (4.5-6.3)* 5.6 (4.8-6.4) 7.53 (5.9-9.2) 11.46 (10.1-12.8)* Group 2 Intact-AITFL -IOL-PITFL-DL 5.5 (5.0-6.0) 5.4 (4.3-6.5)* 5.3 (4.3-6.4) 6.1 (4.8-7.3) 11.1 (9.3-12.9)*	Group 1 - Intact-AITFL -IOL-PITFL-DL 4.0 (3.1-4.9) 4.0 (3.3-4.6) 5.0 (3.9-6.2) 5.7 (4.5-7.0)* 9.8 (8.11-11.5)* Group 2 - Intact-AITFL -IOL-PITFL-DL 4.8 (3.9-5.7) 4.9 (4.2-5.7) 5.64 (5.0-6.3) 5.8 (4.7-6.8)* 10.3 (4.7-6.8)*

Abbreviations: TFO; tibiofibular overlap, TFCS; tibiofibular clear space, MCS; medial clear space, mm; millimeters, nr; number, NR; not reported, AITFL; anterior inferior tibiofibular ligament, IOL; interosseous ligament,
PITFL; posterior inferior tibiofibular ligament, DL; deltoid ligament, p; partial, #; fracture C; Cadaver
*significant difference from intact

Table 5. Summary table for the risk of bias across the included studies

Study	Risk Of Bias				
	Objective(s) And Study Characteristics	Study Design	Methodology Characterization	Descriptive Anatomy	Reporting Of Results
Lui et al. 2005	High	Low	High	Low	High
Yoshimura et al. 2008	High	Low	High	Low	High
Watson et al. 2015	High	High	High	Low	High
Feller et al. 2016	Low	Low	High	Low	Low
Guyton et al. 2017	Low	Low	High	Low	High
Lubberts et al. 2017	Low	Low	Low	Low	Low
Massri-Pugin et al. 2017	Low	Low	High	Low	Low
Lubberts et al. 2018	Low	Low	Low	Low	Low
Massri-Pugin et al. 2018	Low	Low	High	Low	Low
Turky et al.	Low	Low	High	Low	High
D'Hooghe et al.	High	High	High	Low	High

High risk; Red, low risk; Green, unclear risk; Blue

Table 6. Quality assessment of the included clinical studies using the MINORS criteria

Authors	Year	Journal	Evidence	Study design	1	2	3	4	5	6	7	8	Total
Lui et al.	2005	Arthroscopy	II	Cohort study	0	2	1	1	0	0	0	0	6
Yoshimura et al.	2008	Orthopaedic Science	IV	Case series	2	1	0	2	0	1	0	0	7
Turky et al.	2018	Foot And Ankle Surgery	III	Cohort study	2	2	2	1	0	0	0	0	7

Only the non-comparative part of the MINORS criteria was used (i.e. frst 8 questions). The criteria of Methodological Index for Non-Randomized Studies (MINORS) with 0 points when not reported, 1 when reported but not adequate, and 2 when reported and adequate. Maximum score is 16

1. A clearly stated aim: the question addressed should be precise and relevant in the light of available literature.
2. Inclusion of consecutive patients: all patients potentially ft for inclusion (satisfying the criteria for inclusion) have been included in the study during the study period (no exclusion or details about the reasons for exclusion).
3. Prospective collection of data: data were collected according to a protocol established before the beginning of the study.
4. End points appropriate to the aim of the study: unambiguous explanation of the criteria used to evaluate the main outcome which should be in accordance with the question addressed by the study. In addition, the end points should be assessed on an intention-to-treat basis.
5. Unbiased assessment of the study end point: blind evaluation of objective end points. and double-blind evaluation of subjective end points. Otherwise, the reasons for not blinding should be stated .
6. Follow-up period appropriate to the aim of the study: the follow-up should be sufficiently long to allow the assessment of the main endpoint and possible adverse events
7. Loss to follow-up less than 5%: all patients should be included in the follow-up. Otherwise, the proportion lost to follow-up should not exceed the proportion experiencing the major end point
8. Prospective calculation of the study size: information of the size of detectable difference of interest with a calculation of 95% CI, according to the expected incidence of the outcome event, and information about the level for statistical.

Discussion

The most important finding of this study is that the commonly used threshold of 2.0 mm potentially leads to overtreatment and using 3.0 mm of tibiofibular diastasis measured at the anterior portion of the incisura or 3.4 mm of tibiofibular diastasis at the posterior portion seems to be a better cut off value.

Syndesmotic instability can cause significant long-term morbidity if undiagnosed and even subtle persistent syndesmotic instability can already be very disabling. The latter can be difficult to appreciate with clinical maneuvers or with static imaging. This has generated increasing interest in directly visualizing the distal tibiofibular articulation arthroscopically. Despite the fact that ankle arthroscopy has been proposed as the gold standard for diagnosing (subtle) syndesmotic instability, no prior literature review has systematically evaluated the available published research detailing arthroscopic examination of syndesmotic instability.[16] In total, eleven studies were ultimately included in this review, though high heterogeneity didn't allow a formal meta-analysis.
Syndesmotic instability is inherently multidimensional and is comprised of tibiofibular diastasis in the coronal plane, fibular translation in the sagittal plane, and fibular external rotation.[5, 20] The majority of the published literature, however, evaluates the syndesmosis primarily in the coronal plane while applying a lateral fibular "hook test". Several cut off values have been proposed by various authors, including 1 mm with stress application,[11] > 2 mm without stress application,[17] > 2 mm with stress application,[7, 8, 21, 28, 49] > 3 mm without stress application,[52] > 3 mm with stress application,[1, 11, 38] >4 mm without stress application,[8] and >4 mm with stress application.[43] Most studies used 2 mm as a cut off value, but this may over-diagnose syndesmotic instability and 3 mm may instead serve as a better cut off value in the coronal plane.[3, 15, 16, 26, 31, 32, 53] In this review, the weighted mean of syndesmotic instability in the coronal plane with a lateral fibular stress maneuver was 2.9 mm at the anterior portion of the incisura and 3.4 mm at the posterior portion of the incisura.

Syndesmotic instability in the sagittal plane is less well-described in the arthroscopic literature. Those that did investigate sagittal plane instability found that the instability is more visible in the sagittal plane than in the coronal plane in the setting of an unstable syndesmosis.[6, 26, 27, 30, 38, 45, 53, 55] However, the total amount of sagittal plane fibular translation that best serves as a clinical threshold for diagnosing syndesmotic instability remains uncertain. Lubberts et al., created a prediction model based on cluster analysis of data from a cadaveric syndesmotic injury model, which incorporated coronal as well as the sagittal plane measurements for assessing syndesmotic instability.[26] They reported cut off values of 2.2 mm of posterior fibular translation when performing an anterior to posterior hook test and 2.6 mm of anterior fibular translation when performing a posterior to anterior hook test.[26]

Rotational plane stability is rarely assessed arthroscopically in the published literature. One clinical study included in this systematic review evaluated the rotation by assessing the difference between the distance from the anterior border to the incisura and the distance between the posterior border and the incisura.[30] Given that this value can be confounded by concomitant coronal and sagittal plane translation, the arthroscope may not be the preferred method for determining fibular rotation.[30]

Technical factors also influence the amount of tibiofibular diastasis visualized arthroscopically, including **1.** the amount of stress applied and in which direction,[12, 26, 39, 47] **2.** whether a distractor is being used,[27] and **3.** where in the incisura the diastasis is being measured.[15, 26, 31, 32] Stoffel et al. highlighted that stress forces above 100 N do not result in additional diastasis, and therefore numerous studies have standardized a 100N force applied to the fibula 5cm proximal to the tibiotalar joint in either the coronal or sagittal planes.[26, 27, 31, 32, 47] Furthermore, an ankle distractor is almost universally employed during arthroscopic procedures to the ankle, but this traction can mask syndesmotic instability, likely due to the applied tension to the surrounding intact ligaments and other soft tissues. Distraction should therefore be released at the time of measurement, especially if the syndesmotic instability is anticipated to be subtle.[15, 27, 37] Lastly, measurements in the posterior third of the incisura may result in higher values than those anteriorly.[15, 31, 32]

It is important to note that the reported distinction between a stable and unstable syndesmotic measurement value in the literature, as assessed arthroscopically, is a statistical one. The threshold values for instability, as discussed above, are those in which an injury to the syndesmosis has allowed the fibula to translate, either coronally or sagittally, on average significantly more than in the intact state. On the other hand, the degree of diastasis or translation that has clinical implications remains unclear and may or may not entirely correlate with the discussed values. Determination of the clinical effect of the various cut off values will be challenging given that it would require a randomized controlled or a multi-center observational study in which different surgeons use different thresholds.

Ankle arthroscopy does also have some inherent disadvantages. It is an invasive technique and, consequently, available to a select group of patients with either a high level of pre-operative suspicion or patients with a concomitant fracture that independently require surgery. Furthermore, unlike imaging modalities, arthroscopy cannot benefit from using the contralateral side as an internal control, which becomes increasingly useful as instability becomes more subtle, especially in chronic injury scenarios.[13, 24, 36]

Diagnostic techniques that are non-invasive, dynamic, and allow for a bilateral examination at the same time will therefore almost undoubtedly play an increasing role in diagnosing syndesmotic instability in the future alongside the arthroscope. Modalities such as weightbearing CT or dynamic ultrasound fit the above criteria, and their roles should be further explored in both biomechanical and clinical studies.[2, 5, 33, 34]

Two papers included in this review also assessed radiographic or fluoroscopic measurements.[15, 30] They corroborated other radiographic studies highlighting that parameters such as tibiofibular overlap, tibiofibular clear space and medial clear space, do not seem sufficiently sensitive to diagnose syndesmotic instability.[9, 22] This review has some limitations. The overall quality of the included studies was low and there was a high risk of bias. For the experimental studies the low quality was most commonly due to a lack of intra- and inter-observer reliability measurements. Secondly, this study used the AQUA assessment tool, which is specifically designed for evaluating the methodology of an anatomic experiment and was therefore deemed most applicable for inclusion of cadaveric studies, but this tool is only now undergoing the process of being formally validated.[18] Lastly, ligamentous injury pattern was used as a reference standard when comparing the amount of fibular displacement across studies for the same injury and was used to calculate the weighted means. It should be noted that the injury pattern seen in a clinical setting does not invariably correlate with instability.[30, 50, 56] Clinical instability likely also relies on other potential patient factors (e.g. age, weight, and chronicity), but it may also result from a measurement bias given that the forces used in the various stress tests used are often not reported in the literature.

Conclusion

The results have concluded that the commonly used 2.0 mm threshold value of distal tibiofibular diastasis may lead to overtreatment of syndesmotic instability, and that using threshold values of 2.9 mm measured at the anterior portion of the incisura and 3.4 mm at the posterior portion may represent better cut off values. Given the ready availability of 3 mm probes among standard arthroscopic instrumentation, at the very least surgeons should use 3 mm in lieu of 2 mm probes intraoperatively.

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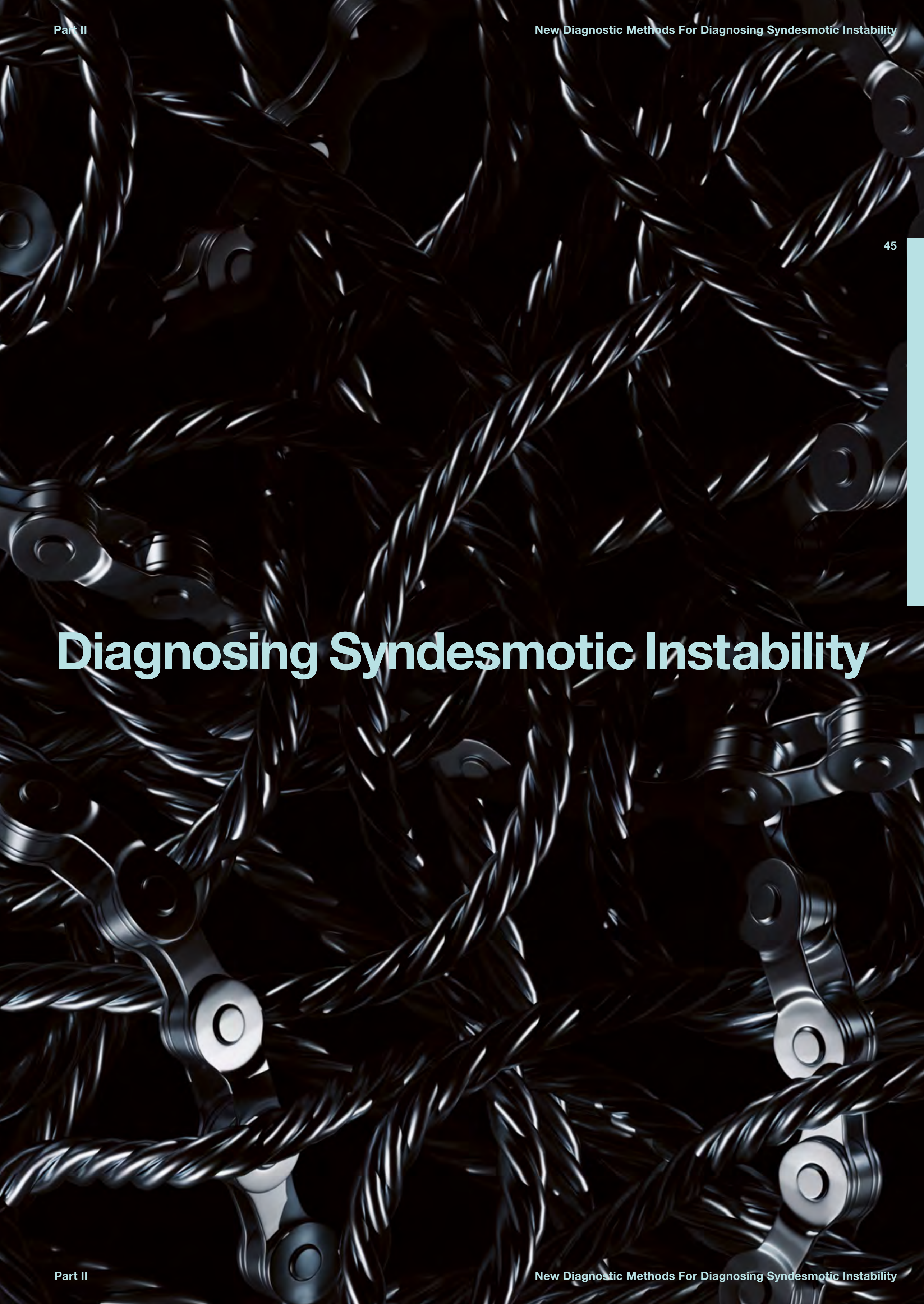
Part II

New Diagnostic Methods For



Diagnosing Syndesmotic Instability

Chapter 3 Diagnosing Syndesmotic Instability With Dynamic Ultrasound - Establishing The Natural Variations In Normal Motion

Hagemeijer NC, Saengsin J, Chang SH, Waryasz G, Kerkhoffs GMMJ, Guss D, DiGiovanni CW

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Abstract

Background

Syndesmotic instability, when subtle, is challenging to diagnose and often requires visualization of the syndesmosis during applied stress. The primary aim was to assess normal distal tibiofibular motion in the sagittal plane using dynamic ultrasound under stress conditions. The secondary aim was to evaluate the reliability of dynamic stress ultrasonography.

Methods

Twenty-eight participants without history of ankle injury were included. Sagittal fibular translation was generated by applying a manual force to the fibula from anterior to posterior and from posterior to anterior. Distance between the ultrasound probe and the fibula was taken at two predefined points: **1.** no force applied and, **2.** during maximum force application. Each participant was scanned twice by two independent examiners, and each scan was analysed by two independent examiners. Three participants were scanned a second time by the same examiner who analysed these films twice to assess for intraobserver agreement. Means of exam 1 versus exam 2 were compared using a mixed linear model. Agreement among observers was calculated using intraclass correlation coefficients (ICC) interpreted as 0.4, poor; 0.4 < ICC < 0.59, acceptable; 0.6 < ICC < 0.74, good; ICC > 0.74, excellent.

Results

Fifty-six ankles were included in the study, including 16 (57%) males and 12 (42%) females. Average anterior to posterior fibular sagittal translation was 0.89 0.6 mm and posterior to anterior fibular sagittal translation was 0.49 1.1 mm. Anterior to posterior translation means of exam 1 versus exam 2 showed no significant differences, means of 0.81mm [0.7-0.9] versus 0.77mm [0.7-1.0], and posterior to anterior means [95% CI] of 0.42mm [0.3-0.5] versus 0.44mm [0.2-0.6] (p-values 0.416 and 0.758, respectively). Excellent Inter- and intraobserver agreement was found for all measurements taken.

Conclusion

Dynamic ultrasound allows one to effectively and readily evaluate sagittal translation of the distal tibiofibular joint. It is able to afford bilateral comparisons, which becomes critical as the amount of syndesmotic instability approaches greater degrees of subtlety.

Introduction

Ankle sprains are a common reason for primary care office and emergency department visit, in the general population the incidence rate of a concomitant syndesmotic injury is about 2.09 per 100,000 person-years.[1, 2] As compared to isolated lateral ankle sprains, high ankle sprains generally entail a longer recovery period with prolonged pain and slower return to sport.[3-8] Critically important to effectively treating such conditions is the ability to identify those injuries that result in syndesmotic instability, which can lead to long term morbidity when left untreated.[6, 9-12]

Subtle syndesmotic instability—typically those cases without fracture or frank radiographic diastasis of the tibiofibular joint—can be difficult to diagnose. When an index of suspicion persists, some have argued that direct arthroscopic visualization should be considered the golden standard for making this determination.[13-20] This represents an invasive and costly approach, however, without comparator. Such surgical inspection can be helpful but exists in isolation because it does not allow evaluation of the contralateral, unaffected side for use as the ideal internal control it would otherwise be. Alternatively proposed modalities, therefore, have included weightbearing radiographs, weightbearing CT, MRI, and ultrasound.[21-23] Amongst these options, ultrasound has several inherent advantages: it is immediately available at the point of care, it can generate high-detail, it carries low cost, it has no radiation, and it enables dynamic evaluation of structures while applying provocative stress.[24] Perhaps most importantly, though, it also allows simultaneous evaluation of the contralateral side as an internal control—an often invaluable attribute given the naturally occurring variations in anatomic configuration of the human distal tibiofibular joint.[25-33] Indeed, prior studies have demonstrated that ultrasound is an accurate and reliable tool for assessing the quality of the anterior inferior tibiofibular ligament (AITFL) and effectively evaluates coronal tibiofibular diastasis when comparing it to MRI.[34-38] None, however, have evaluated its utility while applying a dynamic sagittal stress to the fibulawhich, in vivo, is most readily performed in the sagittal plane.

The purpose of this study was therefore to establish a readily available, non-invasive, low cost, dynamic assessment technique using ultrasound to diagnose subtle syndesmotic instability by evaluating: **1.** the normal references of normal tibiofibular motion in the sagittal plane using ultrasound, **2.** side to side variations, **3.** effect of participant demographics on fibular translation values, and **4.** reliability of the stress examination and measurement methods. Our hypothesis was that little variation would exist between healthy ankles and that different examiners would obtain similar values.

Methods

Participant Population

This phase 1 diagnostic cohort study was performed with the approval of the hospitals' Institutional Review Board, Protocol number, 2017P002793.[39] Between December 2018 and August 2019 a total of 35 potential subjects were asked to participate in this study, 28 participants agreed and 56 ankles were ultimately included in this study. All participants included in this study were study staff or patients from

a foot and ankle clinic in a tertiary center who were older than 18 years and had two uninjured ankles. Participants were excluded if they had an ankle fracture in their medical history, complaints of ankle instability due to recurrent ankle sprains for at least 6 months, or a ligamentous laxity due to a hereditary syndrome. Participants were allowed to have eversion or inversion ankle sprains in the past but were completely asymptomatic at the time of enrolment. Oral consent was provided by all the participants. Seven patients chose not to participate due to time constraints.

Participant demographic data was collected by interviewing the subjects before performing the ultrasound experiment and by retrospective chart review. Demographic data included age, sex, laterality, body mass index (BMI), and tobacco use.

Establishment Of The Ultrasonography Test

The distal tibiofibular joint was examined using an ultrasound probe (2D, gray scale B mode complete ultrasound; Logiq E9, General Electronics Company, ML6-15 and L8-18i-D probes). To detect the anterior to posterior (A to P) fibular translation the participant was positioned in the supine position and to detect the posterior to anterior (P to A) fibular translation the participant was positioned in the prone position. In each position the participant lay with the foot hanging off the examination table.

Standardized probe positions were determined using the tibiotalar joint as an anatomical landmark (Table 1, Figure 2) and fibular translation was simulated in each direction by applying manual force to the distal tip of the fibula in the sagittal plane until more force did not result in additional fibular translation. The dynamic stress exam was captured in real-time video for subsequent analysis.

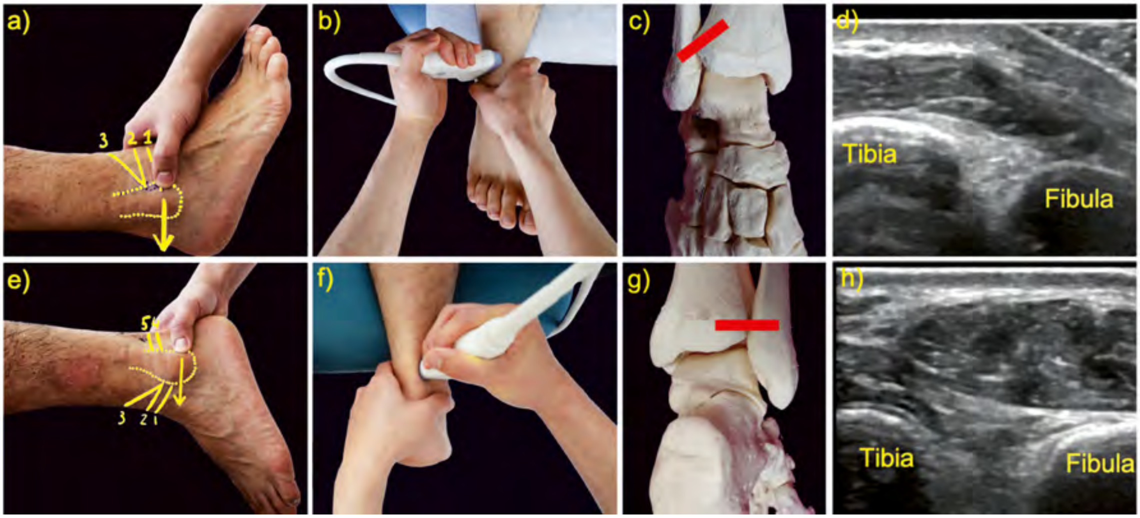
Table 1. Positioning of the probe

Steps – Anterior positioning		
	1	Participant in the supine position with the foot hanging off the examination table
	2	Tibiotalar joint visualization, probe is positioned longitudinally over the anterior tibiotalar joint
	3	A line 10 mm above the tibiotalar joint line is drawn
	4	From the 10 mm line, a line with 30 ° was drawn parallel to the AITFL
	5	The ultrasound probe was placed on the 30 ° line with the middle of the probe covering the anterior incisura
	6	The probe was tilted between 50 and 60 ° from the floor
Steps – Posterior positioning		
	1	Participant in the prone position with the foot hanging off the examination table
	2	Tibiotalar joint visualization, probe is positioned longitudinally over the posterior tibiotalar joint.
	3	A line 10 mm above the tibiotalar joint line is drawn
	4	The ultrasound probe was placed on the 10 mm line with the middle of the probe covering the posterior incisura
	5	The probe was tilted between 0 and 10 ° from the floor

Measurement Methods

The captured real-time films of the bilateral tibiofibular joints were read on the ultrasound device (Logiq E9, General Electronics Company). Positions of the tibia and fibula were subsequently measured at two pre-determined time points: when there was no force (NF) application and at maximum force application (MF). To measure the fibular translation, first positions of the tibia and fibula were determined by measuring the closest distance from the tibial and fibular bones to the probe at no force and at maximum force application (Figure 2). By default the ultrasound device automatically calculated the absolute distance from the ultrasound handset probe to the pointer which was manually located at hyperechoic bony structure closest to the probe. Additionally, the tibiofibular clear space (TFCS) was measured by measuring the TFCS at no force and at maximum force (Figure 3). TFCS was determined by measuring the shortest distance between the tibia and fibula at the beginning of the tibiofibular joint space. During the examination the ultrasound probe was fixed to the tibia, care was taken to have sufficient ultrasound gel between probe and fibula.

Figure 1. Ultrasound probe and hand positioning to detect sagittal translation of the distal fibula



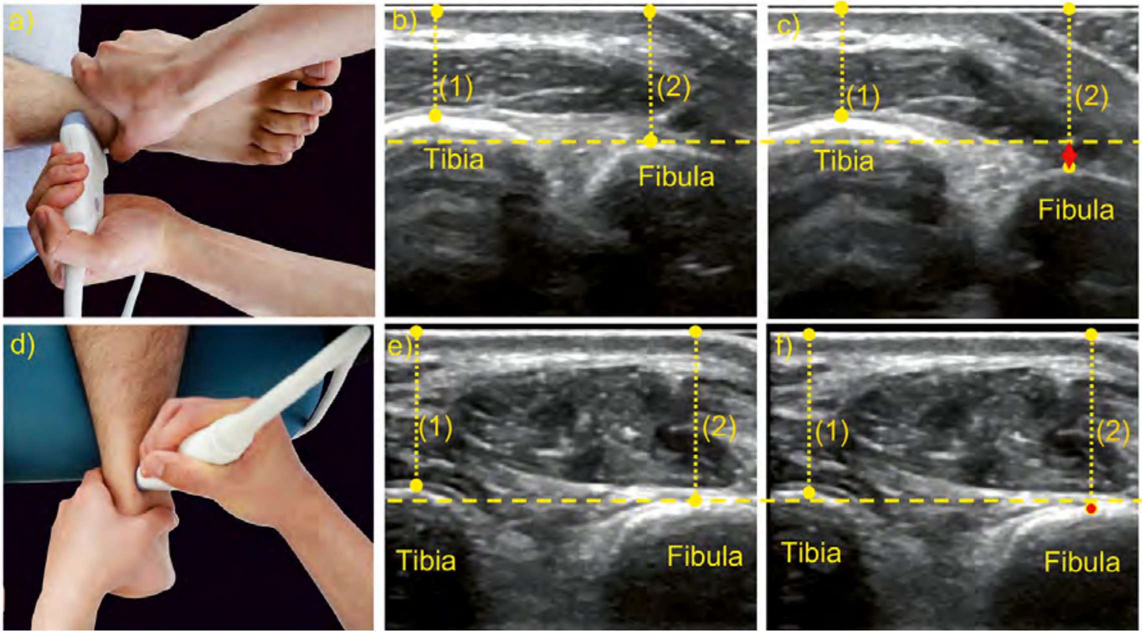
(a to d) Anterior to posterior stress examination: (a) hand positioning; 1 tibiotalar joint line, 2 line 10 mm above the tibiotalar joint, 3 line drawn 30° from the line nr 2 representing probe position, (b) participant in the supine position with the foot hanging offthe table, (c) probe position, (d) corresponding ultrasound image. (e to f) Posterior to Anterior stress examination: (e) hand positioning, (f) participant in the prone position with the foot hanging offthe table, (g) probe position, (h) corresponding ultrasound image.

Ultrasound Outcome

From the captured real-time film the tibiofibular starting position and fibular translation value could be obtained. The starting position of the fibula was defined as the delta height between the tibia and fibula, i.e. TibiaNF-FibulaNF. The fibular translation value was defined as the delta change in fibular movement while maintaining the tibia as a reference (Figure 1), i.e. (TibiaNF-FibulaNF)-(TibiaMF-FibulaMF).

Additionally, tibiofibular clear space (TFCS) opening was calculated by distracting the TFCS at maximum force (TFCSMF) from the TFCS at no force (TFCSNF).

Figure 2. Fibular translation measurement and ultrasound images



(a-c) Anterior to Posterior fibular translation measuring technique, (d-f) Posterior to Anterior fibular transla- tion measuring technique, (c) red diamond resembles Anterior to Posterior fibular translation at maximum pressure force, (f) red dot resembles Posterior to Anterior fibular translation at maximum pressure force.

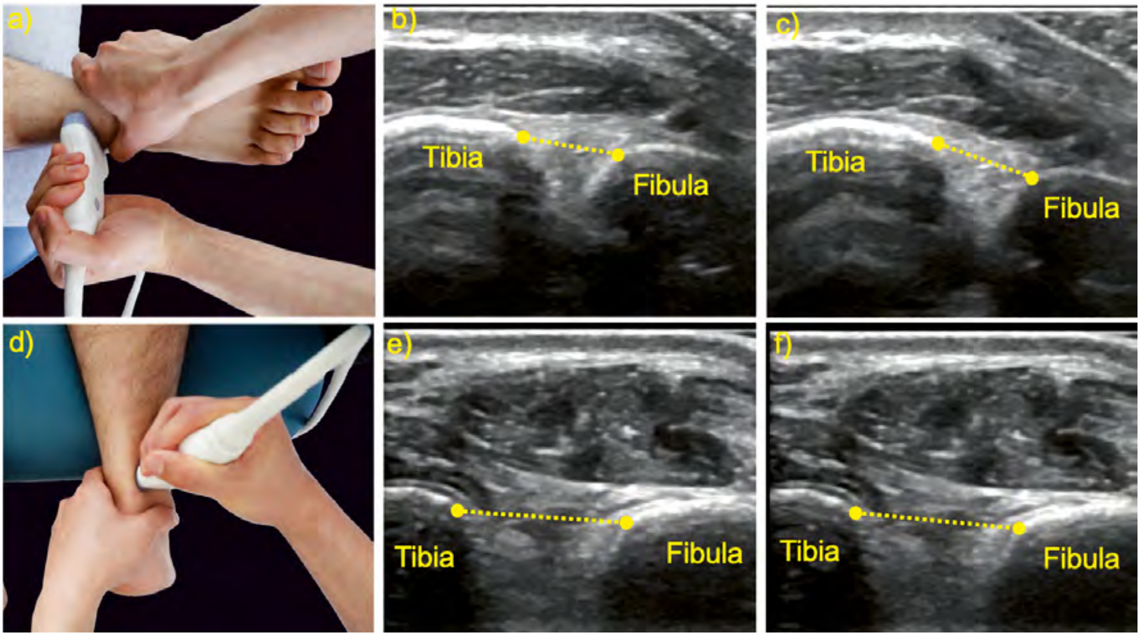
Reliability Measures

Each participant included in the study was scanned twice by two examiners who have experience with musculoskeletal ultrasound for more than 2 years and of whom two are specialized orthopedic foot and ankle surgeons and one a nonsurgical physician (JS, SHC, and NH respectively). To investigate whether the examination could be repeated by the same examiner, three participants were scanned a second time by the same examiner (NH).

