Ankle fractures with associated syndesmotic injuries

Treatment of syndesmosis injuries and the impact of posterior malleolar fractures

by

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Great minds discuss ideas.

Average minds discuss events.

Small minds discuss people.

Eleanor Roosevelt

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Sjusjøen, December 2020.

Abbreviations

AITFL	Anterior inferior tibiofibular ligament
AO	Arbeitsgemeinschaft für Osteosynthesefragen
AOFAS	American orthopaedic foot and ankle society ankle-hindfoot score.
AP	Anterior posterior
EQ-5D	EuroQol five-dimension questionnaire
FDL	Flexor digitorum longus
FHL	Flexor hallucis longus
CI	Confidence interval
CONSORT	Consolidated standards of reporting trials
CT	Computed tomography
FW	Fibular width
ICC	Intraclass correlation coefficient
IOR	Interosseous ligament
IQR	Inter quartile range
MCS	Medial clear space
MICD	Minimal clinically important difference
MOXFQ	Manchester Oxford foot questionnaire
MRI	Magnetic resonance imaging
OA	Osteoarthritis
OMA	Olerud-Molander ankle score
OR	Odds Ratio
ORIF	Open reduction internal fixation
PITFL	Posterior inferior tibiofibular fragment
PMF	Posterior malleolar fracture
PROM	Patient reported outcome measure
PTT	Posterior tibial tendon
RR	Relative risk
SB	Suture button
SPN	Superficial peroneal nerve
SqSS	Single quadricortical syndesmotic screw
SS	Single syndesmotic screw
StSS	Single tricortical syndesmotic strew
Sv	Sievert
TFCS	Tibiofibular clear space
TFO	Tibiofibular overlap
TTFL	Transverse tibiofibular ligament
USG	Ultrasonography
VAS	Visual analogue scale

List of papers

Paper I

Better outcome for suture button compared with single syndesmotic screw for syndesmosis injury: five-year results of a randomized controlled trial.

Ræder BW, Figved W, Madsen JE, Frihagen F, Jacobsen SB, Andersen MR.

The Bone & Joint Journal; 2020 Feb;102-B(2):212–9.

Paper II

Randomized trial comparing suture button with single 3.5 mm syndesmotic screw for ankle syndesmosis injury: similar results at 2 years. *Ræder BW, Stake IK, Madsen JE, Frihagen F, Jacobsen SB, Andersen MR, Figved W. Acta Orthop. 2020 Sep;1–6.*

Paper III

Incidence and clinical significance of posterior malleolar fractures in patients with AO/OTA C type ankle fractures. Results from two randomized controlled trials at 2 years.

Ræder BW, Andersen MR, Madsen JE, Frihagen F, Jacobsen SB, Figved W. (Submitted)

Synopsis of studies

Introduction

The ankle syndesmosis is a complex of 4 ligaments. The four ligaments bind the tibia and fibula together, securing the talus in the ankle mortise. If injured, optimal reduction and fixation is essential to restore stability and reduce post traumatic OA of the ankle joint (1). After the introduction of the suture button nearly two decades ago (2), treatment of syndesmotic injuries and implant choice has been an ongoing debate.

In an ankle fracture, the fracture pattern can involve the lateral malleolus (the distal fibula), the medial malleolus, and the posterior malleolus (distal tibia). The reported incidence of posterior malleolar fractures (PMFs) varies from 7 to 44% in the literature (3-5). With increasing use of CT, PMF has received increased attention. A CT for pre-operative planning is advised for ankle fractures where a PMF is suspected (6). With CT, a PMF can be diagnosed and classified. Several systems for classifications have been made (7-9), in which fracture morphology, rather than size, guides treatment (10).

Aims

The primary aim of this thesis is to analyze outcomes in patients treated with different implants for acute syndesmotic injury. A secondary aim is to state the incidence of a concomitant PMF in patients with AO/OTA C fractures. The last aim is to classify PMFs, assess the reliability of the Haraguchi classification system, and analyze the correlation between fracture pattern and clinical outcome.