All captured real-time films were thereafter measured by two independent observers who worked in separate data files to assess for interobserver reliability (JS and NH). To assess intraobserver reliability of this test, three participants were measured a second time by the same observer after a time period of six weeks after the initial obtainment (NH).

To investigate the variability of the subjective amounts of forces applied by the examiners three orthopedic surgeons and one nonsurgical physician (three men, one woman) were asked to perform the ultrasonography stress examination as described twice with a force sensor attached to their thumb to measure the different forces applied (Tekscan FlexiForce ELF system, Boston). All four were experienced with performing this ultrasound guided stress exam.

Figure 3. Tibiofibular clear space measurement and ultrasound images



(a-c) Anterior tibiofibular clear space measurements, (d-f) Posterior tibiofibular clear space measurements.

Statistical analysis

Descriptive analysis was performed to summarize the baseline characteristics and are presented with frequencies and percentages for categorical variables, with both mean and standard deviations or 95% Confidence Intervals [95%CI] reported for continuous variables. The positions of the fibula and the tibia at no stress application was considered baseline. To evaluate whether laterality, participant characteristics, and examiner had an effect on the sagittal fibular translation values a linear mixed effect model was built for analysis, wherein subject and examiner were crossed random effects using an unstructured covariance matrix. The factors age and height were dichotomized based upon the median, BMI was dichotomized into normal weight (<25) and overweight (≥25). To investigate whether the effect of BMI on translation was different between sexes or age groups, BMI*sex and BMI*age interaction term were entered in the model. A Bonferroni test was used to adjust for multiple comparisons. To assess inter- and intra- observer agreement scores the interclass correlation coefficient (ICC) through a 2-way mixed effects model with absolute agreement were used. Absolute agreement in an ICC assesses how much each measurement performed by one observer differs from the other observer. Interpretation of the ICC values were interpreted as follows: ICC < 0.4, poor; 0.4 < ICC < 0.59, acceptable; 0.6 < ICC < 0.74, good; and ICC > 0.74, excellent.[40]. Two-sided p-values of <0.05 will be considered significant. The number of 28 subjects included in this study was based upon evidence based diagnostic study methodologies, where a number of subjects for establishing reference values in the normal population was handled of 20-30 subjects.[39, 41] All analyses were performed with Stata 13.0 for Mac (StataCorp LP, College Station, TX, USA).

Results

A total of 28 participants, 56 ankles, were included in this prospective stage 1 diagnostic study,[39] 16/28 males and 12/28 females with a mean (SD) age of 33.7 12.6 years, height of 171.0 10.9 cm, and BMI of 25.5 4.4 kg/m² were included in this study.
Two out of the 28 subjects were smokers.

Fibular Translation

The anterior surface of the fibula was situated 0.4 1.7 mm deeper from the probe than the anterior surface of the tibia when scanning with the participant supine. The mean A to P fibular sagittal translation was 0.89 0.6 mm. When applying an A to P directed force no differences in laterality were found. No participant-specific characteristic affected fibular translation values (Table 2). There was no interaction between BMI and sex (p-value 0.780), and BMI and age (p-value = 0.710).

When scanning with the participant prone, the posterior surface of the fibula was situated 3.0 2.0 mm deeper than the posterior surface of the tibia. The P to A fibular sagittal translation was 0.49 1.1 mm. When applying an P to A directed force, no differences in laterality were found. No participant-specific characteristic affected fibular translation values (Table 1). There was no interaction between BMI and sex (p-value 0.948), and BMI and age (p-value = 0.710).

Table 2. Mean fibular translation values in the sagittal plane

Characteristic	Translation (mm) [95%CI]	Translation Difference (mm) [95%CI]	p-value
Anterior to Posterior			
Side (right)	0.85 [0.71-0.99]	0.07 [-0.07-0.20]	0.325
Sex (female)	0.91 [0.74-1.10]	-0.05 [-0.28 – 0.18]	0.676
Age (<30yr)	0.92 [0.74-1.10]	-0.06 [-0.30-0.18]	0.625
BMI (<25 kg/m²)	0.97 [0.81-1.11]	-0.18 [-0.41- -0.06]	0.137
Height (<173cm)	0.90 [0.73-1.08]	-0.04 [-0.28-0.21]	0.763
Posterior to Anterior			
Side (right)	0.54 [0.31-0.78]	-0.10 [-0.36 – 0.15]	0.434
Sex (female)	0.50 [0.20-0.79]	-0.01 [-0.40-0.37]	0.95
Age (<30yr)	0.52 [0.28-0.86]	-0.15 [-0.54-0.24]	0.451
BMI (<25 kg/m²)	0.60 [0.33-0.86]	-0.23 [-0.62-0.16]	0.24
Height (<173cm)	0.54 [0.26-0.82]	-0.09 [-0.49-0.30]	0.644

The translation column contains the translational values of the group indicated in the characteristic column.
The p-value shows whether the fibular translation was affected by the characteristic.
Abbreviations: mm; millimeter, 95%CI; 95% Confidence Interval, yr; year,
kg/m²; kilograms per square meter, cm; centimeter, BMI; body mass index

Tibiofibular Clear Space Values

The anterior TFCS value with no force application was 4.1 0.95 mm and with force application 4.56 0.97 mm, resulting in a TFCS widening of 0.44 0.48 mm. When applying an A to P directed force no TFCS differences in laterality were found. TFCS values were not affected by any participant characteristic (Table 3).

The posterior TFCS value with no force application was 6.10 1.41 mm and with force application 6.08 1.42 mm, resulting in a closing TFCS of -0.03 0.47. When applying a P to A directed force no TFCS differences in laterality were found. TFCS values were not affected by any participant characteristic (Table 3).

Table 3. Mean tibiofibular clear space values

Characteristic	TFCS widening (mm) [95%CI]	Difference (mm) [95%CI]	p-value
Anterior to Posterior			
Side (right)	0.47 [0.37-0.58]	0.07 [-0.19-0.05]	0.255
Sex (female)	0.42 [0.30-0.55]	0.02 [-0.14-0.19]	0.742
Age (<50yr)	0.43 [0.34-0.53]	0.03 [-0.25-0.30]	0.842
BMI (<25 kg/m^2)	0.45 [0.33-0.57]	-0.02 [-0.20-0.15]	0.754
Height (<173cm)	0.39 [0.27-0.52]	0.08 [-0.01-0.27]	0.345
Posterior to Anterior			
Side (right)	-0.004 [-0.15-0.06]	-0.03 [-0.09-0.15]	0.614
Sex (female)	-0.05 [-0.17-0.09]	0.03 [-0.14-0.20]	0.752
Age (<50 yr)	-0.01 [-0.11-0.01]	-0.11 [-0.39-0.17]	0.438
BMI (<25 kg/m^2)	0.03 [-0.08-0.15]	-0.13 [-0.31-0.04]	0.138
Height (<173cm)	-0.04 [-0.17-0.10]	0.02 [-0.17-0.20]	0.867

The TFCS widening column contains the difference between no force and maximum force (TFCSMF – TFCSNF). The p-value shows whether the TFCS was affected by the characteristic. Abbreviations: TFCS; tibiofibular clear space, mm; millimeter, 95%CI; 95% Confidence Interval, yr; year, kg/m^2; kilograms per square meter, cm; centimeter, BMI; body mass index

Reliability Of The Ultrasonography Test

Each participant was scanned twice by two independent examiners. No difference in fibular translation values was found between these two paired exams when scanning in either the supine or prone positions (Table 4). Three participants were scanned a second time by the same examiner to investigate whether similar translation values could be found by the same sonographer. Only the TFCS opening was significantly different between the two examinations obtained by the same examiner, but no differences were found in sagittal plane translation measurements. (Table 4).

Table 4. Repeatability results of the ultrasonography test

Evaluation method	Translation (mean, mm) [95%CI]	p-value
Between examiners		
A to P translation		0.065
Examiner 1	1.11 [0.88-1.24]	
Examiner 2	0.88 [0.67-1.11]	
Examiner 3	0.78 [0.63-0.92]	
P to A translation		0.61
Examiner 1	0.52 [0.22-0.81]	
Examiner 2	0.47 [0.13-0.82]	
Examiner 3	0.48 [0.24-0.72]	
aTFCS opening		0.127
Examiner 1	0.51 [0.37-0.34]	
Examiner 2	0.57 [0.38-0.75]	
Examiner 3	0.35 [0.24-0.47]	
pTFCS opening		0.609
Examiner 1	-0.02 [-0.15-0.10]	
Examiner 2	-0.001 [-0.17-0.16]	
Examiner 3	-0.05 [-0.16-0.06]	
Within examiner		
A to P translation		0.428
Examiner 1.1	1.11 [0.44-0.17]	
Examiner 1.2	0.75 [0.13-1.37]	
P to A translation		0.174
Examiner 1.1	0.97 [0.24-1.70]	
Examiner 1.2	0.25 [-0.48-0.98]	
aTFCS opening		0.475
Examiner 1.1	0.57 [0.18-0.95]	
Examiner 1.2	0.37 [-0.02-0.75]	
pTFCS opening		0.044
Examiner 1.1	-0.12 [-0.29-0.06]	
Examiner 1.2	0.13 [-0.04-0.31]	

Abbreviations: mm; millimeter, 95%CI; 95% Confidence Interval, A to P; Anterior to Posterior, P to A; Posterior to Anterior, aTFCS; anterior tibiofibular clear space, pTFCS; posterior tibiofibular clear space

Reliability Of The Measurement Protocol

To test for the reliability of the measurement protocol, two members of the research team independently read each examination, resulting in excellent interobserver agreement scores. Additionally, three participants' examinations were reviewed a second time, resulting in either excellent or good intraobserver agreement scores (Table 5). Detailed reliability results of the tibiofibular clear space measurements are also outlined in Table 5. To test for the variability of the subjective amounts of forces applied, four examiners performed the ultrasonography stress examination twice with a force sensor attached to their thumb. On average (range) they pushed with 41N (35-48N) of force.

Table 5. Reliability results of the ultrasonography test

Measurement points	ICC measurements [95%CI]	Interpretation
Interobserver		
A->P tibia	0.99 [0.99-0.99]	Excellent
A->P fibula	0.99 [0.99-0.99]	Excellent
P->A tibia	0.98 [0.98-0.99]	Excellent
P->A fibula	0.98 [0.98-0.99]	Excellent
aTFCS	0.78 [0.73-0.85]	Excellent
pTFCS	0.88 [0.85-0.91]	Excellent
Intraobserver		
A->P tibia	0.99 [0.97-0.99]	Excellent
A->P fibula	0.95 [0.92-0.97]	Excellent
A->P tibia	0.99 [0.99-0.99]	Excellent
A->P fibula	0.99 [0.99-0.99]	Excellent
aTFCS	0.86 [0.74-0.93]	Excellent
pTFCS	0.87 [0.75-0.93]	Excellent

0.4, poor; 0.4 < ICC < 0.59, acceptable; 0.6 < ICC < 0.74, good; and ICC > 0.74, excellent.

Abbreviations: A to P; anterior to posterior, P to A; posterior to anterior,

aTFCS; anterior tibiofibular clear space, pTFCS; posterior tibiofibular clear space

Discussion

Syndesmotic instability, when subtle, can be challenging to diagnose—and often requires visualization of the syndesmosis during applied stress. Ultrasound is a dynamic, non-invasive diagnostic tool with the potential to evaluate the tibiofibular joint under stressed conditions at the point of care and with direct consideration of what normative syndesmotic motion should be on an individualized level because of the opportunity for bilateral comparison. This study effectively demonstrates ultrasound's ability to evaluate fibular translation in the sagittal plane and highlights its potential use for diagnosing subtle syndesmotic instability. The uninjured participants in this study demonstrated an average fibular translation of 0.89mm in the A to P direction and 0.49mm in the P to A direction.

Arthroscopy has been argued to be the gold standard in evaluating the syndesmosis given its ability to directly visualize fibular translation in the sagittal plane.[18, 42, 43] However, given the fact that there are anatomical variations within syndesmotic stability between each person, significant variability exists in the published literature regarding arthroscopic cut-off points and methods used to distinguish unstable from stable syndesmosis.[32, 44, 45] The values of sagittal fibular translation found in this study seem to closely correlate with those found in prior cadaveric arthroscopic studies, which ranged 0.2-0.6 mm for A to P translation and 0.4-0.5 mm for P to A translation.[18, 43, 46]

Syndesmotic instability is a multidirectional pathology and ideally its evaluation should integrate multiplanar dynamic stress testing.[17, 18, 23, 42, 43, 47, 48] While the force applied in this study was invariably in the sagittal plane, the 0.44 0.48 mm of anterior TFCS widening with near-zero TFCS widening posteriorly potentially represents an external rotation moment of the fibula during stress testing. Mei Dan et al [36] assessed the tibiofibular clear space using ultrasound while performing an external rotation force on the foot among uninjured athletes as well as athletes with MRI-diagnosed AITFL injury. They found widening of tibiofibular clear space in the setting of AITFL injury and recommended a cutoff value for the TFCS of 0.4mm, analogous to the intact measurement in our study. Furthermore, their measured TFCS in the intact state with the foot in neutral was 4.4 mm, corroborating the values found in our study.
Similar translation values were found between left and right ankles, which has important clinical implications because it allows clinicians to use the contralateral, uninjured side as a reliable internal control. This is critical because numerous studies have underscored that the tibiofibular anatomic relationship visualized with non-dynamic assessment techniques shows large inter-person variations.[31, 49, 50]

It is important to also note that no gender differences were observed between translation value assessments. In contrast, Mei Dan et al., who included a cohort of 110 subjects of which 51 identified as female, did find a larger increase in widening in women as compared to the men.[35] Hypotheses for the etiology of these findings include sex hormones such as progesterone and estrogen which may decrease collagen levels in ligaments leading to increased laxity and, concomitantly, larger translation values.[51, 52] We were not able to corroborate these findings and the issue as a whole becomes less critical when one relies on the contralateral ankle as an internal control rather than absolute threshold values.

The pressure applied to the fibula in our study was based on the amount of pressure at which the fibula did not seem to translate further under ultrasound. While we did not control for the forces applied across all test subjects, the "maximum forces" applied by four different operators when using a newly-designed pressure sensor were interestingly quite similar. Future research may benefit form integrating this pressure sensor in ultrasound examination in the injury setting, specifically as it may be difficult to reproduce the maximal force in an acutely injured limb to permit the ultrasound examination. Likely this dynamic ultrasound assessment technique could be used in the subacute or chronic setting, as patients will experience less pain and may tolerate the test with some analgesic drug during the assessment.

The inter- and intra- observer agreement coefficients of the sagittal translation measurements were excellent, likely benefiting from the software ability of the ultrasound device to automatically calculate the distance from the ultrasound handset probe to the hyperechoic bony structures visualized. It is one of the many benefits attributable to modern ultrasound equipment over those used decades ago.

This study does have several limitations. The examiners in this study had significant prior experience with the use of ultrasound, and the facility with which ultrasound can be used may be more limited among other practitioners. This is arguably true of any newer technology, however, and with the advent of standardized techniques such as those delineated in this study, it is expected that ultrasound examination will become increasingly accessible to a range of practitioners. Second, the exact force applied during the manual stress testing was not specifically measured—although this could be interpreted a strength or weakness of the study. Our multi-examiner application of manual stress could be considered fair replication of the realities of a clinical environment, and it could also be fairly stated that the ability to use the contralateral side as a threshold control rather than using absolute values mitigates much of this limitation. Third, our study also did not randomize to sex, age, height, and BMI, these may have an effect on the results of the fibular translation measurements, absence may be due to the sample size and it is possible that a component of selection bias could exist because the participant population referred to our foot and ankle clinic may not be widely generalizable. Finally, it does not entirely guarantee that more subtle syndesmotic instability effectively be distinguished from natural variation in the clinical setting, especially if awake, injured patients are unable to tolerate the sagittal forces applied.

This study highlights the ability of ultrasound to evaluate the syndesmosis among healthy controls both statically and under dynamic stress. Notably, it is able to do so in a standardized manner that is readily accessible at the point of care, at low cost, and with no ionizing radiation. It is moreover able to afford bilateral comparisons, which becomes critical as the amount of syndesmotic instability approaches greater degrees of subtlety. Additional studies are necessary in the injured setting to further build the argument for the use of ultrasound as the gold standard modality in evaluation the distal syndesmosis.

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Chapter 4 Portable Ultrasound Equals Arthroscopy For Assessment Of Syndesmotic Instability

*Hagemeijer NC,
Sato G,
Bhimani R,
Lubberts B,
Elghazy MA,
Sierevelt IN,
Waryasz G,
Kerkhoffs GMMJ,
DiGiovanni CW,
Guss D*

Submitted

Abstract

Objectives

To evaluate **1.** whether portable ultrasonography can diagnose syndesmotic instability in the sagittal plane, and **2.** how P-US measurements compare to arthroscopic evaluation.

Methods

Eight fresh, above-knee cadaveric specimen were used. The syndesmosis was evaluated with P-US and arthroscopy in the intact state, and thereafter with progressive sectioning of, **1.** anterior-inferior tibiofibular ligament (AITFL), **2.** interosseous ligament (IOL), and 3) posterior-inferior tibiofibular ligament (PITFL). Sagittal plane translation was simulated with 100N of anterior to posterior (A to P) and posterior to anterior (P to A) directed force using a bone hook. Separately, a 50N manual force was applied to the fibular tip and measured with P-US to simulate a fibular "shuck test" performed in the clinical setting.

Results

When all three syndesmotic ligaments were transected, there was a statistically significant increase in fibular motion in the sagittal plane when evaluated using portable ultrasonography with application of 50N of manual pressure and when applying a 100N hook test when measuring total sagittal plane motion ($p=<0.001$ and $p=0.009$). Arthroscopy demonstrated a statistically significant increased motion with a 100N hook test when measuring total sagittal plane motion ($p<0.001$).

Conclusions

P-US performed similarly to arthroscopy when diagnosing syndesmotic instability in the sagittal plane. P-US also offers several advantages over arthroscopy, including availability, non-invasiveness, low cost, and affording contralateral comparison. The promise of this technique suggests it should be further explored as a potential future standard for the diagnostic assessment of occult syndesmotic instability in the sagittal plane.

Introduction

Syndesmotic instability is a three-dimensional (3D) phenomenon, wherein the fibula may translate in the coronal, sagittal, and rotational plane relative to the tibia.[1-5]
Syndesmotic injury mainly affects the young athletic population, especially in collision sports.[6-10] Injury will burden players and cause time loss on the field, moreover, undiagnosed syndesmotic instability can lead to significant and often irreversible morbidity.[7-9,11-14] Clinical examination alone is unreliable in making such diagnoses and the evaluation of syndesmotic instability generally incorporates some sort of imaging modality.

As the instability becomes more subtle, effective imaging of syndesmotic instability becomes increasingly dependent on one of three factors: **1.** the ability to view the distal tibiofibular articulation under stress or physiologic load, **2.** the ability to afford a contralateral comparison, and **3.** the ability to visualize the distal syndesmosis in 3D. Other critical considerations include ease of use, availability, cost, and radiation exposure.
Because of the historic limitations of many imaging modalities, diagnostic arthroscopy is often considered the gold standard to evaluate the distal tibiofibular joint by virtue of allowing direct visualization of the distal tibiofibular articulation with an applied stress. Its invasive nature, cost, and inability to afford a contralateral comparison, however, limits its use. Portable ultrasonography (P-US) is increasingly used to diagnose musculoskeletal injuries because it overcomes many of these limitations. It allows dynamic evaluation of anatomic structures at the point of care with little risk to the patient and at low-cost.[15] Furthermore, its ability to evaluate both the injured and uninjured side is critical given the variable anatomy of the incisura across individuals.[16-19] It therefore intuits that evaluating syndesmotic instability using P-US could serve as a surrogate to arthroscopy.
The aim of this study was, **1.** to evaluate whether P-US is capable of diagnosing syndesmotic instability in the sagittal plane, and **2.** to assess how P-US measurements compare to arthroscopic evaluation. The hypothesis was that P-US and arthroscopy would be capable of differentiating between intact and after subsequent transaction stages of the syndesmosis.

Methods

Specimens

Eight fresh-frozen nonpaired above knee cadaveric specimen were used. Six were male and two were female and the mean age at time of death was 64 (range, 29-91) years. No specimen had signs of ankle osteoarthritis or previous trauma on radiographic evaluation. Soft tissues were maintained to simulate in vivo conditions. Specimens were thawed at room temperature for 24 hours and secured to a board by using four 4-mm Schanz-type pins inserted anteroposteriorly into the tibia.

Sequential Transection Of Ligaments

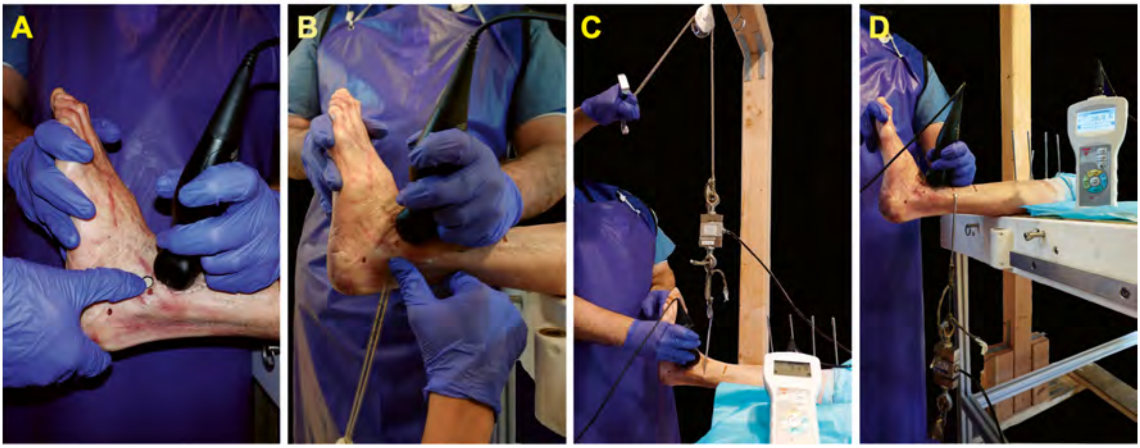
Each specimen underwent an identical sequence of ligamentous transection. After evaluation in the intact state, first the anterior inferior tibiofibular ligament (AITFL) was transected, thereafter the distal 10 cm of the tibiofibular interosseous ligament (IOL), and then the posterior inferior tibiofibular ligament (PITFL).

Ultrasonographic Technique

The distal tibiofibular joint was examined using a portable ultrasound probe (2D, gray scale B mode complete ultrasound; Butterfly iQ, Butterfly Network Inc, Guilford, CT) (Figure 1).

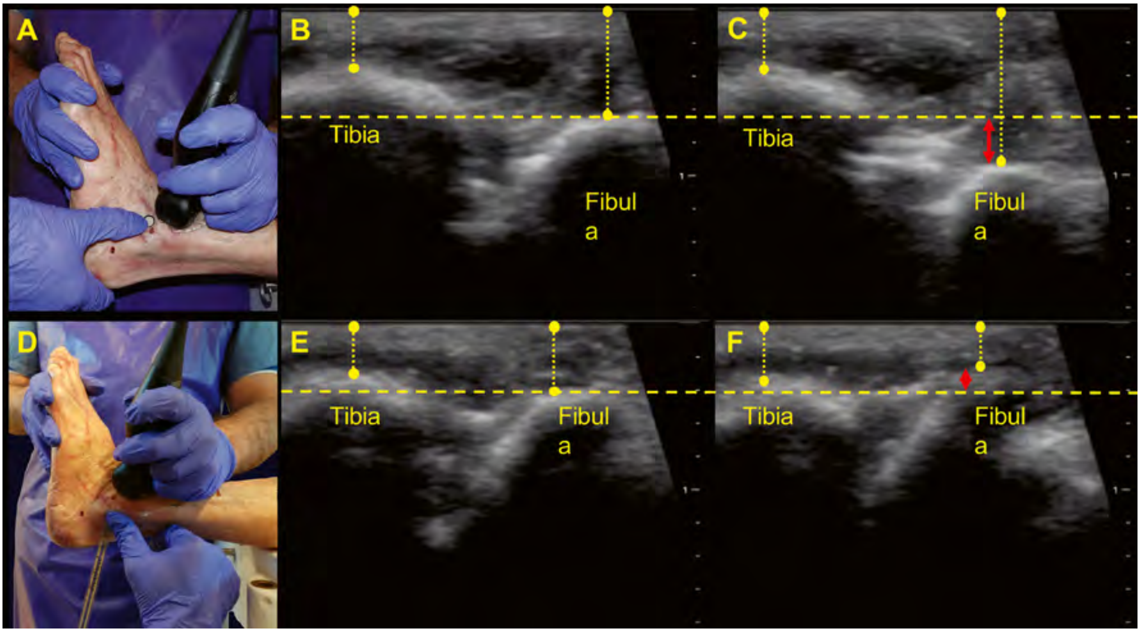
Anterior to posterior (A to P) and posterior to anterior (P to A) fibular translation was simulated by using a bone hook placed around the distal part of the fibula 5 cm proximal to the ankle joint. Using an electronic force gauge (Scientific Industries - Torbal Division, Oradell, NJ) an anteriorly and then posteriorly directed 100N force was applied (Figure 3). The 100N force used in this study was based on a cadaveric study performed by Stoffel et al. which found that forces of more than 100N did not show substantial increase in syndesmotic displacement.[20] In addition to the hook test, a "fibular shuck" test was performed to simulate a physical examination in clinic, wherein A to P and P to A sagittal fibular translation was performed by applying 50N manual force to the fibular tip. The 50N used was decided upon because forces greater than 50N were physically hard to achieve for the investigators and unlikely to be tolerated by awake patients. Manual forces were measured and standardized using a sensor system (FlexiForce ELF System, Tekscan, Boston) which could be placed between the examiner's thumb and the fibula (Figure 1). Standardized ultrasound probe and hand positions were used.[19] The probe was positioned 10mm above the tibiotalar joint line and positioned 30° from this line with the center overlying the tibiofibular clear space. All dynamic stress exams (using a bone hook and manual pressure) were performed at each stage of ligament transection and were captured with real-time ultrasonographic videos. During each ultrasound examination, exact time points for each stress moment were noted and afterwards the captured real-time films of the tibiofibular joint were screenshotted at those determined time points. Images were thereafter imported into imageJ (National Institutes of Health) for analysis. Positions of the tibia and fibula were subsequently assessed by measuring the closest distance from the tibial and fibular bones to the probe when there was no hook force (0Nhook) and at 100N hook force (100Nhook). Similarly, probe-fibular/tibial distances were assessed when there was no manual stress (0N manual) and at 50N manual force (50Nmanual) (Figure 2).[19] Fibular translation was subsequently determined by calculating the delta change in fibular movement while maintaining the tibia as a reference ((Tibia100Nhook – Fibula100Nhook) – (Tibia0Nhook – Fibula0Nhook)) and ((Tibia50Nmanual - fibula50Nmanual) – (Tibia0Nmanual - fibula0Nmanual)) (Figure 2).

Figure 1. Ultrasonographic syndesmotic assessment of a right-sided cadaveric specimen



A) Manual sagittal translation during ultrasound examination. The force sensor which was placed under the thumb during the actual experiment, which is visualized here; (B) Manual P to A sagittal translation during ultrasound examination; (C) Hook A to P sagittal translation during ultrasound examination, (D) Hook P to A sagittal translation during ultrasound examination. Abbreviations: A = Anterior; P = Posterior.

Figure 2. Fibular translation measurement and ultrasound images

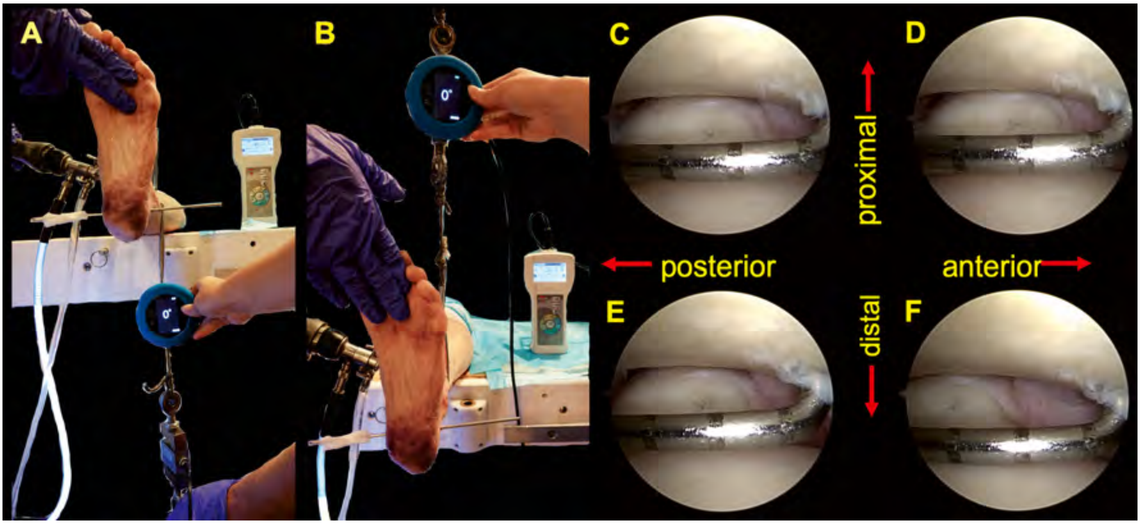


A) Application of manual force to the distal fibula in the A to P direction; B-C: Captured images from a real-time ultrasonographic stress examination at 0N (B) and at 50N (C) manual A to P stress after transection of the AITFL, IOL and PITFL. Vertical discontinued lines resemble the distance from the tibia to the probe. The red arrows in C resemble the A to P translation value. D) Application of manual force to the distal fibula in the P to A direction E-F: Captured images from a real-time stress examination at 0N (C) and at 50N (F) manual P to A stress after transection of the AITFL, IOL and PITFL. Vertical discontinued lines resemble the distance from the tibia to the probe. The red arrows in F resemble the P to A translation value. Abbreviations: A Anterior; P Posterior; PITFL Posterior-inferior tibiofibular ligament; N Newton

Arthroscopic Technique

Ankle arthroscopy was performed through anteromedial and anterolateral portals, utilizing a 2.7-mm, 30-degree, arthroscope (Arthrex, Naples, FL). Using a bone hook, A to P and P to A sagittal fibular translation was simulated in the exact same way as described for the ultrasound measurement technique (Figure 3). Displacement in the sagittal plane was measured by translation of the fibula in the A to P direction with respect to the fixed tibia under 100N. Arthroscopic images were taken in the stressed and unstressed situation. Measurements were attained from these images using ImageJ. All arthroscopic measurements were taken without ankle distraction because this has been previously shown to mask syndesmotic instability, presumptively due to tension of the soft tissue attachments around the ankle.[2]

Figure 3. Arthroscopic syndesmotic assessment of a right-sided cadaveric specimen



(A) A to P sagittal translation during arthroscopic assessment, (B) P to A sagittal translation during arthroscopic assessment, (C) A to P sagittal translation at 0 N, (D) A to P sagittal translation at 100 N, (E) P to A sagittal translation at 0 N (F) P to A sagittal translation at 100 N. Abbreviations: A Anterior; P Posterior; N Newton

Statistical Analysis

A descriptive analysis was performed to summarize the baseline characteristic variables, which are presented with frequencies and percentages for categorical variables and with means and standard deviations and 95% CI for continuous variables. Normality of the data was checked visually and with the use of a Shapiro-Wilk W test. The translation values are reported as mean and standard deviations for the intact stage and as mean and 95% CI for subsequent transection stage in millimeters.