Materials and methods

In study I, a total of 97 patients with an acute syndesmotic injury were randomized to 4.5 mm quadricortical SS (DePuy Synthes, Warsaw, Indiana, USA), or SB (Tightrope®, Arthrex, Naples, Florida, USA). The SS was removed routinely after 10-12 weeks. The primary outcome was the AOFAS. OMA score, VAS, EQ-5D, range of movement, complications, reoperations, and radiological results. CT scans of both ankles were obtained after surgery, and after one, two, and five years.

In study II, 113 patients with an acute syndesmotic injury were randomized to SB (ZipTight™, Zimmer Biomet, Warsaw, Indiana, USA) (n=55) or StSS (DePuy Synthes, Warsaw, Indiana, USA) (n=58). No implants were routinely removed. The AOFAS was the primary outcome measure. Secondary outcome measures included MOXFQ, OMA, VAS, EQ-5D, radiologic results, range of motion, complications and reoperations. CT scans of both ankles were obtained after surgery, and after 1 and 2 years.

In study III, 210 patients treated for an AO/OTA C type fracture with syndesmotic fixation between 2011 and 2017 were included from two randomized controlled trials (RCTs). Presence of a PMF was assessed on plain radiographs and CT. PMFs were classified according to Haraguchi. Patients were assessed at 6 weeks, 6 months, 1 and 2 years. The AOFAS was the primary outcome measure. Secondary outcome measures included presence of OA and malreduction rates. Intraobserver reproducibility and interobserver agreement for the Haraguchi classification were evaluated.

Results

In study I, the five-year follow-up rate was 84%. The SB group had higher median AOFAS (100 (IQR 92 to 100) vs 90 (IQR 85 to 100); p=0.006), and higher median OMA score (100 (IQR 95 to 100) vs 95 (IQR 75 to 100); p=0.006). The 4.5 mm quadricotrical SS group had a higher incidence of OA 24 vs 14 (65% vs 35%) odds ratio (OR) 3.4 (95% confidence interval (CI) 1.3 to 8.8); p=0.009). On axial CT we measured a significantly smaller mean difference in the anterior tibiofibular distance between injured and non- injured ankles in the SB group (0.1 mm vs 1.2 mm; p=0.02).

In study II, the 2-year follow-up rate was 84%. At 2 years, median AOFAS was 97 in both groups (IQR; SB: 87-100, StSS: 90-100, p=0.7), median MOXFQ index was 5 in the SB group and 3 in the StSS group (IQR; SB: 0-18, StSS: 0-8, p=0.2), and median OMA score was 90 in the SB group and 100 in the StSS group (IQR; SB: 75-100, StSS: 83-100, p=0.2). The syndesmotic reduction was similar 2 years after surgery; 19/55 patients in the SB group and 13/58 in the StSS group had a difference in anterior syndesmotic width $\geq$ 2 mm (p=0.3). 0 patients in the SB group and 5 patients in the StSS group had complete tibiofibular synostosis (p=0.03). At 2 years, 10 StSS were broken. Complications, rate of OA and reoperations were similar between the groups.

In study III, 125 of 210 patients (60%) had a PMF. 34% of these PMFs were missed on plain radiographs. Haraguchi type II fractures had a lower AOFAS compared to the no-fracture group at 6 weeks (mean difference -7.5 (95% CI; -15.0 to -0.2), p=0.04) and 6 months (mean difference -8.4 (95% CI; -15.3 to -1.5), p=0.01). The intraobserver agreement was 0.733, (95% CI: 0.629 to 0.884, p<0.001), and interobserver agreement was 0.797, (95% CI: 0.705 to 0.889) p<0.001. The 2-year follow-up rate was 87%.

Conclusions

Five years after syndesmotic injury treated with either SB or 4.5 mm quadricortical SS, we found better AOFAS and OMA scores, and lower incidence of ankle OA, in the SB group. These long-term results favor the use of SB when treating an acute syndesmotic injury compared with a 4.5 mm quadricortical SS.

When comparing SB with a single 3.5 mm SS, we found no clinically relevant differences regarding outcome scores between the groups. These results suggest that fixing an acute syndesmotic injury with StSS is an inexpensive alternative to SB.