Differences between the intact stage and subsequent ligamentous transection stages were calculated using a linear mixed model with the cadaver as random factor. To investigate the correlation between P-US and arthroscopic measurements, the Pearson correlation was calculated. Interpretation to indicate the strength of correlation: slight correlation ($r < 0.2$), low correlation ($r = 0.3$-0.4), moderate correlation ($r = 0.4$-0.7), high correlation ($r = 0.7$-0.9), and very high correlation ($r = 0.9$-1.0).[21] An adjusted two-sided p-value $<.05$ was considered statistically significant.

A power analysis to determine the number of specimens was conducted based on the hypothesis that P-US would be capable of assessing sagittal plane displacement of the syndesmosis between a stable and unstable injury. From a preliminary study in the normal population a mean (SD) of 0.89 ±0.6mm was found.[19] The optimal cutoff point to distinguish stable from unstable injuries is estimated at 2mm for the total sum of anterior and posterior translation.[22] Subsequently, an effect-size of 1.1 was calculated while taking into consideration a type I error of 5%, and a type II error of 80% and using a paired t-test the current study would require seven specimens. Accounting for a potential specimen with a pre-existing bony injury which would lead to exclusion, eight specimens were included in this study.

Two orthopaedic fellowship-trained foot and ankle surgeons performed all arthroscopic and ultrasound measurements in three randomly selected specimens independently to assess interobserver agreement using the intraclass correlation coefficient (ICC) through a 2-way mixed-effects model. Interpretation of the ICC values was carried out according to the guidelines proposed by Shrout as follows: 0.00 to 0.10, virtually none; 0.11 to 0.40, slight; 0.41 to 0.60, fair; 0.61 to 0.80, moderate; and 0.81 to 1.00, substantial.[23]

Results

Ultrasound And Arthroscopic Translation Measurements

P-US and arthroscopic measurement values at each stage of ligamentous transection are summarized in Table 1 and Figure 4.

No syndesmotic instability was visualized in the sagittal plane with isolated transection of the AITFL (Table 1).

With additional transection of the IOL (AITFL + IOL), a statistically significant increase in fibular motion was noted on P-US with 50N of manual pressure in the A to P direction and when measuring total sagittal plane motion of the fibula (A to P + P to A), as well as under arthroscopy with a 100N hook test applied in the P to A direction and when measuring total sagittal plane motion of the fibula.

When all three syndesmotic ligaments were transected (AITFL + IOL + PITFL), there was a statistically significant increase in fibular motion in the sagittal plane when evaluated under P-US with the application of 50N of manual pressure in the A to P and P to A direction, as well as when measuring total sagittal plane motion. P-US evaluation when applying a 100N hook test demonstrated a statistically significantly increased motion in the A to P direction, as well as when measuring total sagittal plane motion. Arthroscopy demonstrated a statistically significantly increased motion with a 100N hook test in the A to P and P to A direction, as well as when measuring total sagittal plane motion.

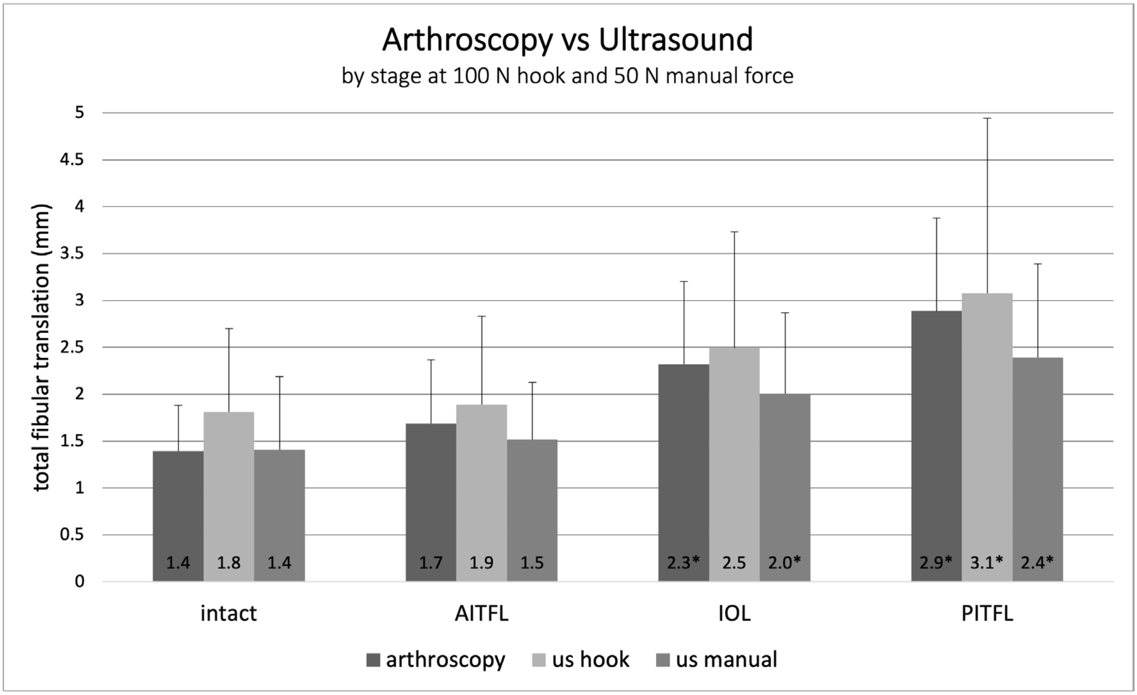
Correlation Between Arthroscopic And Ultrasound Measurements

Using the hook test, a moderate correlation (rho 0.56) was found between the sum of the A to P and P to A fibular translation of the arthroscopic and P-US measurements. Using the hook test during arthroscopy and manual force during P-US assessment, a high correlation was found (rho 0.72). Additionally, a high correlation was found between the P-US assessment using a hook and the P-US assessment using manual force (rho 0.75).

Interobserver Agreement

The ICC [95%CI] for P-US measurements was 0.78 [0.73-0.83] and for arthroscopy was 0.89 [0.86-0.92], indicating substantial agreement among all measurements.

Figure 4. Total sum of sagittal plane fibular translation values among ligamentous transection stages with standard deviations.



Abbreviations: N; Newton, A to P; Anterior to Posterior, AITFL; anterior inferior tibiofibular ligament, IOL; interosseous ligament, PITFL; posterior inferior tibiofibular ligament, us; Ultrasound. *p-value < 0.05 indicating a significant difference between the intact and transection stage.

Table 1. Fibular translation values measured arthroscopically and ultrasonographically

Stress test	Force	Measurement Technique	Transection stage						
			Intact	AITFL		AITFL + IOL		AITFL+IOL+PITFL	
			Mean ±SD translation	Mean [95% CI] translation	p-value	Mean [95% CI] translation	p-value	Mean [95% CI] translation	p-value
Anterior to Posterior									
Hook test	100N	Arthroscopy	0.4 ±0.3	0.4 [-0.2-1.0]	0.976	0.6 [0.0-1.2]	0.161	0.8 [0.2-1.4]	0,003
		Ultrasound	0.9 ±0.6	1.0 [-0.30-2.3]	0.844	1.5 [0.2-2.8]	0.127	1.8 [0.5-3.0]	0,019
Manual	50N	Ultrasound	0.8 ±0.4	0.8 [0.0-1.6]	0.859	1.4 [0.6-2.1]	0.011	1.4 [0.6-2.1]	0,004
Posterior to Anterior									
Hook test	100N	Arthroscopy	1.0 ±0.5	1.3 [0.4-2.2]	0.244	1.7 [0.9-2.6]	0.004	2.1 [1.2-3.0]	<0.001
		Ultrasound	0.9 ±0.5	0.9 [0.0-1.7]	0.964	1.0 [0.2-1.9]	0.516	1.3 [0.5-2.2]	0,055
Manual	50N	Ultrasound	0.6 ±0.3	0.7 [0.3-1.1]	0.124	0.7 [0.2-1.1]	0.364	1.0 [0.6-1.4]	<0.001
Total sum of sagittal translation									
Hook test	100N	Arthroscopy	1.4 ±0.7	1.7 [0.6-2.8]	0.313	2.3 [1.2-3.4]	0.001	2.9 [1.8-4.0]	<0.001
		Ultrasound	1.8 ±0.9	1.9 [0.1-3.7]	0.871	2.5 [0.7-4.3]	0.159	3.1 [1.3-4.9]	0,009
Manual	50N	Ultrasound	1.4 ±0.6	1.5 [0.5-2.5]	0.631	2.0 [1.0-3.0]	0.009	2.4 [1.4-3.4]	<0.001

N = Newton; A to P = Anterior to Posterior; AITFL = anterior inferior tibiofibular ligament; IOL = interosseous ligament; PITFL = posterior inferior tibiofibular ligament

Discussion

This study investigated whether P-US is capable of evaluating fibular motion in the sagittal plane at the distal fibular articulation and found that P-US was indeed capable of diagnosing syndesmotic instability in the setting of progressive ligamentous injury. In addition, the P-US measurements correlated highly with those found during arthroscopic assessment.

Syndesmotic instability can cause significant long-term morbidity when left undiagnosed or inadequately treated. Diagnosing subtle syndesmotic instability is challenging because of its multi-directional nature, as well as the need to visualize the distal tibiofibular articulation dynamically while comparing it to the contralateral, uninjured side.[5, 16, 22] Even though sagittal plane stability is less well described in the literature, it may be more sensitive towards diagnosing subtle syndesmotic instability as compared to coronal plane stability testing.[2, 22, 24-27] Arthroscopy is capable of visualizing the ankle joint while also allowing stress testing in the coronal and sagittal planes but is an invasive and costly assessment technique without the ability to afford a contralateral comparison.[27] In contrast, P-US is a non-invasive, low-cost, dynamic assessment technique that also allows for bilateral visualization critical towards diagnosing instability as it becomes more subtle.[19, 28] This study afforded an opportunity to compare P-US to arthroscopy, hitherto considered by many to be the gold standard.

The comparison between the utility of arthroscopy versus P-US is most rigorously applied with the 100N hook test to replicate intraoperative stress examination. Both arthroscopy and P-US were able to diagnose syndesmotic instability when all three syndesmotic ligaments (AITFL + IOL + PITFL) were transected and when measuring total sagittal plane motion as delineated in prior arthroscopic studies.[4] Furthermore, total sagittal plane motion was also quite similar, with an average of 2.9mm measured arthroscopically and 3.1mm with P-US.

On the other hand, the most clinically relevant comparison is between the 100N arthroscopic hook test and the 50N P-US manual fibular shuck test. This is because the hook test is an invasive examination whose use is limited to the operating room setting. In contrast, by virtue of its noninvasive nature, P-US is ideally used in the clinical setting. The most notable finding of this study is therefore that, to a similar extent as arthroscopy, P-US was able to detect abnormal sagittal plane fibular motion with a manually-applied fibular shuck in the A to P, P to A, and total sagittal (A to P + P to A) direction. This underscores its diagnostic utility in the in vivo clinical setting and at the point of care.

There are some limitations to this study. First, when measuring fibular translation with ultrasound it is important to have sufficient gel between the fibula and ultrasound probe. In a cadaveric setting the ligamentous injury was created by cutting through skin and soft tissues, allowing air to interpose between the fibula and ultrasound probe - space that needed to be filled up with more gel. As the lateral incision extended proximally to 5cm above the ankle joint to transect the IOL, it became more challenging to keep the gel in place than when applying the force manually. This would not be an issue in the in vivo setting where ligamentous injury happens in a closed manner. Second, correlation between P-US and arthroscopy was deemed moderately high for experienced exminers, and each measuring technique has its own error margin due to positioning and stabilization of the P-US probe/arthroscopy camera. Techniques to use P-US will continue to evolve. Third, it must be noted that distinctions between stable and unstable syndesmotic injuries in biomechanical studies like this one become the purview of statistics. It remains unclear to which degree these values correlate with clinical instability and whether absolute threshold values can be defined. Lastly, differential pain tolerance may affect the accuracy of P-US stress examination in certain patients. Additional in vivo studies are necessary to corroborate its use.

Conclusion

P-US performed similarly to arthroscopy when distinguishing syndesmotic instability in the sagittal plane using a hook test as well as using a manually-applied fibular shuck test. The promise of this non-invasive assessment technique suggests it should be further explored as a potential future standard for the diagnostic assessment of occult syndesmotic instability in the sagittal plane.

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ALL-PURPOSE
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Chapter 5

Portable Dynamic Ultrasonography Is An Useful Tool For The Evaluation Of Suspected Syndesmotic Instability: A Cadaveric Study

Hagemeijer NC,
Lubberts B,
Saengsin J,
Bhimani R,
Sato G,
Waryasz G,
Kerkhoffs GMMJ,
DiGiovanni CW,
Guss D

Knee Surg Sports Traumatol Arthrosc. 2023 May;31(5):1986-1993

Abstract

Purpose

Portable ultrasonography (P-US) is increasingly used to diagnose syndesmotic instability. The aim of this study was to evaluate syndesmotic instability by measuring the distal tibiofibular clear space (TFCS) in a cadaveric model using P-US with progressive stages of syndesmotic ligamentous transection under external rotation stress.

Methods

Ten fresh lower leg cadaveric specimens amputated above the proximal tibiofibular joint were used. Using P-US, the TFCS was evaluated in the intact stage and after progressive sectioning of the **1.** anterior-inferior tibiofibular ligament (AITFL), **2.** interosseous ligament (IOL), and **3.** posterior-inferior tibiofibular ligament (PITFL). The TFCS was measured in both the unstressed (0 Nm) state and with 4.5 Nm, 6.0 Nm, 7.5 Nm, and 9.0 Nm of external rotation stress using a bone hook placed on the first metatarsal bone at each stage of ligamentous transection stage using both P-US and fluoroscopy.

Results

When assessed with P-US, partial syndesmotic injury encompassing the AITFL and IOL resulted in significant TFCS widening at 4.5 Nm of external rotation torque when compared to intact state with a TFCS-opening of 2.6 2 mm, $p = 0.01$. In contrast, no significant differences in TFCS were detected using fluoroscopy. Only a moderate correlation was found between P-US and fluoroscopy

Conclusion

P-US is a useful tool in diagnosing syndesmotic instability during external rotation stress examination. TFCS-opening increased as additional ligaments of the syndesmosis were transected, and application of 4.5 Nm torque was sufficient to detect a difference of 2.6mm after the IOL cut.

Introduction

Ankle sprains are among the most commonly reported sports injuries, and up to 18% of ankle sprains involve the syndesmotic ligament complex.[1, 20, 22, 41] Colloquially referred to as a high ankle sprain, the most critical aspect of initial assessment is distinguishing stable from unstable injuries. High ankle sprains are especially caused by a forced external rotation injury, which may result in sequential injury to the anterior inferior tibiofibular ligament (AITFL), interosseous ligament (IOL), and posterior inferior tibiofibular ligament (PITFL).[14, 24, 37]

Failure to diagnose syndesmotic instability can lead to longstanding and often permanent patient morbidity.[11, 19, 33, 35]. On the other hand, the diagnosis of subtle syndesmotic instability remains challenging. Stressed radiographs have low sensitivity, and MRI readily detects injury, but does not allow for dynamic joint evaluation.[23] Arthroscopy has traditionally served as the gold standard; however, it remains a costly and invasive procedure that, furthermore, does not afford a contralateral comparison.[17]
Weight-bearing computed tomography (WBCT) is a promising technique to distinguish stable from unstable injuries by virtue of allowing a bilateral, 3-dimensional (3D) assessment of the distal syndesmosis under physiologic load.[2, 6, 7, 16] It may not be readily available in many clinical settings, and the axial stress applied may not entirely replicate the rotational or sagittal stress that can be applied manually to detect more subtle instability.

Dynamic portable ultrasound (P-US) is increasingly used because of its ready availability, low cost, and ability to dynamically assess the syndesmosis while affording a contralateral comparison. It is a promising and reliable technique to evaluate the tibiofibular clear space (TFCS) under external rotation stress and sagittal fibular translation, as shown in previous studies.[1, 18, 30, 31]

The aim of this study was to evaluate the use of P-US to diagnose syndesmotic instability in a cadaveric model by measuring the TFCS under external rotation stress during progressive stages of ligamentous transection, and compare these results with fluoroscopic measurements. It was hypothesised that P-US could differentiate the intact from the sequent transection stages and that findings are correlated to those detected using fluoroscopy.

Methods

Specimens

The use of cadaveric tissue models for biomechanical testing was exempt by the IRB 2016P001295/MGH. Ten fresh–frozen, nonpaired lower leg cadaveric specimens amputated above the proximal tibiofibular joint were used in this study (mean age at the time of death, 64 years; range, 29–91 of which 7 were male). Before starting the experiment, a fluoroscopic (OrthoScan FD Pulse C-Arm, OrthoScan, Scottsdale, Arizona) and arthroscopic (Arthrex, Naples, Florida) evaluation was performed. Specimens were excluded if there were any signs of ankle osteoarthritis or previous trauma. Soft tissues were maintained to simulate in vivo conditions. Specimens were thawed at room temperature and secured to a board using four 4-mm Schanz-type pins inserted anteroposteriorly into the tibia.

Sequential Transection Of Ligaments

Each specimen underwent evaluation with P-US and fluoroscopy in the intact state and thereafter at each stage of sequential ligamentous transection including the, **1.** AITFL, **2.** distal 10 cm of the IOL, and **3.** PITFL. For the ligament transection, an open incision was made. The ligament transection was performed sharply with a surgical blade No. 10 by a specialised foot and ankle orthopaedic surgeon (JS).

Experimental Setup

The TFCS was examined using a P-US probe (2D, grayscale B mode complete ultrasound; Butterfly iQ, Butterfly Network Inc, Guilford) and fluoroscopy. External rotation torque was simulated by a sharp bone hook (Arthrex, Naples, Florida) placed on the first metatarsal bone, 10 cm distal to the centre of rotation of the ankle. The centre of rotation was confirmed fluoroscopically. An external rotation directed force was then progressively applied, including 0 N (0 Nm), 45 N (4.5 Nm), 60 N (6.0 Nm), 75 N (7.5 Nm), and 90 N (9.0Nm) (FB2K, Scientific Industries—Torbal Division, Oradell, NJ) (Figs. 1 and 2). The foot was manually supported to hold a neutral position of the foot. It was ensured the externally directed force to be paralleled with the ground using a digital goniometer (HALO, halo medical devices HQ, Sydney, Australia). A range of external rotation torque moments was performed because the applied external rotation force in prior studies demonstrated enormous variation, and no previous study assessed the tibiofibular clear space using P-US.[4, 6, 21, 38,43] Even though a selection of the studies used a larger external torque (up to 20 Nm), the maximum amount in this study did not go beyond 9 Nm because patients were not expected to tolerate more torque in the clinical setting,especially in the setting of an acute injury. The experiment and the TFCS measurements were performed by three foot and ankle specialised orthopaedic surgeons (JS, RB, and GS) and one orthopaedic resident (NH).

Portable ultrasound

Standardised ultrasound probe and hand positions were used as previously reported.[18] The probe position was marked 10 mm above the tibiotalar joint line and positioned 30° from this transverse line with the centre covering the tibiofibular clear space. The surgical wound was not closed before application of external loads, however, the skin and soft tissue was retracted to cover the surgical site during the ultrasound experiment. Therefore, the wound would not interfere the ultrasound probe placement. Ultrasound gel was used throughout the experiment to ensure good skin contact. All dynamic ultrasound stress images at each stage of ligament transection were captured while consecutively increasing the external rotation force. After the experiment, the TFCS distances were measured from the captured images using ImageJ (National Institutes of Health). The TFCS values of each stage of ligament transection during each stressed condition were used for analysis. TFCS was determined by measuring the shortest distance between the tibia and fibula at the anterior aspect of the tibiofibular joint space (Figure 1).[18]

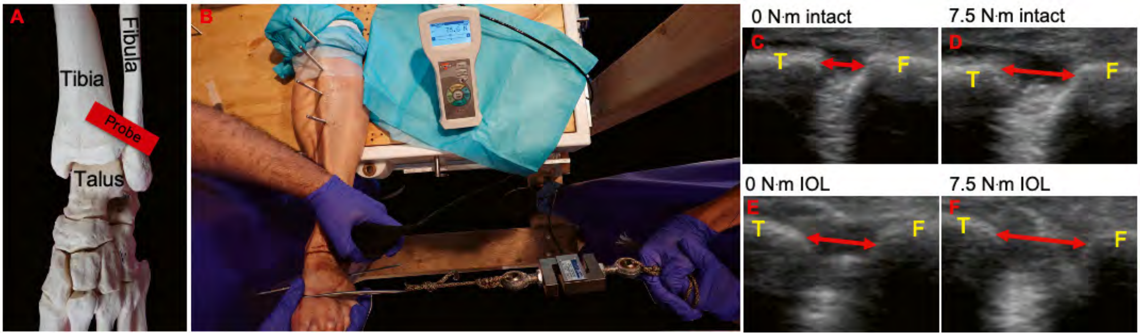
Fluoroscopy

Using fluoroscopy, true anterior to posterior views were obtained for each ligamentous transection stage at each stress moment. The TFCS distance was obtained from each radiograph using ImageJ (Figure 2).

Outcome Measurements

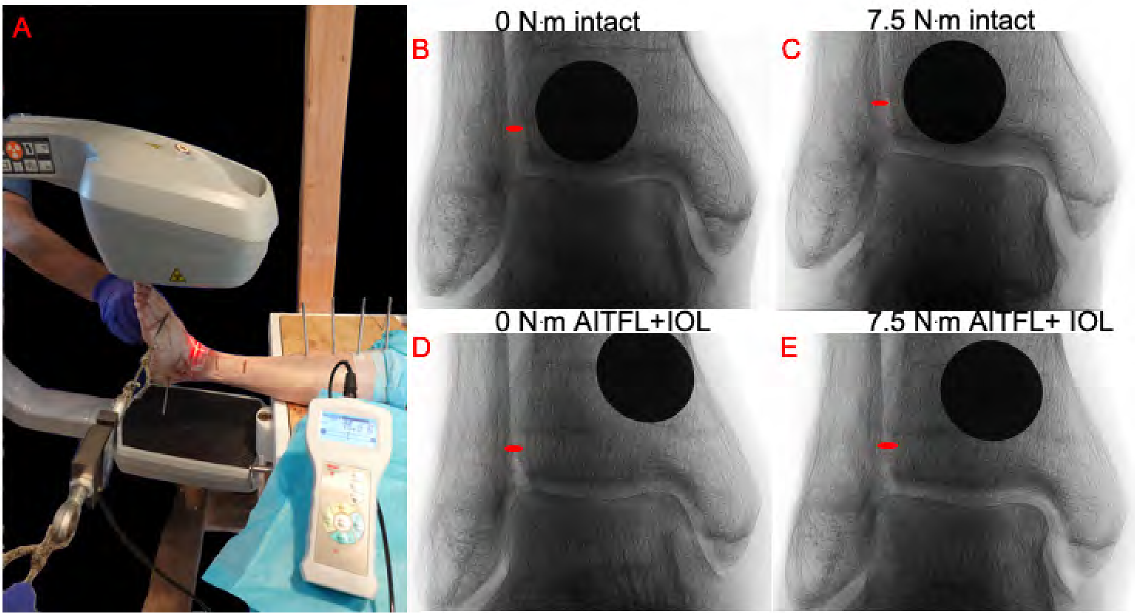
After obtaining all TFCS values using both P-US and fluoroscopy images, TFCS-opening values were calculated by subtracting the intact TFCS values, unstressed and stressed, from the TFCS values of the transection stages. The TFCSopening, therefore, shows the dynamic change after ligament transection and external rotation torque as opposed to the unstressed or stressed intact stage.

Figure 1. P-US experimental setup



A Bone model of probe position. B Ultrasound experimental set up. C–F Ultrasound image of the TFCS at 0 and 7.5 Nm, at the intact stage (C, D) and after AITFL + IOL transection (E, F). Red arrows resemble the TFCS measurements. T tibia, F fibula

Figure 2. Fluoroscopic experimental setup



A Fluoroscopic experimental setup. B–E Fluoroscopic image of the TFCS at 0 and 7.5 Nm, at the intact stage (B, C) and after AITFL + IOL transection (D, E). Red pointer resembles the TFCS measurements. (Same cadaver as Figure 1.)

Outcome Measurements

After obtaining all TFCS values using both P-US and fluoroscopy images, TFCS-opening values were calculated by subtracting the intact TFCS values, unstressed and stressed, from the TFCS values of the transection stages. The TFCSopening, therefore, shows the dynamic change after ligament transection and external rotation torque as opposed to the unstressed or stressed intact stage.

Statistical Analysis

TFCS values are presented with means and standard deviations (SD) in millimetres. In the graphs, TFCS values are presented with means and 95% confidence intervals (CI). The normality of the data was checked visually. The TFCS values of the intact state are considered baseline values. Statistical differences between the transection stages were calculated using one-way analysis of variance (ANOVA). The post hoc Holm–Bonferroni method was used to detect which stages of ligament transection significantly differed from the intact joint. A Pearson correlation was calculated to evaluate a correlation between P-US and fluoroscopy. Interpretation to indicate the strength of correlation was considered as followed: slight correlation ($r < 0.2$), low correlation ($r = 0.3–0.4$), moderate correlation ($r = 0.4–0.7$), high correlation ($r = 0.7–0.9$), and very high correlation ($r = 0.9–1.0$).[15] An adjusted 2-sided p value < 0.05 was considered statistically significant. Two orthopaedic fellowship-trained foot and ankle surgeons performed all P-US and fluoroscopic measurements in three randomly selected specimens independently to assess interobserver agreement. To asses intraobserver reliability, one observer performed all P-US and fluoroscopic measurements in 3 randomly selected specimens twice with 12 months in between. The observers were not blinded for ligament resection stage. The inter- and intraobserver reliabilities were calculated using the intraclass correlation coefficient (ICC) through a 2-way mixedeffects model.[10] Interpretation of the ICC values was carried out according to the guidelines proposed by Shrout as follows: 0.00–0.10, virtually none; 0.11–0.40, slight; 0.41–0.60, fair; 0.61–0.80, moderate; and 0.81–1.00, substantial. The standard error of measurement (SEM) was calculated as the square root of the between-observer as well as the square root within observer variance (i.e. sum of the between-measures variance and the residual variance).[9] In addition, the smallest detectable difference (SDD) (between observers), as well as the smallest detectable change (SDC) (within observer) was calculated from the SEM at individual level (1.96*H2*SEM). A power analysis was conducted based on the hypothesis that a difference of minimally 2 mm in TFCS-opening would be clinically relevant, as there was no previous data available on external rotation stress assessed by P-US. To detect a true difference of 2 mm ± 2 between the paired measurements while handling a chance of having a type error of 0.05 and a type 2 error of 0.80, a sample size of 10 specimens would be required.

Table 1. Ultrasonographic tibiofibular clear space values in sequential ligament sectioning stages among four torque-loading conditions

	TFCS values (mean ± SD) in mm				
Stage	0 Nm	4.5 Nm	6.0 Nm	7.5 Nm	9.0 Nm
Intact	4.6 ±1.1	5.3 ± 1.5	5.5 ± 1.0	5.7 ± 0.9	5.9 ± 0.9
AITFL	5.1 ± 1.3	5.9 ± 1.3	6.2 ± 1.4	6.5 ± 1.4	7.2 ± 1.6
IOL	6.1 ± 1.4	7.9 ± 2.0*	9.1 ± 2.5*	9.7 ± 2.5*	10.6 ± 2.5*
PITFL	6.9 ± 1.2*	9.2 ± 2.3*	9.9 ± 2.4*	10.7 ± 5.0*	11.07 ± 2.5*
p-value	0.001	< 0.001	< 0.001	< 0.001	< 0.001

TFCS tibiofibular clear space

*Corrected p values as compared to the alike (un-)stressed intact state are consecutively IOL stage: $p = 0.01$, $p = 0.001$, $p < 0.001$, $p < 0.001$ PITFL stage: $p = 0.01$, $p < 0.001$, $p < 0.001$, $p < 0.001$, $p < 0.001$

Results

P-US TFCS And TFCS-Opening Values

P-US TFCS values for the intact and sequential ligament sectioning stages among four torque-loading conditions are presented in Table 1. When assessed with P-US, partial syndesmotic injury encompassing the AITFL and IOL resulted in significant TFCS widening as compared to the alike stressed intact state at 4.5 Nm of external rotation torque with an average TFCS-opening of 2.6 mm ± 2.0 mm, adjusted p value = 0.01. With complete syndesmotic injury encompassing the AITFL, IOL, and PITFL, the TFCS widened significantly not only with an applied rotation stress, but also in the unstressed state.

Fluoroscopy TFCS And TFCS-Opening Values

P-US TFCS values for the intact and sequential ligament sectioning stages among four torque-loading conditions are presented in Table 2. When assessed with fluoroscopy none of the TFCS values differed from the alike stressed intact TFCS value, Table 2.

Correlation Between P-US And Fluoroscopy

A Pearson correlation test showed a moderate correlation between P-US and fluoroscopy TFCS values with a rho of 0.52.

Reliability

For P-US, an individual interobserver agreement of 0.95 [95% CI 0.92–0.97] for the TFCS-opening measurement was found, a SEM of 0.9, and a SDD of 2.4. The individual intraobserver agreement for P-US was 0.96 [95% CI 0.94–0.98], with a SEM of 0.7 and a SDC of 1.9. For fluoroscopy, an individual interobserver agreement of 0.46 [95% CI 0.21–0.75] for the TFCS-opening measurement was found, a SEM of 0.9 and a SDC of 2.5. The individual intraobserver agreement for fluoroscopy was 0.56 [95% CI 0.36–0.71], with a SEM of 0.7 and a SDC of 2.0.

Table 2. Fluoroscopic tibiofibular clear space values in sequential ligament sectioning stages among four torque-loading conditions

	TFCS values (mean ± SD) in mm				
Stage	0 Nm	4.5 Nm	6.0 Nm	7.5 Nm	9.0 Nm
Intact	4.0 ±1.3	4.1 ± 1.3	4.2 ± 1.3	4.3± 1.3	4.6 ± 1.3
AITFL	3.9 ± 1.3	4.2 ± 1.2	4.5 ± 1.2	4.7 ± 1.3	5.3 ± 1.6
IOL	4.4 ± 1.1	4.9 ± 1.3	5.3 ± 1.5	5.4 ± 1.5	5.8 ± 1.5
PITFL	4.7 ± 1.5	5.4 ± 1.4	5.5 ± 1.5	5.9 ± 1.6	6.1 ± 1.7
p-value	0.566	0.099	0.114	0.076	0.142

TFCS tibiofibular clear space

Discussion

The most important findings of the present study were that P-US appears to be a useful tool in evaluating suspected syndesmotic instability, detecting widening at the distal tibiofibular articulation after both partial syndesmotic injury to the AITFL and IOL as well as complete syndesmotic disruption of the AITFL, IOL, and PITFL. Furthermore, while complete syndesmotic injuries demonstrate widening at the distal tibiofibular articulation without any applied stress, an external rotation torque of 4.5 Nm seems sufficient to detect syndesmotic instability after a partial tear involving only the AITFL and IOL.

Prior arthroscopic studies have highlighted that syndesmotic instability requires completely syndesmotic disruption of the AITFL, IOL, and PITFL, but that partial injuries to the syndesmosis (AITFL and IOL) can be rendered unstable with deltoid involvement.[25, 29] Isolated injuries to the AITFL and IOL, however, remain stable. These studies, however, relied on coronal and sagittal plane stress manoeuvres applied to the fibula rather than an external rotation torque due to the inherent challenge of externally rotating the ankle with an arthroscope in place. This study highlights the capability of P-US towards evaluating rotational instabilities of the distal tibiofibular articulation.

Subtle syndesmotic injury can cause clinically relevant instability of the ankle joint that can be associated with long-term disability and osteoarthritis when left untreated.[11, 25, 29, 33, 35] Despite the morbidity associated with syndesmotic instability, it remains challenging to identify subtle cases of instability on a large scale due to the limited accuracy, availability, or invasiveness of the assessment method.[6, 17, 23] As a consequence, no consensus has yet been reached on the definition of clinically consequential syndesmotic instability. Ultrasonography is increasingly used in the diagnosis of syndesmotic instability as it allows for a bilateral dynamic evaluation of the ankle joint at the point of care with little risk to the patient and at low cost.[1, 13, 18, 32]

Three clinical studies have assessed the TFCS-opening while providing an external rotation torque to the ankle using ultrasound in patients with a complete AITFL rupture.[1, 31, 40] Baltes et al. found a mean TFCS-opening of 0.4 mm when comparing it to the unstressed injured condition and a mean TFCS-opening of 1.9 mm when comparing it to the stressed uninjured contralateral side. Their result emphasises the importance of the ability to use a contralateral side as an internal control.[1] Mei-Dan et al. and van Niekerk et al. found a TFCS-opening of 1 mm in patients with AITFL rupture.[31, 40]
It is worth noting that among the advantages of P-US is its ability to evaluate the TFCS under stress. Both Baltes et al. and Mei-Dan et al. found dynamic ultrasound assessment technique to be slightly less accurate in detecting AITFL rupture as compared to the MRI, but this explicitly focuses on injury, not instability. It is the latter that drives the decision for surgical management. In this cadaveric study, no statistical difference was found between the intact and AITFL transection stage, underscoring that isolated injuries to the AITFL, whether seen on P-US or MRI, are not inherently unstable.

The TFCS-opening values detected in this study using P-US are similar to those found by Xenos et al. and Shoji et al., who also evaluated the tibiofibular diastasis after sequential transection of the syndesmosis.[36, 43] The study by Xenos et al. evaluated TFCS-opening under an external rotation torque of 5 Nm but using a Storz calliper instead of ultrasound and detected a tibiofibular opening of 1.3 (AITFL), 3.5, (IOL), and 6.3 mm after the PITFL cut as opposed to the unloaded, intact stage.[43] Thereby, shoji et al. already found a significant widening of the tibiofibular distance after the AITFL cut with external rotation stress using ultrasound.[36] The correlation between ultrasound studies and direct measurement techniques highlight the opportunity to evaluate the syndesmosis noninvasively at the point of care.

Various amounts of torque forces have been used in the literature, ranging from 0 to 20 Nm torque.[4, 6, 21, 38, 43] Given that pain will be a limiting factor in vivo when performing stress manoeuvres on an injured ankle, it is critical to be able to diagnose instability with sufficient sensitivity under the least amount of requisite force. In this study, the TFCS was measured during unloaded and after four torque-loading conditions, including 4.5, 6.0, 7.5, and 9.0 Nm. When applying 4.5 Nm, a significant increase in TFCS-opening could be detected with partial syndesmotic injury to the AITFL and IOL as compared to the intact stage. Thus, applying 4.5 Nm of external rotation force to both the injured and uninjured ankle would suffice under clinical conditions and may be better tolerated by patients than higher torque values. In contrast, the fluoroscopic results found in this study corroborate previous literature suggesting that it is insufficiently sensitive for diagnosing rotational plane syndesmotic instability.[8, 23, 34]

Traditionally, the distinction between stable and unstable syndesmosis is primarily based on **1.** ligament disruption as well as on **2.** statistical differences in fibular translation or rotation as compared to the intact state.[3, 12, 25–28, 39, 42] New techniques such as 3D-WBCT scan, CT-scan with rotatory platforms, and (portable) dynamic ultrasonography
carry the potential for reliably evaluating syndesmotic instability noninvasively.[5–7, 13, 18]
The dynamic assessment method presented in this study should be considered when there is suspicion for syndesmotic instability, especially when subtle.

This study has several limitations. First, no information on the premedical history of the cadavers was available. However, no degenerative changes or injury of the ankle joint was detected using arthroscopy and fluoroscopy. Second, this study solely evaluated TFCS values after rotational torque. Syndesmotic instability is a multidirectional pathology, and other stress manoeuvres such as fibular shuck in the sagittal plane may also play a role. Third, it is unclear the degree to which patients will tolerate a 4.5 Nm external rotation torque in vivo, especially after an acute injury. Clinical studies are necessary to hone the application of P-US at the bedside. Lastly, biomechanical properties of the ankle soft tissue structures may have altered due to the freeze/ thaw cycle, as well as the repetitive force loading during the experiment, which may have affected measurements obtained in this setting.

Extrapolated to the clinical setting, P-US may be a useful tool in diagnosing syndesmotic instability during external rotation stress examination clinically. 4.5 Nm of force can be used when comparing to the stressed, uninjured side, and may be better tolerated by patients than higher torque values. The clinical instability cutoff values should be further investigated in a clinical research setting.

Conclusion

P-US is a useful tool in diagnosing syndesmotic instability during external rotation stress examination. TFCS-opening increased as additional ligaments of the syndesmosis were transected, and application of 4.5 Nm torque was sufficient to detect a difference of 2.6 mm after the IOL cut.

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Chapter 6 Range Of Normal And Abnormal Syndesmotic Measurements Using Weightbearing CT

Hagemeijer NC,
Chang SH,
Elghazy MA,
Casy JC,
Waryasz G,
Guss D,
DiGiovanni CW

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Abstract

Objectives

Early recognition of syndesmotic instability is critical for optimizing clinical outcome. Injuries causing a more subtle instability, however, can be difficult to diagnose. The objective of this study was to evaluate both distal tibiofibular articulations using weightbearing computed tomography (CT) in patients with known syndesmotic instability, thereafter comparing findings between the injured and uninjured sides. We also aimed to define the range of normal measurement variation among patients without syndesmotic injury.

Methods

Patients with unilateral syndesmotic instability requiring operative fixation (n = 12) underwent preoperative bilateral ankle weightbearing CT. A separate cohort of patients without ankle injury who also underwent bilateral ankle weightbearing CT were included as comparative controls (n = 24). For each weightbearing CT, a series of 7 axial plane tibiofibular joint measurements, including 1 angular measurement, were utilized to evaluate parameters of the syndesmotic anatomy at a level 1 cm above the tibial plafond. Values were recorded by 2 independent observers to assess for interobserver reliability.

Results

Among those with unilateral syndesmotic instability, values differed between the injured and uninjured sides in 4 of the 7 measurements performed including the syndesmotic area: direct anterior, middle, and posterior differences, and sagittal translation ($P < .001$, $< .001$, $< .001$, and $< .001$, respectively). In the control population without ankle injury, no differences were identified between any of the bilateral measurements (P value range, .172-.961).

Conclusion

This study highlights the ability of weightbearing CT to effectively differentiate syndesmotic diastasis among patients with surgically confirmed syndesmotic instability from those without syndesmotic instability. It underscores the substantial utility and importance of using the contralateral, uninjured side as a valid internal control whenever the need for confirming potential syndesmotic instability arises. Prospective studies are necessary to fully understand the accuracy of weightbearing CT in diagnosing occult syndesmotic instability among patients for whom the diagnosis remains in question

Introduction

Early diagnosis of syndesmotic instability is critical to optimize clinical outcome, but subtle syndesmotic instability can present as a diagnostic challenge.[2, 11] Stress radiographs allow application of physiologic load but have low sensitivity [1, 11] Cross-sectional magnetic resonance imaging (MRI) readily identifies syndesmotic injury but not necessarily instability, by virtue of being an unstressed modality that is almost uniformly unilateral.[4] Similarly, traditional computed tomography (CT) scanning only shows alignment without physiologic load in the unstressed state.[20]

Bilateral weightbearing CT offers several potential advantages over these methods. It not only has the ability to visualize the distal tibiofibular articulation while under physiologic load but also can simultaneously provide direct comparison of the injured and uninjured sides. These capabilities are critical because several studies have demonstrated enormous variability in distal tibiofibular morphology between individuals—emphasizing the value of an internal control whenever evaluating the distal tibiofibular articulation.[6, 12, 17] Prior studies using weightbearing CT to evaluate the distal syndesmosis have described unilateral normal values of the distal tibiofibular articulation in the axial 2-dimensional (2D) plane and found good to substantial reliability for measuring syndesmotic area, fibular diastasis, and fibular translation on weightbearing CT.[2,6,7,13,14,17,19]

The objective of this study was to evaluate the distal tibiofibular articulation using weightbearing CT among patients with known syndesmotic instability, utilizing the contralateral uninjured side as an internal control, and in turn to compare such measurements with those from patients with nonsyndesmotic injuries who underwent similar imaging.[8]

Methods

Study Population And Design

This retrospective study was approved by the hospital's institutional review board. A total of 227 weightbearing CT scans of bilateral ankles and extending to the entire foot were performed at our institution between 2015 and 2018. Patients were included as part of the control group if they had a weightbearing CT to evaluate the Lisfranc joint or a more distal forefoot condition without any associated ankle injury. Patients with syndesmosis instability were defined as those requiring operative stabilization of the syndesmosis. Patients were included only if the injury was unilateral without associated posterior malleolar fracture or other distal tibial fracture extending to the incisura, as well as without contralateral ankle or foot injury. All other patients were excluded from the study. Twelve patients (24 ankles) with unilateral syndesmotic instability requiring operative fixation and 24 patients (48 ankles) with no ankle injury were included in this study. The control group's tibiofibular measurements were compared with the tibiofibular measurements of the study group's contralateral ankle.

The unilateral syndesmotic instability group consisted of 12 patients, of whom 10 had chronic injury and 2 had acute injury, 5 males and 7 females with a median (IQR) age of 26.7 (19.8-38.2) and body mass index (BMI) of 27.2 (23.930.6). Of those 10 chronic patients there were 5 patients who had chronic isolated syndesmotic instability and did not receive treatment before the weightbearing CT was obtained; 3 other patients received a weightbearing CT because they were still symptomatic after initial syndesmosis open reduction and internal fixation (ORIF), and 2 patients became symptomatic after ankle ORIF without syndesmotic repair. A detailed description of these patients is presented in Table 1.

The indications for the weightbearing CT scans of 24 patients without any associated ankle injury were as follows: 19 patients (79%) received a weightbearing CT scan for a Lisfranc joint evaluation, 3 patients (13%) for the evaluation of the forefoot after a reconstructive procedure, 1 patient (4%) for a sesamoid evaluation, and 1 (4%) for an alignment and fragment assessment after multiple base fractures of the metatarsal bones. The control group consisted of 10 males and 14 females with a median (IQR) age of 42.9 (27.1-60.3) years and BMI of 24.9 (23.0-31.3) kg/m^2.

All weightbearing CTs were performed using a PedCAT (CurveBeam, Warrington, PA) that also incorporated the entire foot.

Measurement Methods

A series of 7 axial plane measurements were performed at the distal tibiofibular joint at a standardized level 1 cm above the tibial plafond and as reported by previously published studies (Figure 1). The syndesmotic area was defined as the space between the fibula and the tibia delineated by 2 tangential lines abutting the anterior and posterior cortices of the tibia and the fibula (Figure 1A).[14] The direct anterior and direct posterior differences were measured by first drawing a sagittal line connecting the most anterior point of the fibula with the most posterior point, delineated as the fibular orientation line.[5]
Thereafter, direct anterior and posterior difference lines were drawn perpendicular to this fibular orientation line at the most anterior and posterior points of the fibula, respectively (Figure 1B). The middle difference was the distance between the most central point of the incisura and the nearest point of the fibula (Figure 1B).[17] Fibular rotation was measured as the angle between a line drawn between the anterior and posterior borders of the incisura and the fibular orientation line drawn as described above.[17] The angle was considered positive when the fibula was internally rotated relative to the incisura (Figure 1C).

Table 1 Characteristics of Syndesmosis Instability Patients.

Case	Sex	Age	Diagnosis	Mechanism of injury	time from injury to WBCT scan (months)	Scan for revision	Radiographic widening (radiology report)	MRI	WBCT scan widening (radiology report)	Confirmation of instability
1	male	20	HA sprain	ER injury	4.3	-	no	-	yes	Coronal diastasis visualized during open surgery
2	male	43	HA sprain	PER injury	5.8	-	no	ATFL + AITFL rupture, PITFL avulsion, CFL thickening	yes	Coronal and sagittal diastasis arthroscopically
3	female	19	HA sprain	Inversion injury	60.4	-	no	intact	no	Sagittal fibular translation, + positive anterior drawer while examining clinically under anaesthesia
4	female	16	HA sprain	Twisting injury	48	-	no	ATFL tear, thickening CFL, PTFL, and AITFL	no	Coronal and sagittal diastasis, clinically under anaesthesia and arthroscopically
5	male	24	HA sprain	Unknown	12	-	no	ATFL thinning	yes(subtle)	Coronal and sagittal diastasis, clinically under anaesthesia and arthroscopically
6	female	49	Maisonneuve#	Unknown	0.16	-	yes(mild)	-	yes	WBCT
7	female	29	Closed ankle dislocation	Posterolateral ankle dislocation	0.13	-	no (NWB)	-	yes	WBCT
8	female	18	Missed SI after closed ankle subluxation with talar#	Ankle subluxation, unknown type/direction	12.2*	yes	yes + MCS	-	yes + MCS	WBCT
9	male	34	MR after HA sprain	Inversion trauma	6.6*	yes	no	-	no	Clinical presentation
10	female	54	MR after closed ankle fracture dislocation	Unknown type/direction	9.1*	yes	yes + MCS	-	Yes + MCS	Coronal diastasis visualized during surgery
11	female	29	Missed SI after bimalleolar#	High energy MVA	15.1*	yes	yes(mild)	-	yes	Coronal diastasis visualized fluoroscopically
12	male	24	Missed SI after weberC#	Sports injury, exact mechanism unknown	18	yes	yes	-	yes	WBCT

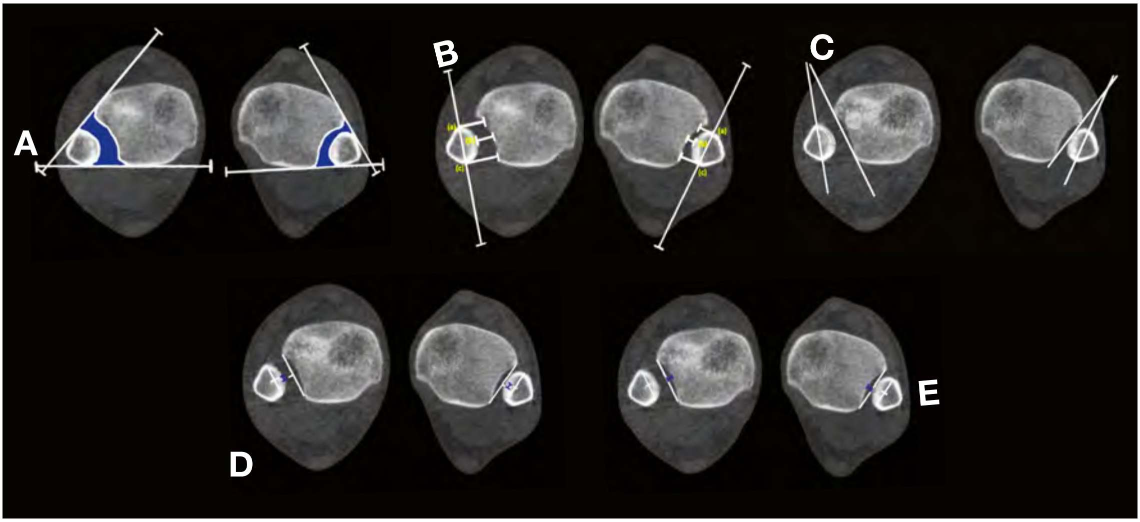
Abbreviations: AITFL, anterior inferior tibiofibular ligament; ATFL, anterior talar fibular ligament; CFL, calcaneal fibular ligament; ER, external rotation; HA, high ankle; MCS, medial clear space; MR, malreduction; MRI, magnetic resonance imaging; MVA, motor vehicle accident; NWB, nonweightbearing; PER, pronation external rotation; PITFL, posterior inferior tibiofibular ligament; PTFL, posterior talar fibular ligament; SI, syndesmosis instability; WBCT, weightbearing computed tomography.

*Time after initial open reduction and internal fixation syndesmosis procedure.

Chapter 6 Range Of Normal And Abnormal Syndesmotic Measurements Using Weightbearing CT

The position of the fibula in the sagittal plane was represented by the difference between the midpoint of the incisura lenght and the midpoint of the fibular lenth line, the latter drawn from the most anterior point of the fibula and sented by the difference between the midpoint of the inci- parallel to the incisura length (Figure 1D).[13] The depth of sura length and the midpoint of the fibular length line, the the incisura was also recorded (Figure 1E).[13] All measurements were performed by 2 independent observers (N.H., research fellow; S.C., orthopedic foot and ankle surgeon) using IMPAX AGFA software with an accuracy of 0.1 mm.

Figure 1. Tibiofibular joint measurements.



(A) Syndesmotic area (shaded area). (B) Direct anterior (a), middle (b), and direct posterior (c) differences. (C) Fibular rotation. (D) Sagittal translation (dark line). (E) Incisura depth (dark line). The patient had rightsided syndesmosis instability after an acute posterolateral ankle dislocation.

Statistical Analysis

A descriptive analysis was performed to summarize the baseline characteristic variables, which are presented with frequencies and percentages for categorical variables and with means and standard deviations and medians and ranges for continuous variables. Dichotomous and categorical demographic data were compared using a chi-square test and continuous variables were compared using a t test. To assess a correlation between separate weightbearing CT measurements, a linear mixed effects model was built, with subject and measurement maker as random factors. This model allowed us to use the collected data from both observers for analysis.

All measurements were independently performed by 2 observers to assess interobserver agreement using the intraclass correlation coefficient (ICC) through a 2-way mixed effects model with absolute agreement. Absolute agreement in an ICC assesses how much each measurement performed by one observer differs from that of the other observer. Interpretation of the ICC values was carried out according to the guidelines proposed by Shrout and Fleiss[18]: 0.00 to 0.10 virtually none, 0.11 to 0.40 slight, 0.41 to 0.60 fair, 0.61 to 0.80 moderate, 0.81 to 1.00 substantial. P values of <.05 were considered significant. All analyses were performed with Stata 13.0 for Mac (StataCorp LP, College Station, TX)

Results

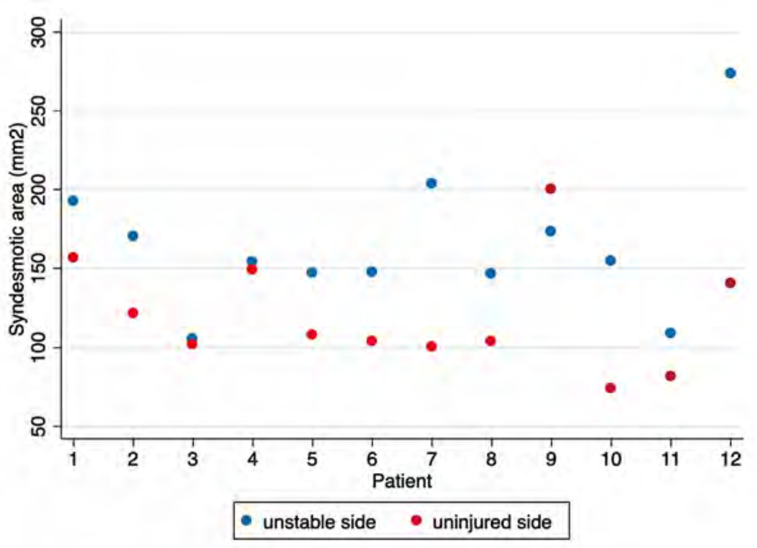
Weightbearing CT Measurements

Among patients with unilateral syndesmotic injuries, measurements including the syndesmotic area, direct anterior difference, middle difference, and direct posterior difference differed between the injured and uninjured side (Table 2). The bilateral syndesmotic area values of the syndesmotic injury group are graphically presented per patient in Figure 2. Patient 9 had a larger area in the uninjured side and did not show a rotational or translational malposition of the fibula; potentially this may have concerned an overcompression of the syndesmosis by the syndesmotic screw fixation.
Among patients without syndesmosis injury, no differences were found based on laterality when comparing any of the syndesmotic measurements (Table 3).

Interobserver Agreement

Two observers performed all measures independently. The ICCs were 0.83 for fibular rotation (95% CI, 0.73-0.89), 0.80 for fibular sagittal plane position (95% CI, 0.68-0.88), 0.97 for syndesmotic area (95% CI, 0.95-0.98), 0.86 for anterior difference (95 CI, 0.77-0.91), 0.92 for middle difference (95% CI, 0.87-0.95), 0.87 for posterior difference (95% CI, 0.80-0.92), and 0.91 for incisura depth (95% CI, 0.85-0.94). The ICCs indicated substantial agreement for all measures except for the position measurement of the fibula in the sagittal plane, which demonstrated moderate agreement.

Figure 2. Bilateral syndesmotic area representation of the syndesmosis instability group



*Patient numbers correlate with the numbers provided in Table 1.

Table 2. Bilateral Axial Plane Weightbearing CT Syndesmosis Measurements of the Syndesmosis Instability Patient Group.a

Measurement	Mean ±SD Median (range) (12 ankles) non-injured	Mean ±SD Median (range) (12 ankles) Unstable	Difference	95%CI	p-value
Syndesmotic area (mm²)	118.7 ±37.7 107.2 (62.5-218.9)	164.8 ±46.8 154.3 (98.6-289.8)	45.72	[30.47-60.98]	<0.001
Anterior difference (mm)	6.0 ±2.1 5.6 (2.7-10.6)	8.4 ±2.4 8.3 (3.8-13.4)	2.36	[1.41-3.31]	<0.001
Middle difference (mm)	4.6 ±1.4 4.6 (1.7-7.6)	6.0 ±1.4 5.8 (3.8-8.8)	1.39	[0.85-1.93]	<0.001
Posterior difference (mm)	9.14 ±2.1 8.4 (6.4-15.3)	11.6 ±3.0 10.7 (7.4-17.4)	2.52	[1.21-3.82]	<0.001
Fibular rotation (degrees)	10.3 ±5.5 11.9 (-1.7-18.4)	8.4 ±7.0 8.3 (-8.1-22.4)	-1.87	[-4.11-0.48]	0.12
Fibular sagittal plane position (mm)	1.7 ±1.1 1.8 (-0.8-3.2)	1.9 ±1.1 2 (-0.7-3.8)	0.28	[-0.32-0.87]	0.36
Depth incisura (mm)	3.5 ±1.0 3.2 (1.5-6.0)	3.3 ±1.3 3.1 (0.5-5.9)	-0,13	[-0.65-0.39]	0.63

Abbreviations: CI, confidence interval; CT, computed tomography; SD, standard deviation.
aValues are given as mean ± SD and median (range), unless otherwise stated.

Table 3. Bilateral Axial Plane Weightbearing CT Syndesmosis Measurements of the Uninjured (Control) Patient Group.a

Measurement	Mean ±SD Median (range) (24 ankles)	Mean ±SD Median (range) (24 ankles)	Difference	95%CI	p-value
Syndesmotic area (mm²)	115.7 ±25.5 109.1 (78.1-164.6)	115.6 ±31.4 110.2 (65.4-192.2)	-0.41	[-5.39-4.57]	0.87
Anterior difference (mm)	6.2 ±1.5 6.0 (3.8-10)	6.3 ±1.4 6.2 (4.0-10.5)	-0.01	[-0.37-0.39]	0.96
Middle difference (mm)	4.5 ±1.01 4.3 (1.7-6.5)	4.6 ±1.1 4.5 (2.5-6.8)	-0.01	[-0.26-0.24]	0.92
Posterior difference (mm)	8.9 ±1.66 9.0 (4.8-11.6)	8.9 ±1.47 8.9 (6.3-13.6)	-0.03	[-0.43-0.37]	0.89
Fibular rotation (degrees)	11.5 ±5.2 10.9 (2.4-24)	12.5 ±6.2 10.0 (3.9-28.5)	0.96	[-0.53-2.45]	0.21
Fibular sagittal plane position (mm)	1.8 ±1.0 1.9 (0-5.1)	1.5 ±1.1 1.3 (0-4.5)	-0.22	[-0.55-0.10]	0.17
Depth incisura (mm)	3.8 ±1.5 3.7 (0.1-7.5)	3.8 ± 1.4 3.5 (2.2-8.6)	0.02	[-0.26-0.30]	0.88

Abbreviations: CI, confidence interval; CT, computed tomography; SD, standard deviation.
aValues are given as mean ± SD and median (range), unless otherwise stated.

Discussion

Accurate detection of syndesmotic instability, especially when subtle, remains challenging. Existing imaging modalities such as weightbearing radiographs are limited by their low sensitivity for diagnosing syndesmotic instability.[1, 11] Alternative modalities such as MRI have high sensitivity for syndesmotic injury but cannot inherently distinguish injury from instability—the latter of which is likely to require and benefit from operative fixation. Weightbearing CT affords the unique ability to evaluate the distal syndesmosis in the axial plane under physiologic load while also allowing comparison with the contralateral uninjured side to serve as an internal control.

Notably, this study demonstrated that the weightbearing CT was able to distinguish between a stable and unstable distal syndesmosis. It also highlighted the utility of bilateral cross-sectional imaging to generate an internal control when evaluating such injuries. Of the various distal tibiofibular joint measurements examined in this study, the syndesmotic area had the highest interobserver agreement and showed the largest difference between normal and abnormal, arguably making it the most applicable for detecting syndesmosis instability in the axial plane.
Syndesmotic area was first described by Malhotra et al,[14] who investigated patients with chronic syndesmosis instability after ankle fracture using bilateral nonweightbearing CT scans and who thereafter underwent operative fixation. They similarly found a larger syndesmotic area on the uninjured side compared with the injured side (121 ± 25 mm^2 vs 171 ± 44 mm^2). Our study, using weightbearing CT, found similar results (119.2 ± 37.9 vs 166.3 ± 48.1 mm^2).

Importantly, we also investigated bilateral weightbearing CT scans of uninjured patients and found that the difference in syndesmotic area based on laterality between the healthy ankles was only 0.41 mm^2 (95% CI, −5.39 to 4.57), whereas the mean difference between ankles in the injured patient was 46 mm^2 (95% CI, 30.47-60.98). Large interperson variability among the population underscores the critical importance of always using the contralateral side as an internal control whenever diagnosis remains in doubt.

Traditionally, nonweightbearing 2D CT evaluation of the tibiofibular joint space has relied on drawing 3 lines from the anterior, middle, and posterior borders of the fibula to the incisura in the axial plane, but such approaches have demonstrated a wide range of normal values.[3, 7, 9, 10, 13, 15-17] Furthermore, only one such study by Lepojärvi et al[13] explored bilateral values, finding no difference based on laterality. The alternative measurement techniques we incorporated in this study were adopted from reports that investigated syndesmosis malreduction, and were explicitly chosen because of their high interrater reliability scores.[5, 19]

Prior studies that have explored the normal syndesmosis using both nonweightbearing CT and weightbearing CT found contradicting results.[9, 15] Hoogervorst et al [9] found no difference in syndesmotic measurements with and without weightbearing, whereas Malhotra et al [15] found that the fibula translated laterally, posteriorly, and externally when under physiological load. Neither study examined the effects of weightbearing in the setting of a syndesmotic injury or known tibiofibular instability. Burssens et al [2] studied syndesmotic injuries on 3-dimensional (3D) weightbearing CT by creating 3D models of an injured ankle with either fractures or high ankle sprains and then superimposing the 3D images of the uninjured side to assess any difference. Measurements were based on the most lateral aspect of the fibula as well as the anterior and posterior fibular tubercles. They found a significant coronal plane translation of the fibula of 1.6 mm, falling in the middle range observed in our study (0.67-2.15 mm). While rigorous in their methodology, the technical availability of 3D weightbearing CT, image mirroring, and subsequent superimposition remains limited, as most practicing orthopedic surgeons continue to rely on the far more simplified image viewer platforms that currently exist.

In our study using 2D weightbearing CT, substantial agreement was found for almost all measurement methods, ranging from 0.83 for fibular rotation to 0.97 for syndesmotic area. The interrater reliability score of syndesmotic area was similar that found by Malhotra et al [14] (0.97), suggesting that this may be the most reliable strategy to evaluate syndesmotic injuries. The other measurements' levels of agreement were slightly higher than those previously reported on in the literature, possibly related to the standardized level of measurement at 1 cm above the plafond.[13, 14, 17, 19]

While our study failed to find a difference in fibular rotation, this may not be the case with all methodologies. For example, Burssens et al [2] did find significant differences in rotation but relied on the superimposition of a mirrored, 3D image of the injured ankle, which may not be as technically accessible as other methodologies. When using a 2D measuring method, fibular rotation is less clearly visible, possibly because it is viewed in 1 image slice rather than in a volumetric manner.

This study has some inherent limitations. It was designed to evaluate whether weightbearing CT is able to identify syndesmotic instability when comparing an injured ankle to its uninjured, contralateral side. Simultaneously, it aimed to confirm that there is no difference between laterality among uninjured controls—proving one's ability to use the contralateral ankle as an internal control when evaluating the syndesmosis. Syndesmotic instability was in turn defined as those ankles that required syndesmotic fixation, so this study suggests but does not yet prove that weightbearing CT can effectively distinguish both subtle and severe diastases. It is also unlikely that the instability values reported in this study are as yet sufficient to represent a true cutoff value for more occult syndesmotic instability.