Plain radiographs underestimate PMF compared to CT. Patients with a Haraguchi type II fracture have a poorer outcome measured by the AOFAS compared to no PMF up to 6 months, but without significant differences at one or two years. Classification of PMF according to the Haraguchi classification is reliable, with substantial agreement between raters.

Norsk sammendrag

Bakgrunn

Syndesmoseligamentkomplekset består av 4 ligamenter (leddbånd) som binder tibia og fibula sammen og sikrer talus' stabilitet i ankelgaffelen. Ved ankelbrudd kan ligamentene bli skadet, og dette kan gi en ustabil ankel. Hvis man ikke behandler denne instabiliteten, kan pasienter oppleve langvarige smerter, med en økt risiko for posttraumatisk ankelartrose. I lang tid har behandlingen av syndesmoseskade vært skruefiksasjon gjennom tibia og fibula, med forskjellige typer og antall skruer. Siden introduksjonen av fibertråd med knapp (suture button) på 2000-tallet, har implantatvalg for å fiksere en syndesmoseskade i ankelen vært tema for diskusjon.

Ved ankelbrudd kan man få bruddlinjer av mediale, laterale og bakre malleol (posterior malleolar fracture (PMF)). Den rapporterte forekomsten av PMF ved ankelbrudd, varierer i litteraturen fra 7 til 44%. En PMF og behandlingen av et slikt brudd er knyttet opp til stabilitet i ankelleddet og syndesmosen. Med økende bruk av CT i den kliniske hverdagen har brudd i PMF blitt hyppigere diagnostisert og fått økende oppmerksomhet. Tidligere var indikasjon for fiksasjon av en PMF størrelse > 25% av leddflate vurdert ved vanlig røntgen, med side, front og gaffel- projeksjon. Størrelsen av PMF har vist seg å bety mindre for ankelstabilitet, derfor mener flere at en PMF skal behandles utfra bruddets utseende og ikke størrelse. Det eksisterer nå 3 forskjellige bruddklassifikasjoner for å vurdere en PMF med CT. I den 3. studien er Haraguchis klassifikasjon blitt brukt.

Mål

Målet med denne avhandlingen er å analysere utfallet for pasienter behandlet med ulike implantater for akutt syndesmoseskade. I tillegg ønsker vi å avdekke forekomsten av PMF, klassifisere en PMF ved ankelbrudd med syndesmoseskade og undersøke hvorvidt det er en sammenheng mellom bruddmønster av PMF og ankelens funksjon etter skade.

Metoder

Studie I er en randomisert kontrollert studie der 97 pasienter med akutt syndesmoseskade er randomisert til SB (Tightrope®, Arthrex) eller kvadrikortikal 4,5 mm SS. Hoved endepunktet i studien er AOFAS. Øvrige endepunkter inkluderer OMA, VAS, EQ-5D, bevegelsesmål, komplikasjoner, reoperasjoner og radiologisk resultat. CT ble utført postoperativt, samt etter ett, to og 5 år.

Studie II er en randomisert kontrollert studie der 113 pasienter med akutt syndesmoseskade ble randomisert til SB (ZipTight™, Biomet) eller trikortikal 3,5 mm SS. Hovedendepunktet i studien er AOFAS. Sekundære endepunkter inkluderer MOXFQ, OMA, VAS, EQ-5D, bevegelsesmål, komplikasjoner, reoperasjoner og radiologisk resultat. CT ble utført postoperativt, samt etter ett og to år.

Studie III er en diagnostisk kohort studie, med pasienter fra studie 1 og 2 inkludert. Tilstedeværelse av en PMF ble målt på røntgen og CT. Videre ble bruddet klassifisert etter Haraguchis klassifikasjon for PMF. Pasientenes funksjon ble målt med AOFAS etter 6 uker, 6 måneder, 1 og 2 år. Sekundære endepunkter inkluderte tilstedeværelse av ankelartrose. Reproduserbarheten av Haraguchiklassifikasjonen ble undersøkt ved å teste inter- og intraobservatør reliabilitet.

Resultater

I studie 1 var 5-års oppfølgingsrate 84%. Gruppen behandlet med SB hadde høyere median AOFAS og OMA sammenliknet med kvadrikortikal, 4,5 mm SS. Vi fant en høyere forekomst av artrose i ankelleddet i SS gruppen. Forskjellen i syndesmosevidde mellom frisk og syk ankel (fremre syndesmosemål) var mindre i SB gruppen. Sidelik syndemosevidde er et tegn på god reposisjon av syndesmosen.

I studie 2 var 2-års oppfølgingsrate 84%. Når man sammenliknet pasienter behandlet med SB og trikortikal SS var kliniske resultater ved 2 årskontroll likeverdige målt med AOFAS, MOXFQ og OMA. De radiologiske resultatene viste samsvarende syndesmosevidde, likt antall reoperasjoner og komplikasjoner. Antallet med komplett synostose var forskjellig: 0 pasienter i SB gruppen og 5 pasienter i SS gruppen hadde komplett forbening mellom tibia og fibula.

I Studie 3 hadde 125 av 210 pasienter (60%) PMF. 34% av PMF ble oversett ved standard røntgen undersøkelse av ankelen. Haraguchi type II ankelbrudd hadde en lavere AOFAS sammenliknet pasienter uten PMF ved 6 uker og 6 måneder, men ikke ved 1 eller 2 år. Ved reliabilitetstesting viser Haraguchiklassifikasjonen betydelig enighet mellom forskjellige observatører, med en intraklasse korrelasjonskoeffisient på 0.7.

Konklusjoner

Fem år etter kirurgisk behandlet syndesmoseskade hadde pasienter behandlet med SB bedre kliniske og radiologiske resultater enn pasienter behandlet med kvadrikortikal SS, med en høyere AOFAS og OMA skår og lavere insidens av ankelartrose. Røntgen underestimerer tilstedeværelsen av PMF sammenliknet med CT. Klassifisering etter Haraguchiklassifikasjonen er reliabel, med en betydelig enighet mellom observatører.

Klinisk relevans

Funn fra studiene støtter bruken av dynamisk syndesmosefiksasjon som SB eller tricortical SS. Kvadrokortikal 4,5 mm SS har signifikant dårligere resultater ved 2 og 5 år sammenliknet med SB, dette er i tillegg det eneste implantatet som må fjernes rutinemessig av implantatene vi har undersøkt. En trikortikal 3.5 mm SS fremstår likeverdig som en SB, der ingen implantater trenger rutinemessig fjerning. SS er et rimelig alternativ til SB. Avhandlingen støtter derfor bruk av enten en 3.5 mm trikortical SS eller en SB for fiksasjon av akutte syndesmoseskader.

Avhandlingen støtter en økt bruk av CT i diagnostisk øyemed ved ankelbrudd, for å avdekke PMF. Haraguchis klassifikasjonssystem av PMF viser i vår studie god reliabilitet og kan anbefales i klinikken og i framtidige studier.

Introduction

Anatomy and biomechanics of the talocrural joint and tibiofibular syndesmosis

The ankle joint complex plays a fundamental role during the gait cycle. The ankle complex is formed by the tibiotalar, tibiofibular, fibulotalar, and talocalcanear joints. The tibia, fibula and talus make the talocrural joint, the only mortise joint in the human body. In the talocrural joint, the trochlea of the talus fits between the distal ends of the tibia and fibula. The articular surface of the tibia is often referred to as the plafond. The load-bearing aspect of the joint is the tibio-talar interface. The trochlea of the talus is cone shaped, widest anteriorly, making the joint more stable in dorsiflexion. The ankle joint has an oblique axis, ascending both in the frontal (8°) and transverse plain (6°), contributing to a complexity beyond a normal hinge joint in plantar and dorsiflexion. The oblique axis combined with the irregular shape of the talus, (broader ventrally and laterally) leads the distal fibula to move laterally, posteriorly and rotates externally when the ankle moves from maximum plantarflexion to dorsiflexion (11). Stability of the talocrural joint is provided by three groups of ligaments: The medial collateral ligaments (deltoid ligament), the lateral collateral ligaments, and the tibiofibular syndesmosis (Fig. 1 and 2).