Our study does, however, underscore the utility of evaluating the distal tibiofibular articulation under physiologic load and looking carefully at any differences in the contralateral control, especially in the chronic cases. Two patients received a weightbearing CT scan after an acute injury. Even though both reports explicitly state that their scans were weightbearing, we are unsure whether these patients were in fact fully weightbearing. This study also suggests that certain measurement techniques, specifically in the syndesmotic area, are perhaps best for assessing syndesmotic instability. One caveat inherent to this measurement technique, however, is that unlike the other syndesmotic measurements that entail distance and angle functions already built into most CT scan viewing programs, the ability to measure an area irregularity at the incisura is still not readily available. This study therefore also highlights the need for ongoing software advancement as a means of empowering orthopedic surgeons to interpret images generated by modern hardware. Lastly, weightbearing CT is a relatively new and costly technique and is therefore not available to all surgeons yet.

Conclusion

This study highlights the ability of weightbearing CT to effectively differentiate syndesmotic diastasis among patients with surgically confirmed syndesmotic instability in comparison with those without instability. The syndesmotic area had the highest interrater agreement and demonstrated the greatest differential between the abnormal and norm,al ankles—suggesting it as the most applicable parameter for detecting syndesmosis instability in the axial plane. Moreover, the data presented emphasize the critical import of using a patient's contralateral, uninjured side as his or her own valid internal control. Additional studies are required to optimally understand the role of weightbearing CT in prospectively diagnosing more subtle cases of syndesmotic instability among patients for whom the diagnosis remains in question.

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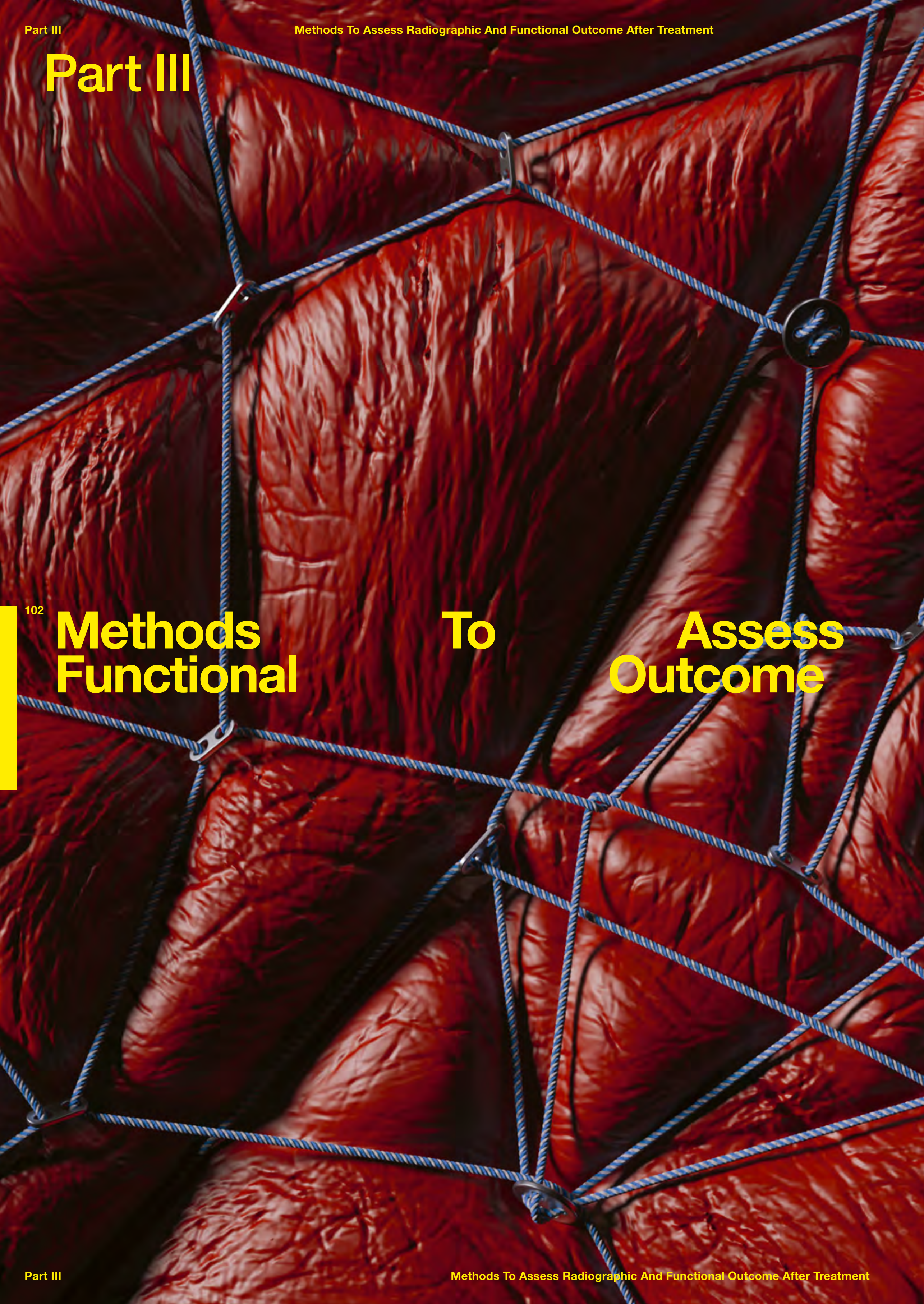

Part III

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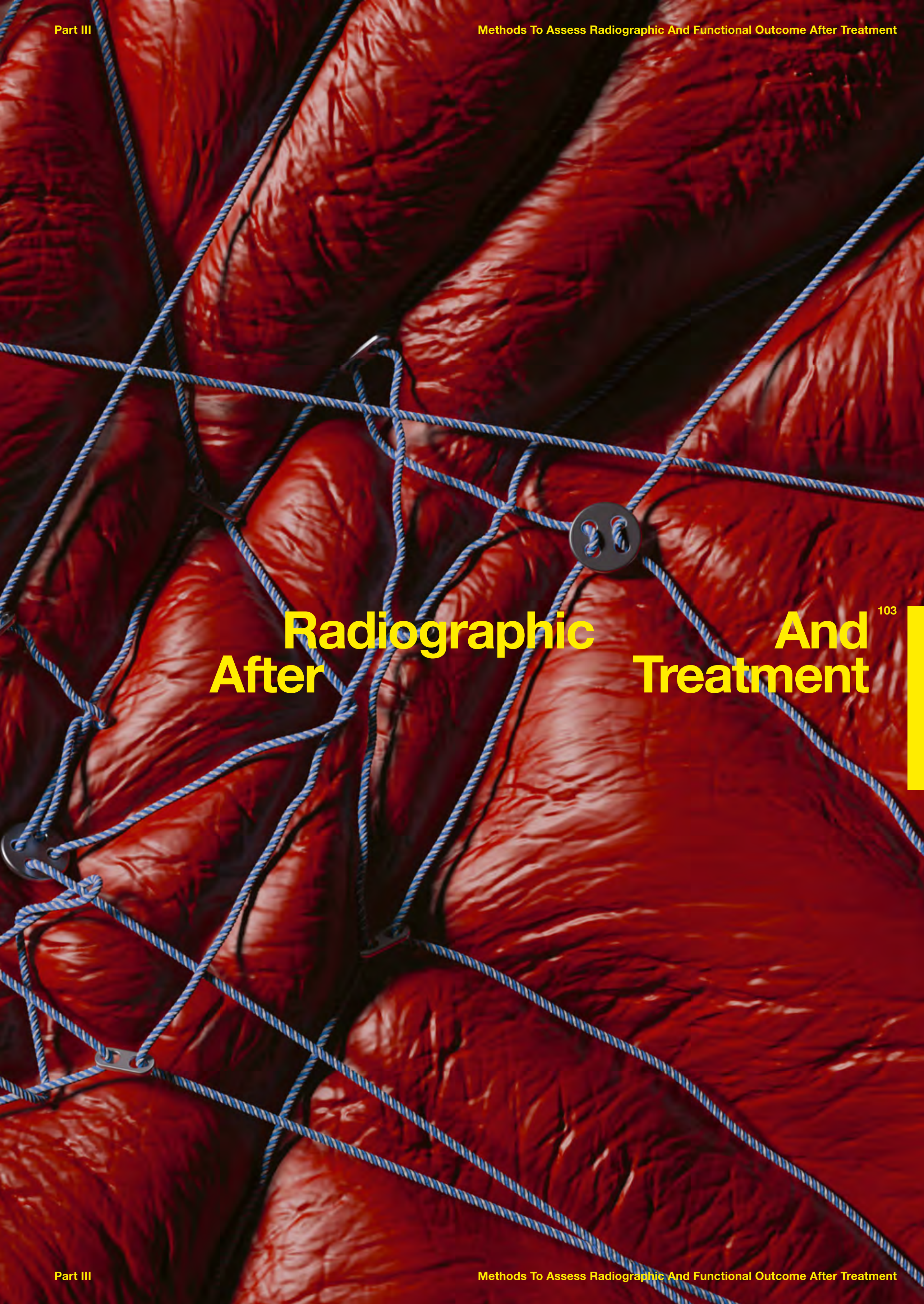
Methods To Assess Functional Outcome



Radiographic And
After Treatment

Chapter 7 Evaluation Of Syndesmosis Reduction On CT Scan

*Elghazy MA,
Hagemeijer NC,
Guss D,
El-Hawary A,
El-Mowafi H,
DiGiovanni CW*

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Abstract

Background

Computed tomography (CT) imaging has traditionally been considered the gold standard for evaluation of syndesmostic reduction, but there is no uniformly accepted method to assess reduction. The aim of this study was to evaluate the intra- and interobserver reliability of published measurement techniques for evaluation of syndesmotic reduction on weightbearing CT scan (WBCT) in hopes of determining which method is best.

Methods

Medical records were reviewed to identify patients who underwent operative stabilization of unilateral syndesmotic injuries. Exclusion criteria included patients younger than 18 years, ipsilateral fractures extending to the tibial plafond, any contralateral ankle fracture or syndesmotic injury, and body mass index greater than 40 kg/m^2. Twenty eligible patients underwent WBCT evaluation of both ankles at an average of 3 years after syndesmotic fixation. The anatomic accuracy of syndesmotic reduction was evaluated by 2 observers using axial CT images at a level 1 cm proximal to the tibial plafond using 9 previously published radiological measurement techniques. Inter- and intraobserver reliability were assessed for each evaluation method.

Results

The syndesmotic area calculation showed the highest interobserver reliability (0.96), the highest intraobserver reliability for observer 2 (0.97), and the second highest intraobserver reliability for observer 1 (0.92). Fibular rotation had the second highest interobserver reliability in our results (0.84), with intraobserver reliability of 0.91 and 0.8 for first and second observers, respectively. The intraobserver reliability of the side-by-side method was 0.49 and 0.24 for the first and second observers, respectively, and the interobserver reliability was 0.26.

Conclusion

Qualitatively assessing syndesmotic reduction via side-by-side comparison with the uninjured ankle had the least intra- and interobserver reliability and should not be relied on to determine syndesmotic reduction quality. In contradistinction, syndesmotic area calculation demonstrated the highest reliability when evaluating syndesmotic reduction, followed by fibular rotation. Given that syndesmotic area measurement techniques are not readily available on standard image viewers, technologically updating image viewers to allow such calculation would make this approach more accessible in clinical practice.

Introduction

Although ankle arthroscopy can evaluate the syndesmosis accurately by providing the surgeon with direct visualization of the tibiofibular articulation under stress, it is invasive and cannot be performed on the contralateral uninjured side to establish a native reference. The ability to review both ankles makes the CT scan a preferred noninvasive method for evaluation of syndesmotic reduction. For the syndesmosis, weightbearing CT scan (WBCT) has the specific additional advantage of dynamic evaluation as shown by significant lateral fibular translation and fibular external rotation relative to the incisura during weightbearing vs nonweightbearing imaging.[16, 20, 22, 25]

Several studies have advocated the use of bilateral ankle CT imaging to determine the accuracy of syndesmotic reduction postoperatively in the axial plane.[7,14] These recommendations resulted in part because of the substantial variation in the anatomic relationship of the normal syndesmosis as demonstrated in a recent systematic review of its normal radiological measurements.[2] Several methods to quantify the syndesmotic relationships and reduction in the axial CT images have been reported. [1, 4, 6-8, 10, 12-15, 18, 21, 24, 26, 28] A side-by-side comparison using the healthy contralateral ankle as a reference seems intuitive and is being commonly used in clinical practice for evaluation of syndesmosis reduction, although its validity as an evaluation strategy remains underinvestigated.

Despite the number of described methods for evaluating the syndesmosis, lack of a standardized method and limited agreement between available studies with respect to the normal and disrupted relationships between distal tibia and fibula at this level suggest a need for further investigation. The aim of this study, therefore, was to evaluate intra- and interobserver reliability of commonly used measurements for evaluation of syndesmosis reduction using axial images of WBCT.

Methods

Patients

After receiving institutional review board approval from Partners HealthCare at Massachusetts General Hospital, a Research Patient Data Registry (RPDR) search was conducted to identify patients who had undergone fixation of unilateral, unstable syndesmotic injuries between January 2008 and December 2016. Exclusion criteria were patients younger than 18 years, ipsilateral fracture extending to the tibial plafond, history of contralateral ankle fracture or syndesmotic injury, body mass index (BMI) greater than 40 kg/m^2, pregnancy or active breastfeeding, and any neurological impairment limiting one's ability to stand independently. Eligible patients were recruited to participate in this study from July 2017 until June 2018 and underwent WBCT evaluation outside their standard orthopedic care as part of this research study. The syndesmotic injury was isolated in 3 patients and associated with ankle fractures in all others, including a transsyndesmotic pattern (Weber type B) in 6 patients and suprasyndesmotic (Weber type C) in 11 patients. The syndesmotic injury was evident on preoperative radiographs for most patients. Five patients underwent preoperative CT scan, and syndesmotic instability was readily apparent in 3 of them. The other 2 patients had subtle syndesmotic instability that was not identified on preoperative CT scan but was confirmed arthroscopically prior to fixation of the syndesmosis. None of the patients had a postoperative infection or required a revision surgery.

Twenty patients were recruited for this study, including 10 men and 10 women with an average age of 43 years (range, 23-67) years. All patients had unilateral syndesmotic instability that required operative fixation alongside an uninjured contralateral side. The mechanism of injury was described as a twisting injury in 13 patients, direct trauma to the ankle in 3 patients, and not mentioned in the records of 4 patients. After fixation of any associated ankle fractures, the syndesmosis was stabilized by a single suture button in 5 patients, 2 suture buttons in 5 patients, a single screw in 6 patients, and 2 screws in 4 patients. Among the screw group, the screw(s) was (were) tetracortical in 3 patients and tricortical in 7 patients. None of the patients had a reoperation due to a complication, and 7 patients had the syndesmotic screw(s) electively removed before obtaining the study scan. WBCT scan was performed for both ankles simultaneously, with an average interval of 3 years (range, 1-7) between the fixation of the syndesmosis and the study scan.

CT Imaging And Measurements

All patients underwent WBCT scan (pedCAT; Curvebeam version 3.2.1.0, Warrington, PA) of both ankles simultaneously using a standardized technique while having the patient stand in an upright, full weightbearing position. Assessment was performed using axial CT images at the level of 1 cm proximal to the tibial plafond. Nine commonly used radiographic measurements (Table 1 and Figures 1 and 2) were chosen for evaluation of syndesmosis.[6, 7, 10, 13, 15, 18, 26, 28]

Measurements from methods 2 to 9 were obtained for both ankles. A picture archiving and communication system (PACS) image viewer was used to obtain the measurements with 0.1 degree of precision for rotation and 0.1 mm of precision for the rest of the measurements. All 9 methods were evaluated independently for all patients by 2 observers. All measurements were repeated after a 6-week time interval. To confirm the reliability of the subjective side-to-side evaluation method, it was further evaluated by 10 other observers with different levels of experience in foot and ankle surgery who independently assessed all patients. The observers were informed of the initial treatment details but were not informed regarding current patient complaints, if any.

Introduction

Statistical Analysis

Interobserver and intraobserver reliability were assessed for each evaluation method. Side-by-side method was assessed using κ interrater agreement, while the reliabilities for all other methods with continuous variables were assessed with interclass correlation coefficients (ICCs) using 2-way mixed-effects model with consistency of agreement. For the first binary evaluation method (subjective side by side), 15 patients were required to have a 95% confidence interval level for 2 independent raters given the probability of 0.5 for each of them to give a positive rating with 0.5 absolute precision. For all other continuous measurements, our study had 80% power to detect a hypothesized ICC of 0.8 against a null ICC of 0.6 using 40 ankles with an α level of 0.05. Analysis was done using STATA 14.2 (StataCorp LP, College Station, TX).

Figure 1. Side-by-side method for evaluation of reduction (reduced or not).

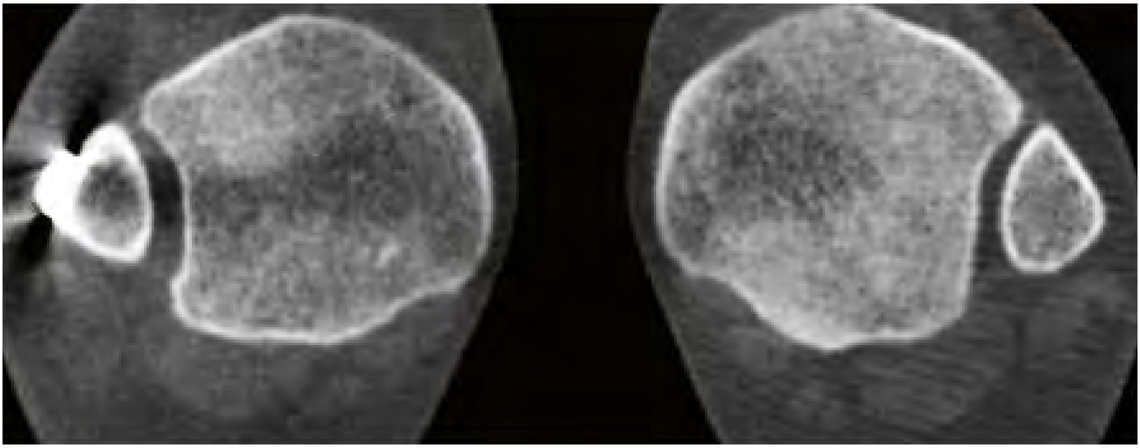
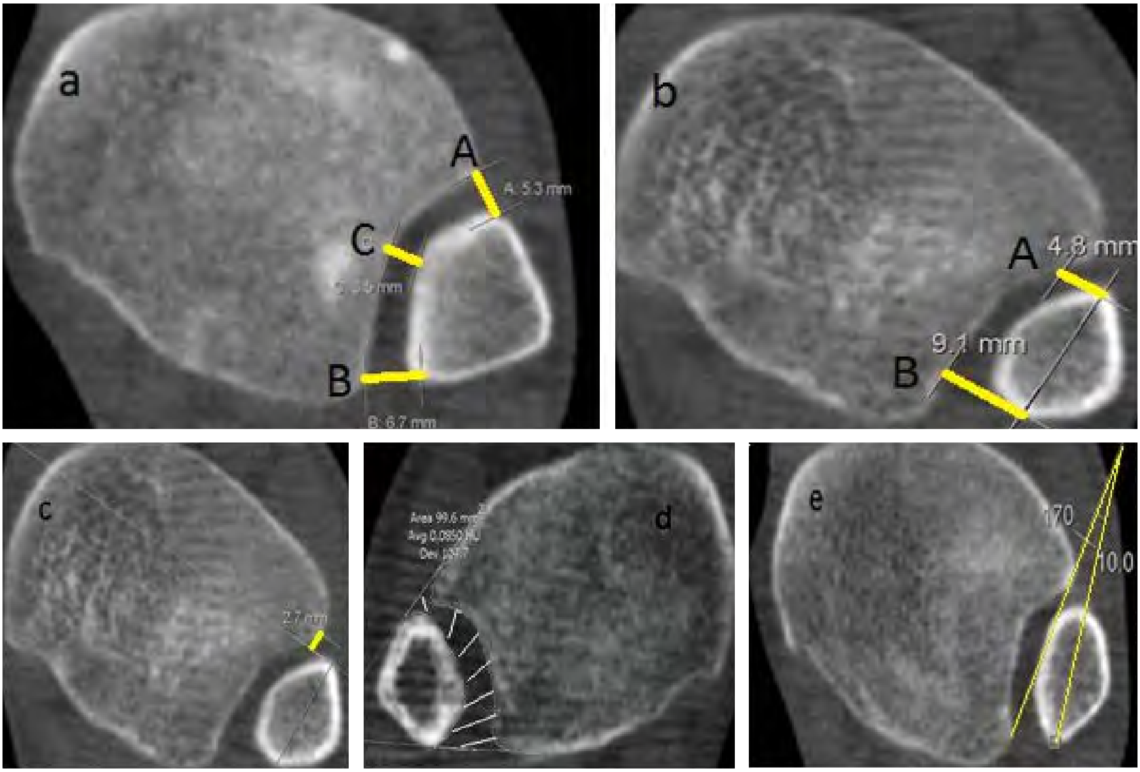


Table 1. Description of Measurement Methods

Method	Description
Side by side (reduced or not)	Subjectively assesses syndesmotic reduction by comparing side-by-side axial images of the injured and uninjured ankles
Anterior difference	The distance between the anterior border of tibial incisura and the most anterior point of the fibula
Posterior difference	The distance between the posterior border of tibial incisura and the most posterior point of the fibula
Middle difference	The distance between the middle of the incisura and the nearest point of the fibula
Direct anterior difference	The distance represented by a line from the incisura and perpendicular to the anterior end of a line representing the fibular orientation
Direct posterior difference	The distance represented by a line from the incisura and perpendicular to the posterior end of a line representing the fibular orientation
Fibular translation	The distance between a line representing the direct anterior difference and the anterior border of tibial incisura. It is positive when the fibula is posterior to the anterior border of incisura.
Syndesmotic area	The space between the lateral cortex of the tibial incisura, the medial cortex of the lateral malleolus, and 2 lines tangential to the anterior and posterior aspects of the tibia and fibula
Fibular rotation	Angle between a line drawn between the anterior and posterior borders of the incisura and a line drawn in the fibula representing its orientation. The angle is positive when the fibula is internally rotated relative to the incisura.

Figure 2. Radiographic measurements.



a) anterior difference (A), posterior difference (B), and middle difference (C). (b) direct anterior difference (A), direct posterior difference (B). (c) Fibular translation. (d) Syndesmotic area. (e) Fibular rotation.

Results

Measurements obtained by first and second observers for all evaluation methods are reported in Table 2, while the agreement results are reported in Table 3. The intraobserver reliability of the side-by-side method was 0.49 and 0.24 for the first and second observers, respectively, while the other 8 radiological measurements ranged from 0.8 to 0.93 and from 0.69 to 0.97 for the first and second observers, respectively. The interobserver reliability for the side-by-side method was 0.26 and ranged from 0.62 to 0.96 for the rest of measurements among the 2 observers. For the side-by-side method, the overall interobserver reliability among the 12 observers was 0.25. The specific interobserver reliability according to the observers' level of experience is listed in Table 4.

Table 2. Results of all evaluation methods obtained by first and second observers.[a]

	Observer 1		Observer 2	
Evaluation Method	**Normal Side (n = 20)**	**Injured Side (n = 20)**	**Normal Side (n = 20)**	**Injured Side (n = 20)**
Side by side (reduced or not)	13 reduced		17 reduced	
Anterior difference, mm	3.8 (1.1)	5.4 (1.4)	5 (1.1)	6.4 (2)
Posterior difference, mm	8.6 (1.2)	9.2 (1.6)	8.7 (1.6)	9.4 (1.6)
Middle difference, mm	3.7 (0.95)	4.6 (1.1)	4.8 (1.8)	5.6 (1.1)
Direct anterior difference, mm	4.5 (1.2)	6.1 (1.3)	5.9 (1.3)	7 (1.6)
Direct posterior difference, mm	9.1 (1.2)	9.7 (2)	9.5 (1)	9.8 (1.5)
Fibular translation, mm	1.2 (1.2)	0.95 (2)	1.6 (1.2)	1.6 (1.8)
Syndesmotic area, mm²	100.5 (16.8)	132.3 (27.8)	110.2 (19.1)	147 (33.1)
Fibular rotation, deg	13.4 (4.8)	6.3 (7.4)	11.6 (5.2)	7.2 (7)

[a]Measurements from methods 2 to 9 are reported as mean (SD).

Table 3. Intraobserver and Interobserver reliability for evaluation methods among first and second observers.

	Intraobserver reliability		
Evaluation Method	**Observer 1**	**Observer 2**	**Interobserver Reliablility**
Side by side (reduced or not)	0.49	0.24	0.26
Anterior difference	0.92	0.83	0.83
Posterior difference	0.93	0.69	0.62
Middle difference	0.93	0.84	0.8
Direct anterior difference	0.93	0.83	0.77
Direct posterior difference	0.8	0.93	0.79
Direct translation	0.9	0.93	0.82
Syndesmotic area	0.92	0.97	0.96
Fibular rotation	0.91	0.8	0.84

Table 4. Interobserver reliability of side-by-side method according to level of experience of the observers.

Years of Experience	Number of Observers	Interobserver Reliability (κ)
0-5	2	0,49
6-10	4	0,26
11-20	4	0,2
>20	2	−0.18

Discussion

While several axial CT measurements have been proposed for evaluating the syndesmosis, it remains unclear which measurement is most reliable for assessing postoperative syndesmotic reduction.[1, 4, 6-8, 10, 12-15, 18, 21, 24, 26, 28] It is also not known which measurements fall within the range of normal and whether or not these can be used as reference standards for defining abnormality. There is wide variation in normal syndesmotic metrics among different CT studies. For example, the mean variation in anterior measurements ranged from 1.7 to 17.4 mm, and the mean variation in posterior measurements ranged from 2.3 to 8.88 mm.[2] The wide interperson variation seen in normal measurements suggests that an absolute cutoff value for detecting syndesmotic pathology may not exist and that, instead, one may need to rely on relative differences with the contralateral ankle as an internal control. Burssens et al [4] recently used the 3-dimensional (3D) CT model of the healthy ankle as a template after being mirrored and superimposed on the 3D model of the contralateral injured ankle and showed significant lateral diastasis and external rotation of the fibula after syndesmotic injury. Side-by-side syndesmotic comparison on axial CT scans had the lowest reliability among all syndesmosis measurements. Because the 2 observers initially had low inter- and intraobserver agreement scores, another 10 foot and ankle surgeons from various countries and with varying experience in the field were asked to assess the tibiofibular joints of all the patients included in the study. After analyzing their results, the overall interobserver reliability was 0.25. After stratifying reliability scores by experience level, however, the interobserver reliability method was noted to decrease as the experience level increased. Interestingly, a higher interobserver reliability for the surgeons with a lower level of experience (0.49 among experience 0-5 years) was found, with the lowest agreement in the group was with the highest level of experience (–0.18 for >20 years). The negative value means that the interobserver reliability was even worse than what can be expected by chance. This low reliability likely stems from both the subjective nature of the evaluation method as well as the fact that no universally agreed-on cutoff value exists to define “successful reduction” or “malreduction.” Moreover, this calls into question the recently advocated use of advanced operative imaging techniques such as intraoperative CT, since these too may not be effective without a preoperative contralateral ankle CT scan as a base of reference.

Several articles have assessed the reliability of CT measurements,[1, 4, 7, 10, 13, 15, 18, 21, 26] but to our knowledge, only Warner et al [26] evaluated the reliability of a subjective side-by-side evaluation of syndesmosis reduction. This group found a substantial result, κ = 0.783, which is a much higher value than found in our study. This difference might be due to several things. The authors included a random and unknown number of patients from their study cohort during their interrater reliability analysis for this subjective evaluation. They also did not provide demographics for their observers or mention whether their observers were blinded—all of which may have increased agreement. Other studies also did not include side-by-side normative assessment evaluations as part of routine comparative assessments for pathology. Even though subjective, visual side-by-side assessment was included in our study as a measurement method because it is still commonly used in practice. We believe this study underscores the critical need to move away from qualitative approaches in favor of more objective, quantitative measurements whenever there is clinical suspicion for instability.

Reliabilities for all other measurements were higher than the side-by-side method. Notably, the syndesmotic area showed the highest interobserver reliability (0.96), the highest intraobserver reliability for observer 2 (0.97), and the second highest intraobserver reliability for observer 1 (0.92). Fibular rotation had the second highest interobserver reliability in our results (0.84) with high intraobserver reliability of 0.91 and 0.8 for first and second observers, respectively.

Syndesmotic area assessment was first described by Malhotra et al,[15] who evaluated 14 patients with chronic syndesmotic instability and reported 0.97 interobserver reliability. Another study by Kocadal et al [13] used syndesmotic area for reduction evaluation, and the intraobserver reliability was 0.885 and interobserver reliability was 0.867, which is very similar to our results. Even though syndesmotic area calculation is not the most commonly used method of measurement to assess syndesmotic reduction, our results suggest that perhaps it should be. Syndesmotic area appears to have higher intra- and interobserver reliability than any other parameter, including anterior difference, posterior difference, middle difference, direct anterior difference, direct posterior difference, and fibular translation. Future studies should continue to focus on investigating the sensitivity of these various measurement techniques for identifying syndesmotic malreduction. Given that the lowest reliability was found in the side-by-side evaluation method, one can make the argument that this technique should be abandoned on both weightbearing and nonweightbearing CT. It also underscores the importance of a contralateral control when evaluating the syndesmosis given such large interpatient variability.

There are certain limitations to our study. We included only what are currently the most commonly employed measurement methods for the assessment of syndesmotic reduction on CT scan, and others that incorporate more advanced techniques such as 3D CT volumetric analysis may also evolve to be useful. Another potential limitation is that we focused only on axial plane images, and perhaps in the future, we may find that other planes afford additional levels of reliability. It could also be argued that our evaluation method should have been correlated to clinical outcome, but this was beyond the aim of this study and would require larger sample sizes even when using the more reliable measurement techniques. Importantly, the most reliable measurement technique identified in this study, syndesmotic area, is not a function readily available on the majority of image viewers currently employed in clinical practice, making this less accessible than other described measures.

In summary, the most reliable means of evaluating distal syndesmotic integrity required comparison of the contralateral uninjured ankle as an internal control through measurement of bilateral distal tibiofibular joint area. It should also be noted that fibular rotation was identified as another promising measurement strategy. Evaluation of syndesmosis reduction using the qualitative and subjective method of side-by-side evaluation of axial CT images had the least intra- and interobserver reliability, however, and should arguably be abandoned. Syndesmotic area calculation appears to offer the highest interobserver reliability of any measurement modality, and as weightbearing CT techniques improve, it is likely to become a predominant analytical tool for future use in identifying syndesmotic pathology. Future image viewer technology will hopefully readily incorporate this capability.