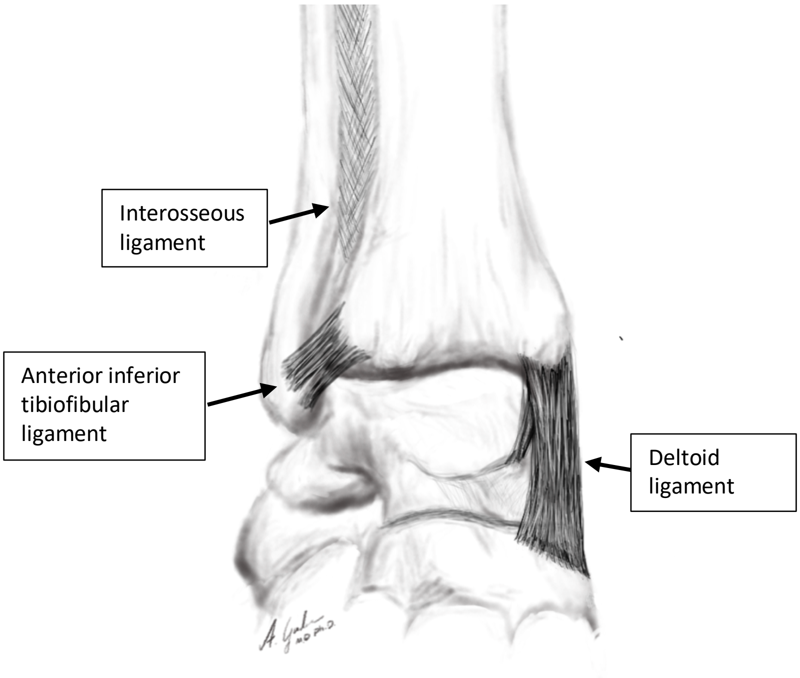


Figure 1: Illustration of the ankle ligaments from anterior view. Illustration by GA. Gundersen.

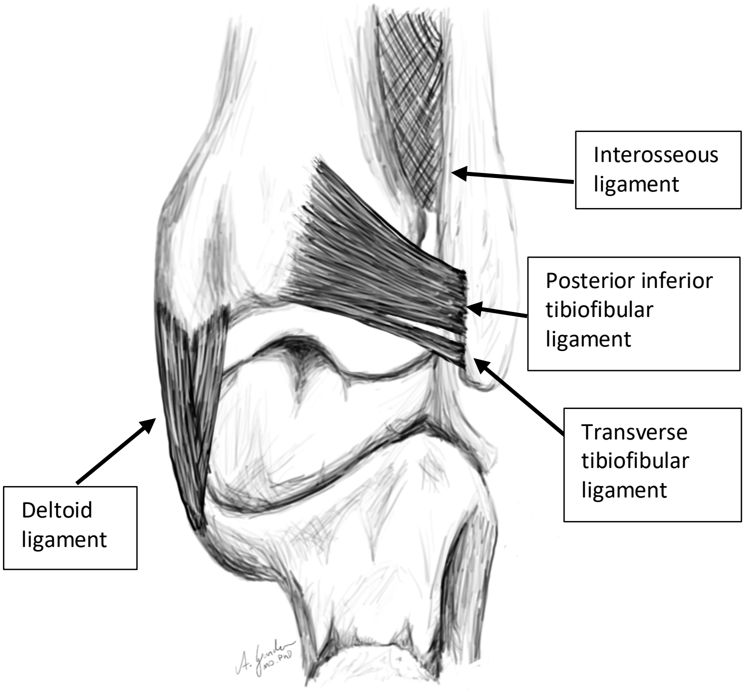


Figure 2: Illustration of ligaments from posterior view. Illustration by GA. Gundersen.