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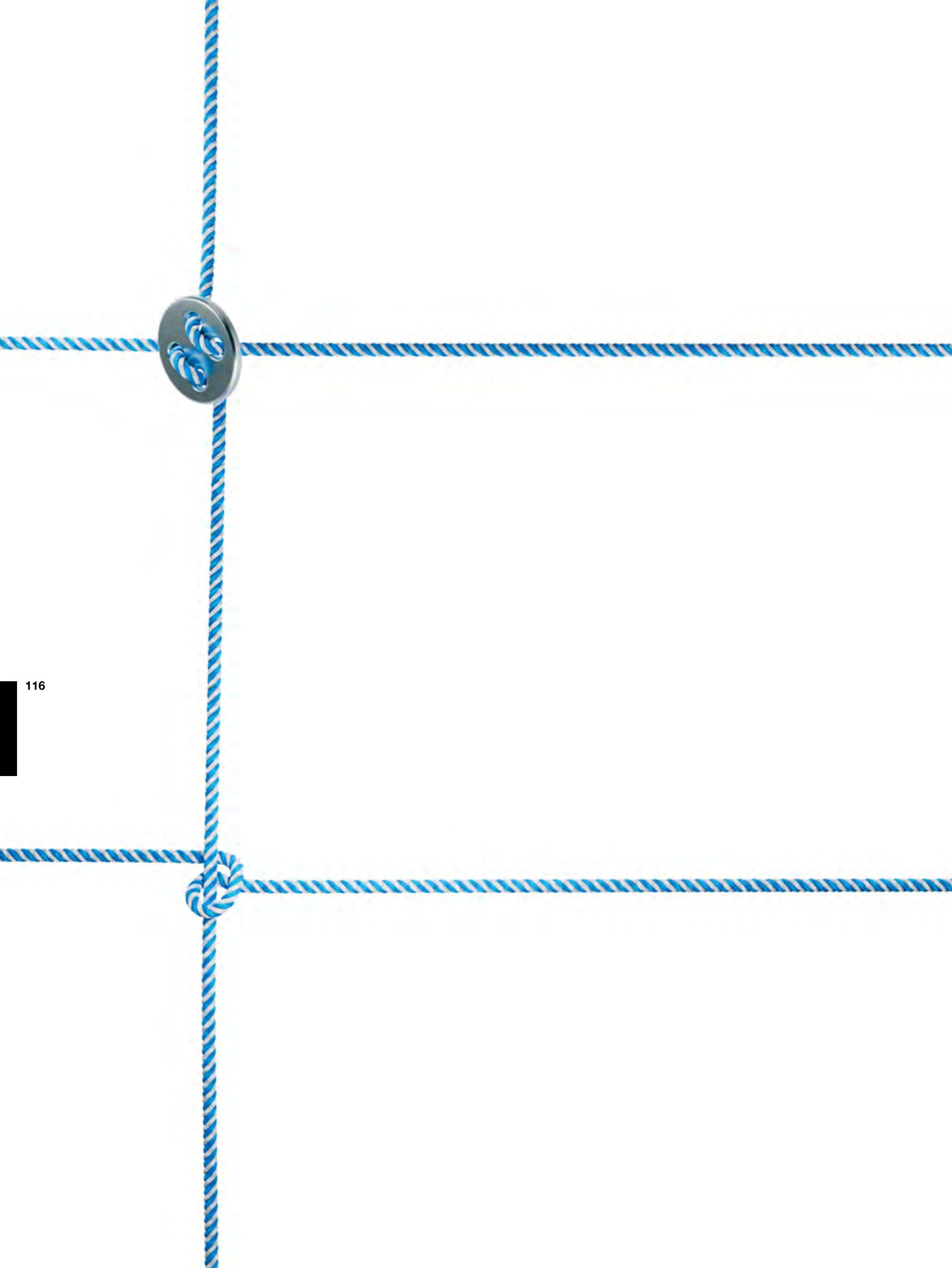


Part III
Methods To Assess Radiographic And Functional Outcome After Treatment

Chapter 8

Screw Versus Suture Button In Treatment Of Syndesmosis Instability:

Comparison Using Weightbearing CT Scan

Elghazy MA,
Hagemeijer NC,
Guss D,
El-Hawary A,
Johnson AH,
El-Mowafi H,
DiGiovanni CW

Foot Ankle Surg. 2021 Apr;27(3):285-290

Abstract

Background

The superiority of screw or suture button fixation for syndesmotic instability remains debatable. Our aim is to compare radiographic outcomes of screw and suture button fixation of syndesmotic instability using weight bearing CT scan (WBCT).

Methods

Twenty patients with fixation of unilateral syndesmotic instability were recruited and divided among two groups (screw = 10, suture button = 10). All patients had WBCT of both ankles 12 months postoperatively.

Results

In suture button group, injured side measurements were significantly different from normal side for syndesmotic area (P = 0.003), fibular rotation (P = 0.004), anterior difference (P = 0.025) and direct anterior difference (P = 0.035). In screw group, syndesmotic area was the only significantly different measurement (P = 0.006).

Conclusion

While both screw and suture button didn't completely restore the syndesmotic area as compared to the contralateral uninjured ankle, external malrotation of the fibula was uniquely associated with suture button fixation.

Introduction

While screw fixation has traditionally been used for syndes-motic instability, the rigidity inherent to screw fixation prevents normal motion of the fibula within the incisura, which may contribute to screw loosening, screw breakage, loss of reduction, and a perceived need for screw removal.

Suture button fixation was designed to restore the distal tibiofibular relationship while allowing some degree of fibular motion.[2] A systematic review article found that suture button removal secondary to soft tissue irritation was necessary in approximately 10% of surgeries, though more recent knotless devices may obviate some of this.[3] Like screw fixation, malreduction remains a potential issue with suture button techniques, though some have argued that the flexibility of these more flexible synthetic devices or, alternatively, the subsequent removal of rigid internal fixation hardware, may allow the fibula to "find its home".[4]

Which fixation technique leads to superior clinical and radiographic results remains a subject of debate, despite multiple investigations.[3] Six randomized trials comparing screw and suture button fixation techniques of the syndesmosis have been published, and five recent systematic reviews summarized these results.[5–15] However, non-validated outcome measures such as the AOFAS score were used to evaluate clinical outcomes.[16]
Furthermore, in their radiographic assessment of accuracy of syndesmotic reduction, these studies predominantly used plain radiographs for post-reduction radiographic measurements, which are considered insufficient to reliably assess the quality of syndesmotic reduction.[1] Three studies utilized non-weightbear- ing CT scans to evaluate the accuracy of syndesmotic reduction after fixation and reported similar malreduction rates for either method.[5, 9, 15] Weightbearing CT scan (WBCT) is a recent tool that has the advantage of dynamic evaluation of the syndesmosis under physiologic load while affording a comparison to the contralateral, unaffected side, which may allow more thorough evaluation of reduction quality than conventional non-weight bearing
CT scan.[17]

Therefore, the primary aim of this study was to evaluate the radiographic outcomes of surgically treated syndesmotic injuries that incorporated screw versus suture button fixation techniques using WBCT scans. Thereby, a secondary aim of this study was to evaluate clinical outcomes using validated Patient-Reported Out-comes Measurement Information System (PROMIS) question- naires. The null hypothesis was that there is no significant difference in terms of the radiographic outcomes using WBCT scan between screw and suture button fixation for syndesmosis instability.

Methods

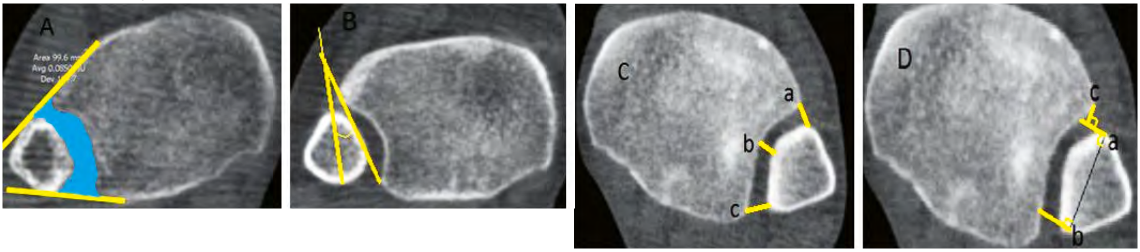
Patient Selection

After IRB approval, medical records at Massachusetts General Hospital, Boston, MA, USA from January 2008 to December 2016 were reviewed to identify patients who had undergone surgical repair of a unilateral syndesmotic injury utilizing either screw or suture button fixation. To avoid potential confounding factors, any patient with the following criteria was excluded from the study: less than 18 years of age, BMI > 40, ankle fracture extending to the tibial plafond, history of syndesmotic injury or ankle fracture in the contralateral ankle, any postoperative infection, any revision surgery other than a planned hardware removal, and any patient who was less than 12 months after the index procedure. All patients underwent weightbearing CT scan (pedCAT; Curvebeam version 3.2.1.0, Warrington, PA) of both ankles simultaneously while standing in an upright, full weightbearing position (Figure 1). Assessment of syndesmotic reduction quality as compared to the contralateral normal side was performed using axial CT images at a level 1 cm proximal to the tibial plafond (Figure 2), through eight previously published measurement techni- ques that were shown to have high reliability (Figure 3) [18–24]. All measurements were obtained for both ankles by two observers independently and were reassessed six weeks later by the same examiner. A Picture Archiving and Communication System (PACS) image viewer was utilized for measurement with 0.18 accuracy for rotation, 0.1 mm accuracy for distances and 0.1 mm^2 for syndesmotic area. In order to assess the clinical outcome, all patients completed four PROMIS questionnaires including: **1.** Pain intensity short form, **2.** Physical function, **3.** Pain interference, and **4.** Depression during their study visit. The PROMIS questionnaires were performed and stored in the institutional RedCAP program.

Figure 1. Patient receiving WBCT scan of both ankles

Figure 2. Level of axial images used for evaluation

Figure 3. Radiographic measurements



(A) syndesmotic area (B) fibular rotation (C) a: anterior difference, b: middle difference, c: posterior difference, (D) a Direct anterior difference, b direct posterior difference, c: fibular translation.

Statistical Analysis

For between group comparisons, a t-test was used for continuous normal data, a RankSum test was used for continuous skewed data, and binary data were analyzed using X2 test. Within each group, the difference in measurements between the injured and normal sides was calculated and analyzed using a one sample t-test. Sidak correction was utilized to adjust for multiple comparisons. Covariable analysis was performed using multilevel regression for each group with the syndesmotic area as the outcome. Sample size calculation based on the work of Malhotra et al.[21] showed that 20 patients (10 in each group) would have 85% power to detect 50 mm^2 difference in syndesmotic area with two sided alpha level of 0.05, based on the assumption that the standard deviation is 35 mm^2. Analysis was done using STATA 14.2 (StataCorp LP, College Station, TX).

Results

After IRB approval and search in the medical records for eligible patients, 100 eligible patients were reached out to and asked to participate in the study. Among patients who responded and agreed to participate, twenty patients were recruited in the period between January 2017 and July 2018. There were no significant differences between the two groups regarding age, follow up time, or BMI (Table 1). Injury characteristics in each group are summarized in Table 2. The mechanism of injury was described as a twisting injury in 13 patients, direct trauma to the ankle in three patients, and was not mentioned in the records of four patients. All patients were fixed in the acute stage except two cases who were subacute (6 weeks to 3 months), both of them in the suture button group, and two patients were chronic cases (> 3 months), one patient in each group. Syndesmotic instability was confirmed intraoperatively in all patients and was stabilized after fixation of any associated ankle fractures. The type and number of implants used for fixation were based on surgeon's preference, as the patients in our study were not operated by the same surgeon.

All patients were fixed by open surgery, although three of them (two in the screw group and one in the suture button group) had undergone diagnostic ankle arthroscopy prior to fixation of the syndesmosis. None of the suture buttons were removed at the last follow up, while seven patients in the screw fixation group had undergone elective screw removal before being recruited for the study. The PROMIS results are summarized in (Table 3). No significant differences between the two groups in any of the four PROMIS domains were found. Differences of radiological measurements between the injured and the normal sides were calculated for all patients and are listed in (Table 4). Also, we looked at the effect of other covariables which might be causes of confounding like the chronicity of injury before fixation, number of implants used for fixation, presence of medial malleolus fracture and removal of the screw. All these covariables didn't have any significant effect with considering the syndesmotic area as the outcome of interest (Table 5).

Table 1. Demographics of both groups

	Suture Button Group N = 10	Screw Group N = 10	p-value
FU time, mean (SD)	31 (19) months	42.6 (28) months	0.3
Age, mean (SD)	43.6 (15) years	43 (16) years	0.9
Male	4	6	0.4
Right side	4	7	0.2
BMI, median [IQR]	26.95 [25.7-28.7]	28.1 [26.5-30]	0.4
Type 2 DM	1	0	0.3
Osteopenia	2	0	0.1
Ex-smoker*	0	3	0.06

*quit at least 3 years before study participation

Table 2. Injury and surgical characteristics of both groups

	Suture Button Group n = 10	Screw Group n = 10	p-value
Injury type			0.7
Weber B	2	4	
Weber C	4	4	
Maisonneuve	2	1	
Isolated Posterior malleolus fracture	1	0	
Isolated Ligamentous syndesmosis injury	1	1	
Medial malleolus fracture	1	2	0.5
Talus osteochondral lesion	2	2	1
Number of syndesmosis implants			0.7
1	5	6	
2	5	4	
Removal of syndesmotic implant	0	7	0.001

Table 3. PROMIS scores for both groups represented as median and IQR.

PROMIS	Suture Button Group	Screw Group	P value
	N = 10	N = 10	
Pain intensity	30.7 [30.7-30.7]	33.25 [30.7-35.8]	0.3
Pain interference	38.7 [38.7-38.7]	38.7 [38.7-50.1]	0.4
Physical function	57.35 [53.1-66.1]	53.35 [51.3-57.5]	0.3
Depression	37 [34.2-46.1]	45.7 [43.8-48.7]	0.2

Table 4. The difference between injured and normal sides in both groups,
Measurements are presented in mean ± SD, P value for radiological measurements for each group difference

Radiological Measurement	Difference	p-value	Difference	p-value
	(Injured-Normal)		(Injured-Normal)	
Syndesmotic area (mm²)	27.99 ± 16.2	0.003	40.9 ± 25.98	0.006
Fibular rotation (○)	-7.77 ± 4.6	0.004	5.16 ± 7.6	0.4
Anterior Difference (mm)	1.7 ± 1.35	0.025	1.57 ± 1.9	0.2
Posterior Difference (mm)	-0.41 ± 1.6	0.99	1.15 ± 1.6	0.3
Middle Difference (mm)	0.67 ± 0.95	0.4	1.11 ± 1.11	0.1
Direct Anterior Difference (mm)	1.62 ± 1.4	0.035	1.42 ± 2.2	0.5
Direct Posterior Difference (mm)	- 0.34 ± 1.4	0.99	1.39 ± 1.6	0.2
Direct Translation (mm)	±1.5	0.99	0.85 ± 1.7	0.8

Table 5. Covariable analysis using multilevel regression for each group with Syndesmotic area as outcome.

Covariable	Group 1: Suture Button		Group 2: Screw	
	Effect (mm²)	p-value	Effect (mm²)	p-value
Chronicity (Acute or non-acute)	9.7	0.4	-26.4	0.3
Fracture of Medial Malleolus	-5.1	0.8	-10.8	0.6
Number of Syndesmotic Hardware	9.3	0.4	-11.3	0.4
Implant removal*	-	-	17.2	0.4

*Subgroup analysis using two sample t-test.

Discussion

In our study, both the screw and suture button groups still had a significantly higher post fixation syndesmotic area when comparing the injured and uninjured sides. Interestingly, only the suture button group demonstrated a significant asymmetry in fibular external rotation and anterior measurement (anterior and direct anterior differences). These differences are arguably related in the sense that a more externally rotated fibula is likely to precipitate widening of these anterior metrics. Notably, similar results were reported in the study of Sanders et al.[5] They randomized 102 patients with syndesmotic instability in the setting of ankle fractures to undergo syndesmotic fixation with either two 3.5 mm screws or a single suture button device. When evaluating the distal tibiofibular articulation and comparing the injured to the uninjured ankle, the suture button group demonstrated a significantly increased syndesmotic diastasis at the anterior and midportion of the incisura, whereas such differences were not observed in the screw fixation group.[5]

It should be pointed out that most published studies investigating post-reduction alignment of the syndesmosis have utilized either plain film examination—which has been shown to be unreliable [1] —or non-dynamic cross-sectional imaging such as nonweightbearing CT scan, which does not evaluate the ankle under physiologic load or stress.[5, 15, 22, 25] A true radiographic assessment of one's ability to recreate normal distal tibiofibular alignment after a destabilizing injury must arguably do so under physiologic, weightbearing conditions.

While both types of now commonplace syndesmotic fixation have demonstrated reasonable utility with respect to their intended purpose, relative biomechanical disadvantages of each device have been pointed out by previous studies. When screws are used for conferring syndesmotic reduction and stability, they lock distal tiboifibular motion at the incisura. While intuitively non-physiologic in the setting of an uninjured ankle, however, some surgeons feel that such "locking" may actually be beneficial in the setting of a destabilizing injury. In contradistinction, when suture buttons are chosen for fixation and stabilization of the syndesmosis, some authors have reported comparatively poor control of fibular rotation during finite element analysis assessment.[26] One cadaveric study done by LaMothe et al. reported that the suture-button allowed significantly more fibular sagittal plane motion than syndesmotic screws.[27] Mounting data suggest that we have yet to land on the ideal approach to, or hardware for, repairing the unstable syndesmosis.

Perhaps the most overlooked aspect of treating the unstable syndesmosis, however, lies not in the fixation hardware, being screw fixation or suture button repair, but rather the reduction and repair technique itself. A screw's ability to stabilize the distal tibiofibular articulation is irrelevant if the fibula is clamped in a malreduced position before placing the screw. In this sense, studies that find fewer malreductions with suture buttons as compared to screws may actually reveal the ability of the hardware to tolerate initial fibular malposition (the fibula subsequently "finds its home") rather than any sort of inherent superiority of hardware biomechanics. While in some scenarios this may be beneficial, the ability of the fibula to find its home also implies an anatomically reduced fibular fracture, an appropriate physiology to the surrounding syndesmotic ligaments, as well as a less robust ability to resist sagittal translation, which may not be desirable in severely unstable injuries. Cosgrove et al. have highlighted that clamp position, especially the medial tine, is critical towards successfully realigning the syndesmosis.[28]

To this end, some of the authors in the current study have migrated towards a lag screw technique rather than peri-articular clamping when using screw fixation for mildly displaced syndesmotic injuries to avoid clamp malreduction. With significantly displaced syndesmotic injuries, the same authors further consider attaining a CT scan not only of the injured ankle, but also a WBCT scan of the contralateral ankle to understand exactly where a clamp needs to be placed to recreate normal anatomy, which has been shown to vary across individual patients.[29] Ultimately, reducing a displaced syndesmosis with a clamp is analogous to using a bony tenaculum to reduce a displaced fracture, especially when using a screw—any initial malposition is likely to persist. Clearly, more attention must also be stressed to the endpoints achieved with respect to fibular and ligament anatomy during treatment of these injuries if optimized outcomes are to be expected following syndesmotic instability management.

In our study, there did not appear to be a clinical benefit of one fixation method over the other after an average follow up of three years as indicated by PROMIS scores, including pain intensity, pain interference, physical function and depression.

Previous studies have evaluated the clinical difference between the two fixation techniques.
In the study of Sanders et al.,[5] all patients completed questionnaires including the Foot and Ankle Disability Index (FADI) and Work Productivity Activity Impairment Questionnaire (WPAI) at a minimum of 12 months and also underwent evaluative bilateral nonweightbearing ankle CT scans at 3 months. They found no difference in clinical outcome scores, though they were admittedly underpowered to discern such differences, despite of having the largest number of patients in a published randomized trial till now. They were, however, powered to detect radiographic differences and reported a higher malreduction rate with screw fixation as compared to suture button (39 % vs. 15 %, p = 0.03).

Another study by Kortekangas et al. [15] randomized 43 patients with unstable syndesmoses to suture button fixation or fixation with a single, tricoritcal screw. At two years there was no difference in clinical outcome scores, including the Foot and Ankle Outcome Score and RAND-36. Interestingly, intraoperative CT found a higher malreduction rate in the suture button group as compared to the screw fixation group (7 vs. 1), but identified that this was dependent on foot position, with the suture button malreduction self-correcting if the ankle was held at neutral dorsiflexion. At two year follow up, CT scan revealed no significant difference in malreduction rate nor rates of osteoarthritis.

This study has a number of strengths. We used PROMIS measures as part of our study, as opposed to non-validated questionnaires such as the AOFAS score.[16, 30, 31]
PROMIS measures have greater precision (less error) than most conven- tional measures, which enhances power in a less costly way than increasing sample size. Furthermore, syndesmotic reduction was assessed using WBCT imaging, allowing not only for cross- sectional evaluation of the distal tibiofibular articulation in a way not possible with plain radiographs, but also doing so under physiologic load, contrasting with prior studies that relied on non-weight bearing CT. Notably, the WBCT included bilateral ankles, allowing use of the contralateral, uninjured ankle as an internal control. Lastly, unlike prior studies, evaluation of syndesmotic reduction included a measurement of syndesmotic area, which has been shown to be the most reliable means of assessing syndesmotic reduction.[24]

There are a number of limitations to our study. Recruited patients were those who were willing to return to the research institution years after their initial treatment, which may have introduced bias if only those patients doing well or poorly were willing to participate. Furthermore, due to the timeline at which the collection of PROMIS scores was initiated at the research institution, participating patients did not have preoperative scores to allow a comparison. In addition, the study was powered to identify anatomic differences on WBCT rather than clinical outcomes. Although PROMIS have greater precision than the conventional measures, our study might be underpowered to detect clinical difference. The results of the PROMIS measures in our study may guide further studies aiming to use PROMIS to evaluate clinical outcome after syndesmosis injuries. Lastly, the retrospective and non-randomized nature of this study did not predicate how the decision was made to use a screw versus a suture button device. It is therefore conceivable that more severe injuries were more likely to have undergone screw fixation. Also, the patients in our study didn't have the surgery done by the same surgeon. The fact that all participants with an associated fibular fracture had undergone anatomic reduction of the fibula prior to syndesmotic fixation, however, obviates some of this compromise inherent to retrospective studies.

Conclusion

While neither screw nor suture button fixation entirely restored normal syndesmotic area anatomy when compared to contralateral normal ankle measurements on WBCT, suture button fixation techniques uniquely failed to restore normal fibular rotation, with residual external rotation of the fibula noted. Long-term follow up is needed to evaluate the long-term clinical implications of such malreductions, and further investigation will be required to continue modifying our fixation techniques for syndesmotic instability in order to maximize both short and, more importantly, long term patient outcome.

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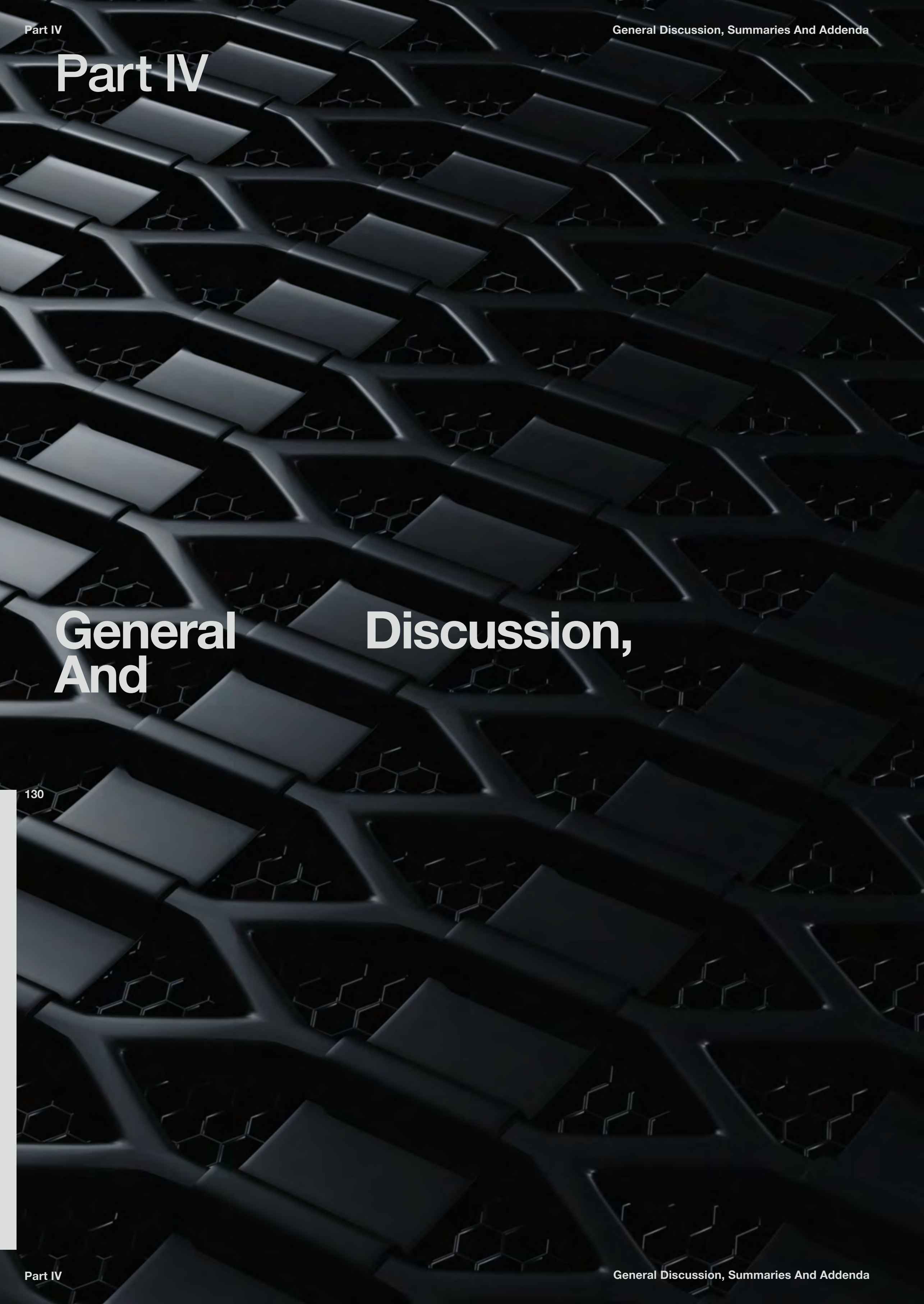

Part IV

General Discussion, And

Summaries
Addenda

Chapter 9 General Discussion And Future Perspectives

General Discussion

Persistent subtle syndesmotic instability can be disabling and causes long-term morbidity. A subtle syndesmotic instability can be difficult to appreciate with clinical maneuvers or with static imaging. The assessment of syndesmotic instability is particularly challenging because of its multidimensional aspect with lateral displacement of the fibula in the coronal plane, fibular translation in the sagittal plane, and external rotation of the fibula in the rotational plane.[7, 17, 42] Vertical translation, i.e. shortening, of the fibula may occur but to a minimal degree if there is no concomitant fibula fracture present.[7, 10, 17] The focus of this thesis was to further explore existing diagnostic tools, as well as to develop new dynamic diagnostic assessment techniques with the objective of distinguishing stable and unstable syndesmotic injuries.

Arthroscopic Assessment For Diagnosing Syndesmotic Instability

Traditionally, arthroscopy has been considered the gold standard for diagnosing syndesmotic instability as it allows both direct visualization of the distal tibiofibular joint and allows immediate treatment of syndesmotic instability, associated fractures and/or osteochondral lesions if necessary.[21, 55, 63, 64] Various arthroscopic methods have been investigated clinically and in cadaveric study settings to define syndesmotic instability. Most studies have performed an arthroscopic evaluation of the stability of the syndesmotic joint in the coronal plane, often by evaluating the distal tibiofibular joint while applying a so called 'lateral hook test'. By pulling the fibula outward the distance between the distal tibia and fibula expands. The separation between the fibula and tibia is also called the diastasis. As summarized in **Chapter 2** of this thesis, various cut off values for coronal plane syndesmotic instability are reported throughout the literature; 1mm diastasis with stress application,[20] > 2 mm without stress application,[29] > 2 mm with stress application,[13, 15, 32, 64] > 3 mm without stress application,[67] > 3 mm with stress application [1] and, > 4 mm without stress application.[31] Ankle arthroscopy can also assess distal fibular translation in the sagittal plane. Similar to coronal plane assessment, the surgeon will use a bone hook to pull the distal fibula in the anterior or posterior direction of the sagittal plane. Even though sagittal plane stability of the fibula is not often described in-vivo, there are several biomechanical studies that claim syndesmotic instability may be more evident in the sagittal plane.[11, 42-47, 61, 68, 69] A biomechanical study by Lubberts et al. incorporated all coronal and sagittal translation data into one mathematical model, the arthoscopic syndesmotic assessment (ASA) tool. The ASA tool seems to be more reliable and accurate compared to separate evaluation of data points.[42] The downside of this assessment tool is that it will take more time in the operative room and requires calibrated probes which are not available yet, constraining the clinical applicability of this tool. The assessment of rotational plane stability with arthroscopy is described in the literature but due to anatomical and technical constraints, arthroscopic assessment in the rotational plane is not a reliable assessment technique to assess syndesmotic instability.[43, 47] In a systematic review of the literature in **Chapter 2** a weighted mean of 2.9 mm coronal plane fibular translation was found to distinguish between an intact and all syndesmotic cut.[27] The 2.9 mm coronal plane fibular translation is a value which derived from cadaveric studies and represents the translation of the fibula that, on average, was significantly more than the intact translation. It therefore remains unsure whether these values correlate to a clinically relevant value. For example, if more cadavers were to be included it is likely that the instability cut off value will drop as significance will be reached more easily. However, evaluation of the threshold clinically will be challenging as it requires a randomized controlled or a multi-center observational study in which different surgeons use different thresholds.

New Diagnostic Methods For Diagnosing Syndesmosis Instability

Ultrasound assessment technique for evaluation of syndesmotic instability will be the way to go in the future to be able to distinguish stable from unstable syndesmotic joints.

Portable ultrasound is an assessment technique that can be for a bilateral dynamic stress examination; the technique has low risks and carries low cost making it a high potential technique for diagnosing syndesmotic instability. Its applicability for diagnosing syndesmotic instability has therefore been a major subject of this thesis. Prior in vivo studies have demonstrated that ultrasound is an accurate and reliable technique to evaluate the AITFL as well as the tibiofibular clear space without stress application [39, 53, 66] and with stress application.[4, 12, 51, 52, 60] No studies investigated sagittal plane syndesmotic instability and therefore in **Chapter 3**, a dynamic ultrasound examination technique was developed to evaluate syndesmotic stability in the sagittal plane in the normal population. In this newly developed examination technique the examiner handles the ultrasound probe and stresses the fibula in the sagittal plane with their thumb while capturing in real-time. Indeed, sagittal translation of the fibula could be detected reliably by different operators using ultrasound.[28] The normal sagittal translation values found, 0.89 mm in the anterior to posterior direction and 0.49 mm in the posterior to anterior direction, correlated with the intact sagittal translation values found in the literature using arthroscopy.[28, 42-44, 68] The reliability scores of this test were excellent and comparable or even better than the reliability scores seen in the literature for arthroscopy.[44] Likely because there was less variability within the data as only the intact state was evaluated and, importantly, the ultrasound software used could automatically calculate the distance from the pointer to the probe, which made the measurement making easier and faster for the measurement makers. Of note, this automated calculation of a distance is a good example of how technique advances should complement clinician performance.[26] Additionally, as already demonstrated by previous studies, similar translation values were found between left and right ankles if not injured.[12, 22, 41, 54] This means that the contralateral, uninjured, side is the preferred control to use clinically, especially since there is high variability between individuals.[22, 26, 41, 54]

In **Chapter 4** the established ultrasound assessment technique for sagittal plane syndesmotic instability was taken into the biomechanical laboratory to evaluate how it compared to the considered gold standard in diagnosing syndesmotic instability, arthroscopy. For this study a portable ultrasound device was used, as such devices can be used more easily in the outpatient clinic. The sagittal plane syndesmotic stability was evaluated in the intact state, and thereafter with progressive sectioning of the **1.** anterior-inferior tibiofibular ligament (AITFL), **2.** interosseous ligament (IOL), and **3.** posterior-inferior tibiofibular ligament (PITFL). Sagittal plane translation was performed with a bone hook with 100 N of anterior to posterior (A to P) and posterior to anterior (P to A) directed force. To simulate a clinical setting 50 N manual force was applied to the fibular tip and measured with ultrasound alone to simulate a fibular shuck test, as performed in the clinical setting. A maximum of 50 N was decided upon as it was physically hard for all the examiners to perform more force with their hands. As the 100 N hook test is an invasive stress technique the most important comparison in this study was the 100 N hook test using arthroscopy and the 50 N manual test using portable ultrasound, by virtue of its non-invasive nature. Interestingly both measuring techniques provided significant change in translation as of the IOL stage as compared to the intact showing that portable ultrasound could detect sagittal translation after sequential transection of the syndesmotic ligaments in a similar fashion as arthroscopy but then without related risk to a patient and with the ability to have a reliable control clinically.

As syndesmotic injury is commonly caused by an external rotation type injury, one may expect tibiofibular joint displacement to occur when applying an external rotation directed force to the ankle. Indeed, numerous biomechanical studies suggest that syndesmotic instability is most apparent when applying an external rotation torque.[8, 10, 17, 30, 65, 69] Presumably, because the external rotation of the foot causes the talus to open the syndesmosis, thereby directly stressing the syndesmotic ligaments. Therefore it is interesting to evaluate the change in distance between the tibia and fibula, also called the tibiofibular clear space (TFCS) or ankle diastasis, while stressing the ankle externally. Others have previously evaluated the tibiofibular clear space (TFCS) using ultrasound while applying external rotation stress and showed that ultrasound could detect TFCS opening in patients with or without AITFL injury in a clinical study.[4, 51, 66]
To further investigate whether ultrasound would indeed be an applicable technique for distinguishing stable from unstable injury this thesis investigated to what extent the TFCS opening would increase after sequent transection of the syndesmosis using dynamic portable ultrasound in a controlled laboratory setting. In **Chapter 5** the TFCS was assessed using portable ultrasound and fluoroscopy in the intact and after sequent transection of the **1.** anterior-inferior tibiofibular ligament (AITFL), **2.** interosseous ligament (IOL), and **3.** posterior-inferior tibiofibular ligament (PITFL). The external rotation directed force was applied by a bone hook placed on the first metatarsal bone; 10 cm distal to the center of rotation of the ankle. An external rotation directed force was then applied while consecutively providing 0 N (0 Nm), 45 N (4.5 Nm), 60 N (6.0 Nm), 75 N (7.5 Nm), and 90 N (9.0 Nm) external rotation torque. Several rotation torque conditions were investigated as applied external rotation torque varies largely within the literature.[8, 10, 30, 62, 69] A statistical difference was found using portable ultrasound between the intact and IOL transection stage as of 4.5 Nm, which implies that 4.5 Nm should be sufficient for detecting syndesmosis instability. It is important to know the lower limit of stress required as, clinically, the success of the test will also depend on patient tolerance. In this study the portable ultrasound results were compared to fluoroscopy, an assessment technique which is already known to be unfavorable for the assessment of syndesmosis instability.[16, 37, 57] Nevertheless, it remains part of the evaluation in the clinical setting spurring the use of other imaging modalities such as dynamic ultrasound or weightbearing CT-scan.[5, 16, 37]

Weightbearing CT scan is a relatively new diagnostic modality to evaluate the syndesmosis bilaterally under an axial physiologic load with the foot, naturally, being a plantigrade position.[48] In **Chapter 6** the syndesmosis was evaluated on bilateral weightbearing CT scans of a group of patients who were surgically treated for syndesmotic instability as well as a healthy control group. The area of the distal tibiofibular joint space showed the largest difference between normal and abnormal syndesmosis in a weightbearing condition with a mean difference of 46 mm^2 and had the best agreement score of the assessment methods measured in this study. Similar to findings in **Chapter 3** and the literature this study found no differences between uninjured left and right ankles emphasizing the importance of obtaining bilateral imaging.[41] Moreover, other studies, published by the same research group further explored the use of weightbearing CT for assessing syndesmotic instability and demonstrated that volumetric (3D) measurements even further improve the ability to detect instability in a non-invasive manner.[3, 9]
With a sensitivity of 96% and a specificity of 84% for detecting clinical syndesmotic instability when using the contralateral ankle as the internal control weightbearing CT should be considered a valuable assessment technique for syndesmotic instability. It should, however, be noted that the weightbearing aspect might not be the determining factor why weightbearing CT seems to be a better and more reliable assessment technique as compared to non-weightbearing CT. In a cadaveric study setting the addition of axial load application did not affect the syndesmosis measurements even after injury.[36]

However, seemingly, weightbearing CT scan does offer optimal scanning conditions; due to the standing position it standardizes the plantigrade foot position and it allows for bilateral scanning. Stressing the foot externally with axial loading (i.e. a standardized plantigrade foot position) does affect syndesmotic measurements and seems to be the optimal maneuver for detecting syndesmotic instability on weightbearing CT.[10] Combining the above would mean that the assessment of syndesmotic instability using CT scan should be as follows; bilateral scanning, with the foot in a plantigrade position (probably with some degree of axial loading), appliance of rotational torque, and use of 2D and 3D syndesmotic assessment techniques. Currently it is not possible yet to have all these conditions combined clinically and future research should focus on designing a tool to allow the clinician to scan the ankle under optimal conditions to detect syndesmotic instability.

Methods to assess radiographic and functional outcome after treatment

The last part of this thesis aimed to evaluate radiographic outcome after syndesmotic repair techniques, i.e. a rigid technique using one or two screws or a dynamic technique using one or more tightropes. The goal of reducing the syndesmosis surgically using either technique is to restore normal ankle mechanics. However, which of these fixation techniques leads to superior radiographic and clinical results remains subject of debate. To date, seven randomized controlled trials have compared the suture button and syndesmotic screw devices,[2, 18, 19, 35, 38, 50, 70] and in response to, five systematic reviews summarizing these trials have been published.[14, 23, 25, 56, 59] They often suggest that the dynamic fixation could be superior to static fixation in terms of clinical outcomes and complication rates. However, recently a meta-analysis evaluated the robustness of the outcomes of those systematic reviews investigating fixation techniques and found the outcomes sensitive for error as slight changes in methods could easily change outcomes, and thus, outcomes should be interpreted carefully.[49] Of note, the majority of these studies assessed non-validated patient reported outcomes measures such as the AOFAS hindfoot and ankle score and the Olerud–Molander score.[6, 33] Additionally, the radiographic outcome parameters predominantly involved plain radiographs for assessing the reduction, which is insufficient to reliably assess the syndesmotic reduction.[24]

Three of the seven randomized controlled trials incorporated uni-or bilateral CT-scans, albeit, non-weightbearing.[2, 34, 70] True radiographic assessment to recreate normal distal tibiofibular alignment after a destabilizing injury must arguably be performed under stressed conditions. As postsurgical syndesmotic reduction had not been assessed using a dynamic imaging technique before, as a first step, the reliability of previously published measurements on non-weightbearing CT-scan for the evaluation of the reduction on weightbearing CT-scan were evaluated in **Chapter 7**. As found in **Chapter 6**, the 2D syndesmotic area measurement turned out most reliable. Interestingly, in this study the so called 'side-by-side' measurement technique was also investigated, which is often used clinically. As described in the initial study protocol, only two observers performed side-by-side measurements on all patients but in the analyzing phase it was noticed that both observers had very low inter- and intra-observer scores. Therefore, it was decided to ask ten more international observers with various years of experience within orthopedic surgery to eyeball the reduction images as well. Surprisingly, the higher the experience level, the lower the reliability score emphasizing the fact that there is no universally agreed-on cutoff value to define a "successful" reduction. We may therefore have to reconsider the use of advanced operative imaging techniques including 3D fluoroscopy or intraoperative CT without a contralateral ankle as a control or when only eyeballing the imaging material.

Then as a second step, in **Chapter 8** the postsurgical reduction was evaluated after both rigid and dynamic reduction techniques. A total of 20 patients who were treated with either suture button(s) fixation (10 patients) or with screw(s) fixation (10 patients) were asked to return to the hospital at a minimum of one year after the fixation procedure to undergo bilateral weightbearing CT-scan and to fill out questionnaires. Both groups had a larger syndesmosis area as compared to the uninjured contralateral side which might explain development of moderate osteoarthritis as seen in a recently published study by Lehtola et al. with a minimum follow up of six years.[40, 58] Only in the suture button group an asymmetry in external rotation and anterior measurements was also detected which were not seen in the screw group. No differences between the fixation techniques were found in terms of patient reported outcomes. One may, however, argue with the latter result as this study was not powered to assess clinical outcomes and the lack of preoperative scores to allow a comparison. Nevertheless, more research is required using validated reported outcomes as well as dynamic radiographic outcome parameters to evaluate optimal fixation techniques for treating syndesmotic instability.

This thesis aimed to evaluate several existing techniques for diagnosing (subtle) isolated syndesmotic instability. Regardless of the technique used, it is best to use the contralateral ankle as the internal control, if possible. Even though considered the golden standard arthroscopy did not seem to have the ingredients to be the optimal assessment technique to investigate syndesmotic instability clinically.

A secondary aim was to analyze a new technique, the portable ultrasound. Portable ultrasound was found to be a reliable technique in evaluating (subtle) syndesmotic instability at the point of care while providing sagittal- or rotational torque stress. It performed similarly to the arthroscope when measuring sagittal plane syndesmotic instability and it outperformed fluoroscopy when measuring rotational plane syndesmotic instability.

Another aim of this thesis was to evaluate the clinical value of weightbearing CT scan for diagnosing syndesmotic instability. Weightbearing CT scan showed to be a reliable and useful technique for diagnosing syndesmotic instability and may also be used to assess syndesmotic reduction after surgery.

Future Perspectives

Isolated syndesmotic instability is a three-dimensional injury in which sagittal, coronal, and rotational planes are affected. When left untreated or mistreated syndesmotic instability can lead to longer recovery period with prolonged pain and slower return to sport and degeneration of the ankle joint over time. This thesis focused on finding new dynamic diagnostic assessment tools to evaluate the syndesmosis in the several planes. Future research should further evaluate the diagnostic value of the studies assessment methods, including dynamic ultrasound and (weightbearing) CT scan for detecting syndesmotic instability and malreduction following surgical intervention in prospective clinical settings. Future research projects should focus on improving these assessment methods and investigate which methods, such as ultrasound sagittal, ultrasound external rotational, weightbearing CT scan, CT scanning with the foot held in the external rotated position, or a combination of measurements, correlate with clinical outcomes. Artificial intelligence (AI) may play an important role in improving the assessment methods, such as objectified in the ASA tool and as seen in **Chapter 3** where an automated calculation of the distance between pointer and probe could already make the measurement much easier and led to the best reliability scores within this thesis.

To develop and implement these technical advances collaboration with technicians and the radiology department will be rudimental. The suggested new dynamic assessment methods are non- or less invasive techniques offering a dynamic evaluation at relatively low cost, allow for contralateral side as an internal control, and especially portable ultrasound is widely available. Values from this thesis presented in **Chapters 4, 5, and Chapter 6**, can be used as a guidance in creating new study protocols and new treatment algorithms for determining isolated syndesmotic instability. Considering increasing healthcare costs and current climate change, it is becoming critically important to emphasize that sustainable healthcare is non-delivered healthcare that should not have been delivered in the first place and vice versa. Hopefully, elaborating on this thesis will provide the opportunity to develop cost-effective, sustainable, and tailored assessment techniques for diagnosing syndesmotic instability or malreduction.

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Chapter 10 Summary

Summary

Chapter 1 provides a general introduction of syndesmotic injuries. If not treated or missed, syndesmotic instability may lead to osteoarthritic changes over time and impact patient quality of life and function. Therefore, syndesmotic instability should be treated surgically with either a static or dynamic treatment strategy. This thesis aims to improve existing diagnostic assessment techniques of the syndesmosis and to develop new ones in three parts, including **I.** arthroscopic assessment for diagnosing syndesmotic instability, **II.** new methods for diagnosing syndesmotic instability using portable ultrasound and weightbearing computed tomography (CT), **III.** methods to assess radiographic and patient functional outcomes after treatment.

Part I - Arthroscopic Assessment For Diagnosing Syndesmotic Instability

Arthroscopy is widely used for diagnosis of syndesmotic instability, especially in subtle instability cases. **Chapter 2** systematically reviews the literature to evaluate which instability values should be used. A total of eleven studies were included for review of which eight cadaveric and three clinical studies. The weighted mean associated with syndesmotic instability in the coronal plane is 2.9 mm. These data suggest that during arthroscopic surgery surgeons should use a 3.0 mm probe instead of 2 mm probes to distinguish stable from unstable syndesmotic injuries.

Part II - New Methods For Diagnosing Syndesmotic Instability Using Portable Ultrasound And Weightbearing Computed Tomography

Chapter 3 describes a prospective clinical study of healthy subjects that aimed to assess the motion of the tibiofibular joint using portable ultrasound in the sagittal plane. This study resulted in a novel assessment technique. Both ankles of 28 participants were scanned and evaluated independently by two examiners. The study shows that ultrasound was able to detect fibular translation and that the translation values are similar to the normal values found with arthroscopy in cadaveric studies. Bilateral comparison showed no difference emphasizing the importance of having the ability to use the uninjured contralateral side as internal control. Even though ultrasound is known to be operator dependent the two examiners found similar translation values of the syndesmosis and were able to reliably read the measurements with substantial agreement.

To investigate whether this newly developed assessment technique is able to measure syndesmotic instability, portable ultrasound measurements were compared to measures taken with ankle arthroscopy in a cadaveric study presented in **Chapter 4**. Sagittal translation was assessed with both assessment techniques in the intact and after progressive sectioning of the syndesmosis; **1.** Intact, **2.** anterior inferior tibiofibular ligament (AITFL), **3.** Interosseous ligament (IOL), **4.** posterior inferior tibiofibular ligament (PITFL)). Sagittal translation forces were mimicked by placement of a bone hook around the fibula which was pulled with 100 N from anterior to posterior and vice versa. Separately, a 50 N manual force was applied to the fibular tip and measured with portable ultrasound alone to simulate a fibular "shuck test" as performed in the clinical setting. This study shows that portable ultrasound can detect sagittal translation after sequential transection of the syndesmotic ligaments in a similar fashion as arthroscopy but then without related surgical risk to a patient. Compared to the intact stage, a statistical difference was seen in both the arthroscopic and ultrasound measurements after the IOL cut with a total fibular translation of 2.3 mm seen with arthroscopy and 2.0 mm with portable ultrasound. Whether these numbers correlate with clinical instability should be further explored in a clinical setting.

Syndesmotic injury is commonly caused by an external rotation type injury and, therefore, in **Chapter 5** portable ultrasonography and fluoroscopy are used to evaluate the tibiofibular joint after applying an external rotation torque to the ankle in a cadaveric study model with progressive stages of syndesmotic ligamentous transection; **1.** Intact, **2.** AITFL, **3.** IOL, **4.** PITFL. The external rotation force was applied using a bone hook placed on the first metatarsal bone; 10 cm distal to the center of the ankle while consecutively providing stress from 0 Nm, 4.5 Nm, 6.0 Nm, 7.5 Nm, and 9.0 Nm external rotation torque. Two examiners performed all portable ultrasound and fluoroscopy measurements in three randomly selected cadavers. This study showed that portable ultrasound can detect a change in tibiofibular clear space reliably with substantial interobserver agreement. With 4.5 Nm external rotation stress, a significant difference in tibiofibular clear space opening (2.6mm) could be detected after the IOL was transacted. Thus applying 4.5 Nm external rotation torque should suffice under clinical circumstances. When assessed with Fluoroscopy no differences in any of the syndesmotic ligamentous transection stages were detected.

In **Chapter 6** the distal tibiofibular articulation is evaluated in twelve patients who were surgically treated for unilateral syndesmotic instability and had received a preoperative bilateral weightbearing CT scan. Additionally, a control group of 24 patients with bilateral CT scans were included as a comparison. All measurements were performed by two observers. The results show that weightbearing CT scan can differentiate stable from unstable syndesmotic injuries with differences detected in four axial plane measurements including the syndesmotic area, anterior difference, middle difference, and posterior difference. Notably, the syndesmotic area shows the largest difference with 46 mm^2 and has the highest interobserver agreement score of 0.97. Further clinical research studies should focus on volumetric measurements of the tibiofibular joint, and, if more data becomes available, a sensitivity analysis should be performed to determine preliminary syndesmotic instability cut off values.

Part III - Methods To Assess Radiographic And Functional Outcome After Treatment

Accurate reduction of the syndesmosis is rudimental for the restoration of normal ankle mechanics and prevention of secondary degenerative changes of the ankle joint. Previously, postsurgical assessment of reduction was preferably performed on CT scan. This thesis explores the role of the weightbearing CT scan for the assessment of syndesmotic reduction.

First, in **Chapter 7**, the intra- and interobserver reliability of published assessment techniques for evaluation of the tibiofibular joint on CT scan are evaluated on weightbearing CT scan. This study shows that the syndesmotic area has the highest intra- and interobserver reliability scores. Other measurements of the tibiofibular joint including, anterior difference, posterior difference, middle difference, direct anterior difference, direct posterior difference, direct translation, and fibular rotation showed moderate to substantial reliability scores. The so called 'side by side' measurement was performed by twelve observers with various levels of experience. All observers were asked if they could eyeball the image and decide if they found the syndesmosis properly reduced or not. This subjective binary assessment method had the lowest reliability with an interobserver score of 0.25 and should not be used on CT scans – including scans taken under weightbearing.

Chapter 8 describes a clinical study including subjects that received surgical reduction of an unstable syndesmosis. Ten subjects were treated with flexible fixation technique, while the other ten subjects received rigid fixation of the syndesmosis. Syndesmotic instability was evaluated using weightbearing CT scan after a minimum of twelve months postoperatively. In this study patient reported outcomes were also collected. After a flexible fixation technique, the syndesmotic area, fibular rotation, anterior difference, and direct anterior difference were different as compared with the contralateral intact measurements after an average follow up of 31 months. In the rigid fixation group, only syndesmotic area was significantly increased as compared to the contralateral intact side. Which means that only in the flexible fixation group an external rotation of the fibula was detected. No differences were seen in any of the four patient-Reported Outcome Measurement Information System (PROMIS) domains **1.** Pain intensity short form, **2.** Physical function, **3.** Pain interference, and **4.** Depression after an average follow up time of three years. A result which should be handled carefully as this study was not powered to evaluate patient reported outcomes and no preoperative scores were available disallowing a comparison to baseline.

Chapter 11 Nederlandse Samenvatting

Nederlandse Samenvatting

In **Hoofdstuk 1** wordt een algemene introductie gegeven over de enkelsyndesmose. De enkelsyndesmose bevindt zich boven in de enkel en bestaat uit drie ligamenten die de tibia en de fibula met elkaar verbinden, ook wel het tibiofibulaire gewricht genoemd. Deze ligamenten zijn belangrijk voor het stabiliseren van je enkelvork als je bijvoorbeeld wandelt of sport. De syndesmose bestaat uit; het anterieure inferieure tibiofibulaire ligament (AITFL), het interossale tibiofibulaire ligament (IOL) en het posterieure inferieure tibiofibulaire ligament (PITFL).

Enkeldistorsie is een van de meest voorkomende blessures en betreft vooral de sportende jonge populatie. In de algemene populatie is syndesmose letsel aanwezig in 5%-10% van de enkeldistorsies. Echter in de sport populatie is syndesmose letsel in ongeveer 18% aanwezig en dit stijgt tot wel 63% bij hoog risico sporten. Voorbeelden van hoog risico sporten zijn contactsporten (Rugby, American Football, worstelen) en sporten waar de enkel gefixeerd is in een hoge schoen (ijshockey of skiën). Syndesmose letsel kan geïsoleerd (ligamentair) voorkomen of niet-geïsoleerd indien er tevens sprake is van een fractuur.

Letsel aan de syndesmose wordt meestal veroorzaakt door exorotatie van de voet en enkel met de voet in pronatie en de enkel in dorsiflexie. Indien onbehandeld of gemist, kan instabiel letsel van de syndesmose leiden tot te veel beweging en een andere drukverdeling in je enkelgewricht. Deze disbalans kan dan leiden tot artrose van je enkelgewricht en kan derhalve een negatieve invloed hebben op de kwaliteit van leven door toenemende pijn en verminderende mobiliteit. Om deze disbalans te voorkomen moet instabiel letsel van de syndesmose chirurgisch worden gestabiliseerd met een statische of dynamische behandelstrategie. Aan de andere kant is het ook belangrijk om stabiel letsel adequaat te herkennen. Dit om patiënten niet aan onnodige operatierisico's bloot te stellen, maar ook omdat we zorg moeten dragen voor onze steeds maar stijgende zorgkosten en rekening moeten houden met de milieu impact van onze behandelingen.

De meest gebruikte gradering om geïsoleerd letsel van de syndesmose te bepalen is als volgt. Een Graad I letsel betreft partieel of een volledige ruptuur van de AITFL, Graad II letsel betreft een volledig geruptureerde AITFL en partieel letsel van de IOL. Graad III letsel betreft een volledige ruptuur van alle drie de ligamenten van de syndesmose; AITFL, IOL en de PITFL. In deze classificatie is Graad I letsel altijd stabiel, Graad II letsel kan zowel stabiel of instabiel letsel betreffen, en Graad III letsel is altijd een instabiel letsel. Een instabiel Graad II letsel wordt ook wel subtiel instabiel syndesmose letsel genoemd.
Patiënten met geïsoleerd syndesmose letsel presenteren zich meestal met een exorotatie trauma en pijn van de enkel welke verergerd bij dorsiflexie, een exorotatie beweging, of wanneer er druk op de syndesmose wordt uitgeoefend. Patiënten hebben vaak ook aan de binnenzijde en buitenzijde van de enkel pijnklachten. Wanneer er klinisch een verdenking is op syndesmose letsel zal vervolgonderzoek moeten worden ingezet. Beginnende met röntgenfoto's om eventueel geassocieerde fracturen uit te sluiten. Een MRI scan kan gedetailleerd laten zien of en hoe veel schade er is aan de ligamenten van de syndesmose. In het geval van een subtiel letsel kan subtiele instabiliteit hier echter niet mee aangetoond of uitgesloten worden.

Om stabiliteit te beoordelen kan het beste het enkelgewricht in beweging geëvalueerd worden. Bijvoorbeeld doormiddel van een kijkoperatie (artroscopie). De chirurg beweegt de fibula dan met een haakje naar buiten toe (lateral hook test) of naar voren/achteren (sagittal hook test) en kijkt dan met een camera naar de beweging die de fibula aflegt t.o.v. de tibia. De mate van beweging die gezien wordt bepaald dan of er sprake is van instabiliteit en indien daar sprake van is kan deze direct chirurgisch behandeld worden.
Ondanks veel onderzoek is er nog steeds geen consensus in de literatuur over hoe veel beweging in het tibiofibulaire gewricht afwijkend is. Daarbij is de artroscopie een invasief diagnosticum waar in geval van twijfel niet altijd naar gegrepen kan worden. Derhalve zou een niet invasief dynamisch diagnosticum een toegankelijkere optie zijn.

Potentiele technieken zijn bijvoorbeeld de echografie en de CT-scan. Echografie kan gebruikt worden voor de beoordeling van de AITFL maar zou ook gebruikt kunnen worden om real-time de beweging van de fibula t.o.v. de tibia in beeld te brengen tijdens manuele manipulatie van het enkelgewricht door de zorgverlener (zoals een exorotatie beweging of sagittale translatie van de fibula) zonder bijkomende risico's voor de patient. Ook met een CT scan kan een 'actie-moment' gecreëerd worden. De weightbearing CT scan is hier een voorbeeld van. Dit is een relatief nieuw type CT scan waarin de patiënt staat, waardoor er tijdens de scan zwaartekracht wordt uitgeoefend op het enkelgewricht. In theorie zou zo'n 'actie-moment' ook gecreëerd kunnen worden met de patiënt liggend in de scan met een mal die de voet en enkel in een exorotatie en dorsiflexie stand fixeert. Behoudens dat deze meettechnieken minder invasief zijn hebben ze nog een belangrijk voordeel; je kunt direct de contralaterale enkel afbeelden en gebruiken als vergelijking met de aangedane enkel.

Dit proefschrift heeft als doel om dynamische diagnostische technieken voor het beoordelen van syndesmose stabiliteit te verbeteren en nieuwe dynamische diagnostische meettechnieken te ontwikkelen in drie delen:

I. Artroscopische beoordeling voor het diagnosticeren
van instabiel letsel van de syndesmose.

II. Nieuwe dynamische methoden voor het diagnosticeren
van instabiel letsel van de syndesmose met echografie en weightbearing CT scan.

III. Toepassen van dynamische methoden om radiologische en functionele uitkomsten van de patiënt na het stabiliseren van de enkelvork te beoordelen.

Deel I – Artroscopische beoordeling voor het diagnosticeren van instabiel syndesmose letsel.

Een artroscopie van de enkel kan worden gebruikt voor de diagnose van instabiel letsel van de syndesmose, vooral bij subtiele instabiliteit. **Hoofdstuk 2** biedt een systematisch literatuuroverzicht om te bepalen welke afkapwaarden voor syndesmose instabiliteit worden gehanteerd in de literatuur. In totaal zijn elf studies geïncludeerd, waarvan acht kadaver en drie klinische studies. Het gewogen gemiddelde dat geassocieerd wordt met een instabiliteit van de syndesmose in het coronale vlak is 2,9 mm. Deze gegevens suggereren dat chirurgen tijdens een artroscopische ingreep een meetinstrument van 3,0 mm zouden moeten gebruiken in plaats van 2 mm, om onderscheid te kunnen maken tussen stabiel en instabiel syndesmose letsels.

Deel II – Nieuwe Methoden Voor Het Diagnosticeren Van Syndesmose Instabiliteit Met Behulp Van Echografie En Weightbearing CT Scan

Hoofdstuk 3 beschrijft een prospectieve klinische studie met proefpersonen zonder letsel aan de enkel of voet, waarin middels echografie de beweging van het tibiofibulaire gewricht in het sagittale vlak in kaart werd gebracht. Deze studie resulteerde in een nieuwe beoordelingsmethode voor syndesmose instabiliteit. Van 28 deelnemers werden beide enkels door twee onderzoekers gescand. Alle beelden werden hierna onafhankelijk beoordeeld door twee onderzoekers. De resultaten tonen aan dat echografie in staat is fibulaire translatie in het sagittale vlak te detecteren en dat de gemeten translatiewaarden overeenkomen met de normale waarden die in kadaver studies via artroscopie zijn vastgesteld. Bilaterale vergelijking toonde geen verschil, wat het belang onderstreept van het kunnen gebruiken van de niet-aangedane contralaterale zijde als interne controle. Hoewel bekend is dat echografie operator-afhankelijk is, vonden beide beoordelaars vergelijkbare translatiewaarden van de syndesmose en konden zij de metingen betrouwbaar interpreteren.

Om te onderzoeken of deze nieuw ontwikkelde beoordelingstechniek in staat is om syndesmose instabiliteit te detecteren, werd in **Hoofdstuk 4** in een kadaver model de echografie vergeleken met de artroscopie. In het sagittale vlak werd translatie van de fibula beoordeeld met beide technieken, in de intacte toestand en na stapsgewijze doorsnijding van de syndesmose: **1.** Intact, **2.** AITFL, **3.** IOL, en **4.** PITFL. De sagittale translatiekrachten werden gesimuleerd door een metalen haak op de fibula te plaatsen, die vervolgens met 100 N werd getrokken van anterieur naar posterieur en omgekeerd. Daarnaast werd een manuele kracht van 50 N uitgeoefend door met de duim op de fibulapunt te drukken. Deze test werd uitsluitend met echografie gemeten ter simulatie van een klinisch uitgevoerde "fibular shuck test". Deze studie toont aan dat echografie sagittale translatie van de fibula kan detecteren na sequentiële doorsnijding van de verschillende syndesmose ligamenten op vergelijkbare wijze als artroscopie maar zonder het bijbehorende chirurgische risico voor de patiënt. Na doorsnijding van het IOL werd in zowel de artroscopische als de echografische metingen een statistisch significant verschil waargenomen ten opzichte van de intacte situatie, met een totale fibulaire translatie van respectievelijk 2,3 mm en 2,0 mm. Of deze waarden correleren met klinische instabiliteit dient verder onderzocht te worden in een klinische setting.

Zoals beschreven in **Hoofdstuk 1** wordt syndesmose letsel meestal veroorzaakt door een exorotatie-trauma. In **Hoofdstuk 5** worden daarom echografie en fluoroscopie ingezet om het tibiofibulaire gewricht te beoordelen na het toepassen van een exorotatie kracht op de syndesmose in een kadaver model. De tibiofibulaire ruimte werd gemeten na doorsnijding van de ligamenten: **1.** Intact, **2.** AITFL, **3.** IOL, **4.** PITFL. De exorotatie kracht werd toegepast met een beugel rond het eerste metatarsale bot, 10 cm distaal van het centrum van de enkel. De stress werd stapsgewijs verhoogd: 0 Nm, 4,5 Nm, 6,0 Nm, 7,5 Nm en 9,0 Nm. Tevens verrichten twee beoordelaars onafhankelijk van elkaar alle metingen met zowel echografie als fluoroscopie bij drie willekeurig geselecteerde kadavers. De resultaten toonden aan dat echografie in staat is om veranderingen in de tibiofibulaire ruimte betrouwbaar te detecteren, met goede interobserver-overeenstemming. Na doorsnijding van het IOL kon bij 4,5 Nm exorotatie kracht een significante toename van de tibiofibulaire ruimte (2,6 mm) worden vastgesteld met de echografie. Dit suggereert dat 4,5 Nm exorotatie in klinische omstandigheden toereikend is. Met fluoroscopie werden in geen enkele fase van ligamentaire doorsnijding een significante verschil waargenomen.

In **Hoofdstuk 6** onderzochten we in een retrospectieve studie de toepasbaarheid van de weightbearing CT scan voor het beoordelen van instabiliteit van de syndesmose. Hiervoor werden de preoperatieve bilaterale weightbearing CT beelden van de distale tibiofibulaire gewrichten van twaalf patiënten met peroperatief vastgestelde instabiliteit van de syndesmose geanalyseerd. Daarnaast werd een controlegroep zonder letsel aan de syndesmose of enkel van 24 patiënten met bilaterale weightbearing CT scan geïncludeerd. Metingen werden verricht door twee onafhankelijke beoordelaars. Metingen bestonden uit bestaande meetmethodes gebruikt voor de CT scan. De resultaten tonen dat men met behulp van weightbearning CT scan onderscheid kan maken tussen stabiel en instabiel letsel van de syndesmose met significante verschillen in vier axiale vlakmetingen: het syndesmotisch oppervlak, het anterieure, middelste en posterieure verschil. Het syndesmotisch oppervlak vertoonde de grootste afwijking (46 mm^2) en had de hoogste interobserver-overeenkomst.

Deel III – Methoden Voor Het Beoordelen Van Radiologische En Functionele Uitkomsten Na Behandeling

Een accurate chirurgische repositie van de syndesmose is essentieel voor het herstel van normale enkelmechanica en ter preventie van secundaire degeneratieve veranderingen. De beoordeling van de repositie postoperatief wordt bij voorkeur verricht met een CT scan. In dit proefschrift wordt de rol van de weightbearing CT scan onderzocht voor de evaluatie van de repositie van de syndesmose.

In **Hoofdstuk 7** wordt de intra- en interobserver-betrouwbaarheid geëvalueerd van reeds bestaande meetmethoden op CT-beelden, toegepast op weightbearing CT. De resultaten tonen aan dat het syndesmotisch oppervlak de hoogste intra- en interobserver-betrouwbaarheid heeft. Andere metingen zoals het anterieure, posterieure en middelste verschil, directe anterieure en posterieure verschillen, directe translatie en fibulaire rotatie, vertoonden matige tot substantiële betrouwbaarheid. De zogenaamde "side-by-side"-methode werd door twaalf beoordelaars met uiteenlopende ervaring toegepast. Deze subjectieve binaire beoordelingsmethode had de laagste interobserver-betrouwbaarheid (ICC 0,25) en wordt daarom niet aanbevolen voor gebruik op CT, als ook niet voor gebruik op de weightbearing CT scan.

Hoofdstuk 8 beschrijft een prospectieve klinische studie onder patiënten die een chirurgische repositie van een instabiele syndesmose hadden ondergaan. Patiënten die minimaal een jaar geleden waren behandeld met een flexibele fixatietechniek of een rigide fixatie techniek werden uitgenodigd om deel te nemen aan deze studie. Stabiliteit van de syndesmose werd geëvalueerd met weightbearing CT scan. Daarnaast werden tevens patiënt gerapporteerde uitkomsten verzameld. In de groep met flexibele fixatie waren het syndesmotisch oppervlak, fibulaire rotatie, het anterieure verschil en directe anterieure verschil afwijkend ten opzichte van de contralaterale, intacte zijde, bij een gemiddelde follow-up van 31 maanden. In de rigide fixatiegroep werd alleen het syndesmotisch oppervlak significant vergroot waargenomen. Dit betekent dat een exorotatie stand van de fibula werd vastgesteld tijdens belasting van de enkel in de flexibele fixatie groep. Er werden geen significante verschillen gevonden in de vier domeinen van het Patient-Reported Outcome Measurement Information System (PROMIS): **1.** Pijnintensiteit, **2.** Fysieke functie, **3.** Pijninterferentie, en **4.** Depressie. Deze uitkomst dient echter met voorzichtigheid geïnterpreteerd te worden, aangezien de studie niet was ontworpen om patiëntgerapporteerde uitkomsten te evalueren en preoperatieve scores ontbraken, waardoor vergelijking met de beginsituatie niet mogelijk was.

Chapter 12 Appendices

Ph.D. Portfolio

Name PhD student	*Noortje Hagemeijer*
PhD period	01-03-2017 to 05-12-2025
Promoter	Prof dr. G.M.M.J. Kerkhoffs & Prof. C.W. DiGiovanni
Co-promoter	Dr. B. Lubberts

1 *PhD Training*

		Year	ECTS
General Courses			
•	*Musculoskeletal Ulstrasound at the Point-of-Care: Diagnostic and Procudural Applications* - Massachusetts General Hospital, Harvard Medical School	2017	0.7
•	*Why Can't They Just Stop? Understanding Substance Use Treatment Strategies* - Norman Knight Nursing Center for Clinical and Professional, Massachusetts General Hospital	2017	0.2
•	Applied Biostatistics, Harvard Catalyst	2018 / 2019	4.0
•	Leadership strategies for the Researcher (Harvard Catalyst)	2018	0.5
Specific Courses			
•	*IATA shipping Dangerous Goods Training* (Class 6.2 Infectious Substances, Class 9 Miscellaneous Goods)	2017	0.2
•	*ATLS provider course*	2019	1.3
•	*AO Trauma Blended Course* - Basic Principles of Fracture Management	2021	3.0
•	Stralingsbescherming voor medisch specialisten die gebruik maken van röntgenapparatuur	2023	1.3
•	*OTC I: Gesloten fractuurbehandeling* – The Beginning	2023	0.8

Seminars, Workshops And Master Classes	*Year*	*ECTS*
• Monthly Grands Rounds	2017 - 2019	1.0
• Weekly research meetings	2017 - 2019	4.0
• Journal club	2017 - 2019	0.2
• Unleash Global innovation lab to help reach the Sustainable Development Goals (SDGs), Shenzen	2019	1.5

Presentations

- *Intermetatarsal Ligament Release As Primary Operative Management for Morton's Neuroma: The Carpal Tunnel of the Foot? JSSF/AIG meeting November 2018, Japan*
- *Tibial Stress Fracture After Ankle Arthrodesis. JSSF/AIG meeting November 2018, Japan*
- *Opioid Prescription Patterns After Foot and Ankle Procedures: Results of a Post-op Pain Management Survey. JSSF/AIG meeting November 2018, Japan*
- *Does use of a peripheral nerve block influence the postoperative pain management protocol? JSSF/AIG meeting November 2018, Japan*
- Opioid consumption rate after foot and ankle surgery. AOFAS Specialty day 2019
- Normal variation and instability values of the tibiofibular joint on Weightbearing CT. AAOS – 2019 & EOA 2019
- Portable dynamic ultrasonography versus fluoroscopy for the evaluation of syndesmotic instability– a cadaveric study. AOFAS Annual Meeting 2020
- In vivo assessment training; ultrasound of the ankle, knee, and wrist. Workshop at ORS 2021 annual meeting

		Year	ECTS
General Courses			
•	*18th ESSKA Congress*, Glasgow	2018	0.5
•	*AOFAS annual meeting*, Boston	2018	0.5
•	Combined meeting of *the 43rd Annual meeting of Japanese Society for Surgery of Foot* (JSSF) & *the 5th Ankle Instability Group Annual Meeting* (AIG)	2018	0.5
•	*AAOS Annual meeting*, Las Vegas	2019	0.5
•	*AOFAS meeting*, Chicago	2022	0.5
•	*20th ESSKA Congress*, Paris	2022	0.5
•	*ISAKOS CONGRESS*, Boston	2023	0.5
•	*NOV jaarcongres*	2023	0.1
•	*NOV jaarcongres*	2025	0.1
Other			
•	Traumaplatform - Challenge 2016: *Ride for Research*	2016	0.5
•	*Arthrex Nanoscope cadaver workshop*	2019	0.1

2 Teaching

		Year	ECTS
Lecturing			
•	Statistics class 1: *univariate analysis*	2018	
•	Statistics class 2: *multivariate analysis*	2018	
•	Basic STATA class 1: *Build up & analysis*	2018	
•	Basic STATA class 2: *Analyzing dataset and creating tables*	2018	2.0
Tutoring, Mentoring			
• *Jan de Bruin BSc* (Netherlands)	• *Mohamed A. Elghazy, MD* (Egypt)	2017 - 2019	
• *Quinten Rikken BSc* (Netherlands)	• *Song Ho Chang, MD PhD* (Japan)		
• *Kathryn Whitelaw BSc* (USA)	• *Jirawat Saengsin, MD* (Thailand)		
• *Thomas Mobley undergraduate* (USA)	• *Go Sato, MD* (Japan)		
• *Mary Coogan BSc* (USA)	• *Rohan Bhimani, MD* (India)		
• *Shivesh Shah BSc* (USA)	• *Gabrielle Donahue, BSc* (USA)		
• *Jack Casey undergraduate* (USA)	• *Matteo Buda, MD* (Italy)		
• *Ariella Goldberg undergraduate* (USA)	• *Liu Ying, MD* (China)		
• *Jafet Massri-Pugin, MD* (Chile)	• *Li Yu, MD* (China)		
• *Escar Kusema, MSc* (USA)	• *Peter Kvarda, MD* (Switserland)		22
Supervising			
•	Interim director of the Foot & Ankle Research and Innovation Lab, Massachusetts General Hospital, Harvard medical school.	2017 - 2019	15

3 *Parameters of Esteem*

		Year
Grants		
•	AOFAS Research Grant – 15.000 dollar. Project: *Ultrasonography for Diagnosing Medial Sided Ankle Instability: A Cadaveric Study*	2019
•	*Butterfly iQ.* – Non-financial research support	2019
•	Arthrex – Non-financial research support	2019
Awards and Prizes		
•	*Amsterdam University Fund* – 400 euro	2016
•	*Amsterdam University Fund* – 700 euro	2018
•	*EOA 2019* EOA Sam A. Labib, MD Donor Award	2019
Other		
•	*Opened new research and innovation centre:* FARIL MGH, Harvard	2018

List Of Peer Reviewed Publications

Publications In Thesis

- **Hagemeijer NC**, Elghazy MA, Waryasz G, Guss D, DiGiovanni CW, Kerkhoffs GMMJ. Arthroscopic coronal plane syndesmotic instability has been over-diagnosed. Knee Surg Sports Traumatol Arthrosc. 2021 Jan;29(1):310-323
- **Hagemeijer NC**, Saengsin J, Chang SH, Waryasz GR, Kerkhoffs GMMJ, Guss D, DiGiovanni CW. Diagnosing syndesmotic instability with dynamic ultrasound - establishing the natural variations in normal motion. Injury. 2020 Nov;51(11):2703-2709
- **Hagemeijer NC**, Lubberts B, Saengsin J, Bhimani R, Sato G, Waryasz GR, Kerkhoffs GMMJ, DiGiovanni CW, Guss D. Portable dynamic ultrasonography is a useful tool for the evaluation of suspected syndesmotic instability: a cadaveric study. Knee Surg Sports Traumatol Arthrosc. 2023 May;31(5):1986-1993
- **Hagemeijer NC**, Sato G, Bhimani R, Lubberts B, Elghazy MA, Sierevelt IN, Waryasz G, Kerkhoffs GMMJ, DiGiovanni CW, Guss D. Portable ultrasound equals arthroscopy for assessment of syndesmotic instability submitted to ISAKOS
- **Hagemeijer NC**, Chang SH, Abdelaziz ME, Casey JC, Waryasz GR, Guss D, DiGiovanni CW. Range of Normal and Abnormal Syndesmotic Measurements Using Weightbearing CT. Foot Ankle Int. 2019 Dec;40(12):1430-1437
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- **Hagemeijer NC**, Claessen FM, de Haan R, Riedijk R, Eygendaal DE, van den Bekerom MP. Graft Site Morbidity in Elbow Ligament Reconstruction Procedures: A Systematic Review. The American journal of sports medicine 2017:363546517693836.
- **Hagemeijer NC**, van den Bekerom MP, Kerkhoffs GMMJ. A new predicting model for syndesmotic injuries? Injury. 2018 Jan 31. pii: S0020-1383(18)30021-4.
- B Buda M, Kink S, Stavenuiter R, **Hagemeijer NC**, Chien B, Hosseini A, Johnson AH, Guss D, DiGiovanni CW Reoperation Rate Differences Between Open Reduction Internal Fixation and Primary Arthrodesis of Lisfranc Injuries. Foot Ankle Int. 2018;:1071100718774005.
- Donahue GS, **Hagemeijer NC**, Johnson AH. How Will the Foot and Ankle Orthopedic Community Respond to the Growing Opioid Epidemic? Foot & Ankle Orthopaedics. 2018;3(3):2473011418764463.
- Buda M, **Hagemeijer NC**, Kink S, Johnson AH, Guss D, Digiovanni CW. Effect of Fixation Type and Bone Graft on Tarsometatarsal Fusion. Foot Ankle Int. 2018;:1071100718793567
- Coogan MK, Mobley T, **Hagemeijer NC**, Abbott B, Guss D, et al. (2018) Herpes Zoster: An Atypical Cause of Foot Drop - Case Report and Review of the Literature. Int J Foot Ankle 2:020
- Kvarda P, **Hagemeijer NC**, Waryasz G, Guss D, Digiovanni CW, Johnson AH. Opioid Consumption Rate Following Foot and Ankle Surgery. Foot Ankle Int. 2019;:1071100719848354.
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- **Noortje C. Hagemeijer**, Thomas P. A. Baltes, Alex B. Walinga, Daniel Guss, Gino M. M. J. Kerkhoffs. Diagnosis of Syndesmotic Instability: Clinical Evaluation, Radiographs, Ultrasound, (Weightbearing) CT Scan, MRI, and Arthroscopy. Tech Foot Ankle Surg. 2025. E-pub ahead of print

Gino M.M.J. Kerkhoffs
The Netherlands

Christopher W. DiGiovanni
United states of America

Daniel Guss
United states of America

Mohamed A. Elghazy
Egypt

Gregory Waryasz
United States of America

Jirawat Saengsin
Thailand

Song Ho Chang
Japan

Go Sato
Japan

Rohan Bhimani
India

Anne E. Johnson
United States of America

Bart Lubberts
The Netherlands

Inger N. Sierevelt
The Netherlands

Jack C. Casey
United States of America

Ahmed El-Hawary
Egypt

Hani El-Mowafi
Egypt

Chapter 13

Allereerst wil ik graag iedereen bedanken die betrokken is geweest bij mijn promotietraject.

Prof. dr. Gino Kerkhoffs. Beste **Gino**, Één vraag van jou na mijn presentatie over wrong-side surgery mondde uit in een groot en impactvol avontuur. Ik wil je bedanken voor je onvoorwaardelijke steun en vertrouwen dat jij mij hebt gegeven. We hebben naast het delen van een passie voor ons vak ook een bijzondere vriendschap opgebouwd. Met misschien wel als hoogtepunt ons project *MUSTANG.*

Lieve **Gino**, helaas heb ik mij in de afgelopen jaren beseft hoe ongelooflijk waardevol dit avontuur en onze vriendschap voor me is geweest. Ik zou zeggen; op naar de volgende!

Dr. Christopher DiGiovanni. Dear **DiGi**, I owe a deep debt of gratitude to you, as Chief of the Foot and Ankle Division at Massachusetts General Hospital, for believing in me and for creating an environment in which I was both able and inspired to reach my full potential. Your leadership and your extraordinary ability to motivate others are qualities I deeply admire and aspire to learn from. Only three months after my arrival, you entrusted me with the opportunity to serve as Interim Director of the Foot and Ankle Research and Innovation Laboratory (FARIL)—a vision that, through hard work, became a reality during my time. I am truly honored to be part of the Foot and Ankle family, and I sincerely hope our paths will cross again.

Dr. Guss. Dear **Daniel**, I honestly don't know anyone with the same boundless energy, creativity, and sense of humor that you have. At times, I truly thought you must be from another planet. And perhaps you are—but most likely you are simply one of the smartest people I've ever met, and my brain just needed some extra time to process your brilliance. It has been both an honor and a great pleasure to spend time with you. I will never forget our early morning drives to Waltham, during which you generously shared your valuable morning time with this "crazy Dutchie." Despite your demanding schedule filled with work and family, you were always an accessible mentor to me, and you added tremendous value to our work together.

Above all, it is simply a blessing to know that I have such a good friend on the other side of the pond.

Dear **DiGi** and **Daniel**, I am beyond words grateful for how incredibly quick and thoughtful you both have responded last year, it truly has brought light in my darkest days and that's something I will never, ever forget.

Acknowledgements

Dear **Bart**, I took over your position at the MGH Foot and Ankle team. About the first thing I heard when I arrived was; 'Noor, just so you know; you have big shoes to fill'. That turned out to be no understatement. I am so happy that from the start we could get along so well. You helped me start up, wrap up, and finish this big project. I was very lucky that at the end of my time in Boston you returned as the director of the Foot and Ankle Laboratory, and it has been a joy to have finally worked with you closely. Even though I didn't always make things the easiest (like losing all our lab data;).

You are truly one of a kind: working tirelessly, competing in Ironmans on the side, yet somehow managing to remain relaxed, enjoy a night out, and nurture a wonderful and growing family. Bart, I believe you can be deeply proud of the choices you've made and where they have brought you in life. Thank you for being my co-promoter.

Dear **Song Ho**, **Jirawat**, **Go**, and **Rohan**,
I consider myself incredibly fortunate to have had you as my closest colleagues throughout this journey. Each and one of you has contributed to the quality of my dissertation.

Song Ho, I will never forget your help in developing the initial ultrasound test, and how you and Jirawat stepped in to include patients for our study when I was sidelined with a fractured wrist. I am deeply grateful for the warmth with which you welcomed both me and Prof. DiGiovanni to your hometown of Tokyo. The Christmas cards from you and your lovely family still bring me warmth every year.

Jirawat, **Go**, and **Rohan**, the time we spent together in "The Lab" is something I will always treasure. Perhaps the loss of all our data—even if it felt catastrophic at the time—was in its own way a blessing because it allowed us to relive the process together. And yes, Coin! still crosses my mind at least every other week.

You are more than colleagues; you are in my heart,
and I will remain forever grateful for the friendship we built together.
This time will never be stolen from us.

Beste **Jan** en **Quinten**, wat heb ik geluk gehad met jullie.
Naast dat jullie natuurlijk echte toppers waren in dingen snel oppakken, hard werken en onderzoek doen, waren jullie ook een geweldig duo om erbij te hebben.

Ik ben super trots op wat we daar samen hebben neergezet en ben heel blij dat we nog steeds contact hebben.

Lieve **Johanna**, dit is natuurlijk veel te weinig tekst om te beschrijven wat jij voor mij hebt betekend in Boston. Wat een geluk voor mij dat jij toen ook net in New York ging wonen. Vele hoogtepunten van mijn Boston avontuur heb ik met jou beleefd. Zoals vakantie vieren in de gigantische Brickstone in Brooklyn waar jij op de kat van een bekende curator mocht passen, de keg party in de achtertuin, de tripjes naar Upstate New York, Maine, het strand, de logeerpartijen in Boston, fietsen naar Walden Pond (jij volledig ongetraind).

Maar het allergrootste persoonlijke hoogtepunt was wel onze roadtrip dwars door Amerika heen in de JEEP waar we allerlei avonturen hebben beleefd. 'These girls went to school, but they did not learn how to read'. Ook in de afgelopen jaren ben jij er door dik en dun vanuit New York geweest. In de toekomst leveren we de cilinders in en pakken we de fiets, ik kijk nu al uit naar dit avontuur!

Lieve Appeltoni's; **Sjors**, **Stijn**, **Stijn**, **Lauren**, **Hannah**, **Joeky**, **Sabine**, **Rens**, **Claire**, **Yassine**, **Nick**, **Michiel**, **Olivier**. Wat een heerlijke tijd hebben wij gehad in die brickstone van ons aan de Appleton 88 St. Ik heb echt genoten van alle etentjes, stoop seshes en fantastische feestjes. In specifiek wilde ik graag toch het volgende benoemen;

Lieve **Joeky**, je was mijn fiets-en skate maat. De tripjes naar Concord en samen op onze boards langs de Charles waren echt heerlijke onderbrekingen van het werk, ik kan je funkyness wel weer gebruiken.

Sjors, wat een geluk heb ik gehad dat je de zomers steeds weer bij ons wilde komen wonen. De stoop seshes in de zomer waren altijd al fantastisch maar toch pas echt compleet als jij erbij was. Love de kampeer trips die we hebben gemaakt en wie weet wat voor andere grote avonturen wij nog gaan beleven in onze toekomst;).

Lieve **Claire**, vanaf het moment dat jij op de Appleton kwam wonen startte eigenlijk mijn sociale leven in Boston pas echt. Jij had in een paar weken een groter sociaal netwerk dan ik in een jaar, en het goede nieuws voor mij; je nam mij gewoon mee. **Claire** je bent een harde werker, een fantastisch mens en een fantastische vriendin, ik ben super blij dat ik je heb mogen leren kennen.

Yassine, toen jij bij ons kwam wonen kwam er eigenlijk een gratis warmtebron bij. Jij hebt echt een gave om mensen op hun gemak te stellen en de cohesie te behouden, je bent echt een topper.

Dear **Hannah** and **Rue**, how could you keep up with all those crazy Dutchie's? I just want to say thanks for your patience with us and for coping with our, at times, ridiculous behavior. I mean, you'll have to bring a lot to the table to get Hannah off guard. I really respect you for it and I'm proud you became a pediatrician as you always wanted, and I hope to see you again in the future!

Dear **Nick**, it was so cool to have you as our roommate. We were super lucky that you wanted to live with us! Thanks for our trips together and I am happy we are still in contact. I'm really sure you and Kayla are going to be bad ass good parents, hope to see the family in the future.

To all; oh how I miss our stoop sesh.

Lieve **Quirine**, Ik heb echt een super waardevolle tijd met je gehad en ben heel blij te zien dat je nu echt goed op je pootjes terecht bent gekomen bij de sportgeneeskunde en je mooie gezinnetje.

Lieve **Claire**, **Livia** en **Nynke**, had ik jullie maar eerder in mijn avontuur in Boston ontmoet. Ik voelde me meteen thuis bij jullie. Dank voor de vele heerlijke etentjes, avondjes uit en de trip naar Maine. En niet onbelangrijk, door jullie heb ik ook **Nava** mogen leren kennen.

Dear **Nava**, I feel so rich to have met you and I am very grateful for the friendship we continue to have till today. As you know, I keep my hopes up that you and **Johan** will come to live in Amsterdam one day.

Lieve **paranimfen**, lieve **Juul** en **Pim**.
Ik ben ongelooflijk trots jullie als paranimfen te hebben. Met jullie kan ik de wereld aan. Jullie zijn allebei powervrouwen en ik heb ongelooflijk veel respect voor wie jullie zijn. Ontzettend veel dank voor jullie geweldige ondersteuning.

Lieve **Juul**, ik had me echt geen betere zus dan jij kunnen wensen. Het is voor mij zo waardevol dat we in de afgelopen jaren zo ontzettend naar elkaar toe zijn gegroeid. Ik wil jou nooit meer kwijt, en accepteer niet anders dan meer tijd met jou (en natuurlijk kleine **Robin** en **Nicolas**).

Lieve **Nic** en **Inke**, hoe bijzonder was het telefoontje in Boston dat ik trotse tante zou worden. **Nic**, je bent er onvoorwaardelijk voor mij en mag super trots zijn op jullie prachtige gezinnetje!
Ik heb veel zin om een keer samen naar de Efteling te gaan!

Lieve **Char**, **Charlie**, **Suus** en **Sanne**, wij zijn een superheldenteam. Dank voor al jullie onvoorwaardelijke steun en het gedogen van mijn afwezigheid.

Lieve geneeskunde **Skyfall buddies**; **Lauren**, **Rogier**, **Clasine**, **Ruud**, **Ramon**, **Sebastiaan** en **Fabienne**, wat een geluk heb ik dat ik jullie allemaal als vrienden heb.

Lauren; **Julliene** en **Anna** krijgen de groetjes van **Mina**.

Beste **Chamois** fietsvrienden **Eline**, **Meike**, **Doreth** en **Jozien**, op naar vele volgende avonturen!

Vochtige streken; **Isabelle**, **Ratna**, **Leanna**, **Maura**, **Emma**, **Fréderique**, **Jikke**, **Simone** (**Shiva**), **Doreth** en **Jozien**, jullie zijn allemaal fantastisch, creatief, grappig en hebben onuitputtelijke energie. Wat een cadeau dat we elkaar hebben weten te vinden.

Jari, hoe gaaf was het geweest als wij samen in Boston hadden gezeten. Ik ben blij dat ik je heb leren kennen en heel blij met onze vriendschap.

Kim, hoe badass ben jij? Heel badass zeg ik;). Je bent er echt voor me en ik vind het ongelooflijk gezellig. Op naar een volgende zombie sessie!

Carlijn, wat een cadeau dat we elkaar als collega hebben mogen treffen. Dankjewel voor je steun en positiviteit waarmee je mij het afgelopen jaar hebt overladen.

Lot, jij en **Patries** zijn absolute lichtpuntjes geweest in de afgelopen jaren, dank hiervoor.

Lieve **Irene**, **Fabiënne**, **Dennis**, **Mees**, lieve **schoonfamilie**.
Vanaf moment één hebben jullie mij opgenomen in de fam.
Dat is niet vanzelfsprekend maar wel ontzettend waardevol.

Lieve **Mees**, dank dat ik gebruik heb mogen maken van jouw creatief master brein voor de kunst en inhoud van dit boekje,
ik heb genoten van onze samenwerking!

Lieve **mama** en **papa**. Dank voor al jullie vertrouwen en steun wat jullie mij al vanaf jongs af aan hebben gegeven. Wat ontzettend gaaf dat jullie me ook in Boston zijn komen opzoeken. We hebben 2 zware jaren achter de rug maar het heeft ons enkel dichter bij elkaar gebracht, ik hou van jullie.

Lieve **Jojanneke**, lieve **Jo**. Save the best for last, period.
Wij zijn nu vijf en een half jaar samen en ik kan me geen leven meer voorstellen zonder jou. Het maakt niet uit wat er gebeurt, want met jou heb ik al gewonnen. Zo heb ik mij, zelfs in de afgelopen jaren, iedere dag kunnen voelen. Je bent er onvoorwaardelijk voor mij en ik ben er onvoorwaardelijk voor jou. We raken niet uitgepraat wij. Ik kijk heel erg uit naar wat de toekomst ons nog komt brengen!

Lieve **Rien**, ook al ben je er niet meer, ik denk nog steeds bijna iedere dag aan je. Ik weet dat je ongelooflijk trots was geweest. Ik had echt alles ervoor over gehad dat jij hierbij had kunnen zijn, zo oneerlijk. Zonder jou was ik überhaupt niet op dit toneel verschenen. Ik mis je ontzettend.

Reinier, we hebben veel goede gesprekken gehad in Boston,
je was onderdeel van het avontuur daar. Je koos anders.
Rust zacht lieve vriend.


SEP
Massachusetts
6HF 679

Chapter 14 About The Author

Noor Hagemeijer werd geboren op 18 september 1990 in Oirschot, als jongste telg van ***Freek Hagemeijer*** en ***Hannie Meulenbroeks***. Zij groeide op met haar oudere broer en zus ***Nic*** en ***Juul***. Van jongs af aan was zij gedreven, sportief, eigenzinnig, maar ook zorgzaam. Hockey, skimboarden, bomen beklimmen, en kattenkwaad wisselde zij af met een rol als mantelzorger voor buurman ***Rien***. Mede dankzij zijn steun wist zij vanuit het vmbo door te stromen naar het vwo. En ook hij was het die haar inspireerde om geneeskunde te gaan studeren aan *de Universiteit van Amsterdam*.

De studie geneeskunde bleek voor ***Noor*** al snel niet voldoende. Ze werd actief bij de studievereniging *MFAS* en maakte deel uit van de buitenlandse reiscommissie. In haar derde jaar werd zij lid van studentenvereniging *LANX* en het dispuut *Chloë*, waarin zij uiteindelijk ook een bestuursfunctie vervulde. Maar ook op sportief gebied zat Noor niet stil. Ze ruilde hockey in voor voetbal waar ze een aardig balletje leerde trappen. Dit zette ze in op het Nederlands kampioenschap voetgolf, waar ze voor de grap aan meedeed en verrassend tweede werd.

Tijdens haar laatste coschap leidde een creatief en grappig praatje tot een promotieplek in Boston, waar zij al snel het *Foot and Ankle Research and Innovation laboratory* mocht leiden. Hier kreeg zij vele internationale orthopedisch chirurgen onder haar hoede waaraan ze een groot internationaal netwerk aan collega's en vrienden heeft overgehouden.

Haar studie, promotie traject en de bijbehorende nevenactiviteiten leidde uiteindelijk tot een mooie opleidingsplek binnen de orthopedie. Eenmaal in de opleiding zette zij zich in voor een duurzamer energiebeleid binnen het *OLVG*. Later pleitte zij via de commissie *Cultuur van de NOV* voor meer aandacht voor minderheden binnen de orthopedie
en een inclusievere zorg.

Haar opleiding werd onderbroken door een periode van ziekte, maar ondanks deze tegenslagen voltooide zij met doorzettingsvermogen en vastberadenheid haar proefschrift.

Naast haar werk is Noor een fanatiek fietser, creatief denker en maakt ze de lekkerste kopjes koffie van Amsterdam Noord. Samen met haar partner ***Jojanneke*** en hun hondje ***Mina*** gaat zij met energie en optimisme nieuwe avonturen tegemoet.

Dear reader,

The supplemental imagery found within this thesis, designed using 3D-modeling software, and presently found on the cover, chapter and part indicating pages, feature both thematic and personal objects or scenes.

The thematic imagery is fairly self-evident, but the non-thematic images, of a more personal nature, are more esoteric than anything. These images are very serene, abstract and sober depictions of Noor's joyous research adventure, only to be understood by her, her fellow researchers and related figures.

In general I wanted the visuals to be very clinical, yet aesthetically pleasing and inspired by medical text books, anatomic articles and scholastic literature, where technological figures often have a certain stock photo flair to it (Chapters) and organic figures are often detailed cutouts and seemingly puzzling to a commoner (Parts).

The graphic design and layout of this thesis plays around with thesis design conventions, though it doesn't entirely break from it. More often than not the design of theses leave little to no breathing space, with each following chapter, and their textual content, claustrophobically blending together. Text followed by more text, without space to reflect. In many ways this edited procession of prior thesis designs has shaped the layout to become more magazine-esque in look and feel.

I thank Noor for giving me the opportunity to design this thesis and trusting me with its innards.

- Mees Joachim van Amesfoort

Amsterdam Movement Sciences

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Amsterdam Movement Sciences conducts scientific research to optimize physical performance in health and disease based on a fundamental understanding of human movement in order to contribute to the fulfillment of a meaningful life.