The deltoid ligament stabilizes and restricts eversion and valgus stress (12). The lateral collateral ligaments limits varus stress and reduces inversion and rotation (13). The deep portion of the medial collateral ligaments and the lateral collateral ligaments contributes to some syndesmotic stability, as it prohibits talar displacement (14). The tibiofibular syndesmosis resists axial, rotational and translational forces between the tibia and fibula during talocrural motion, securing the talus in the ankle mortise (15). The fibula lies in the tibial incisura. There is a great inter-individual variance in the shape of the incisura and the tibiofibular relationship (16). When comparing sides on axial CT scans, Dikos et al. found a mean variability in tibiofibular clear space in the incisura of 0.7 mm (SD 0.6), concluding with a low variance between sides within individuals (16). The ligaments of the syndesmosis consist of the anterior inferior tibiofibular ligament (AITFL), the interosseous ligament (IOL), the posterior inferior tibiofibular ligament (PITFL), and the transverse tibiofibular ligament (TTFL) (Fig. 1 and 2). The AITFL has its proximal attachment at the distal tibia, with its origin at the anterior tibial tubercle (Tillaux-Chaput), in average 5 mm above the articular surface. The ligament is trapezoid in shape, running obliquely, with a wider tibial insertion. The AITFL inserts at the anterior aspect of the lateral malleolus (Wagstaffe) (17). The length of the

AITFL varies from 12 to 20 mm. The AITFL width at the fibular insertion varies from 7 to 12 mm and the width of the tibial insertion varies from 9 to 22 mm (18). In some cases a distal fascicle runs separately from the AITFL, commonly referred to as the Bassett ligament (Fig. 3) (17,19).

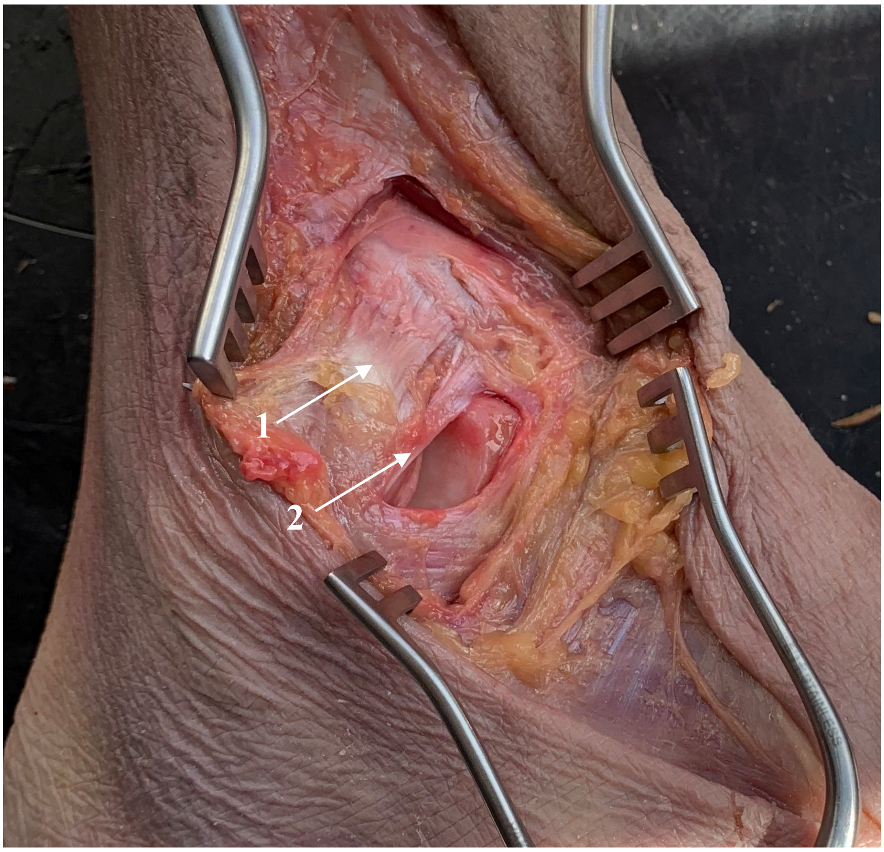


Figure 3: Specimen dissected to visualize the AITFL (1) and the Bassetts ligament (2). Photo by MR. Andersen and BW. Ræder.

The IOL is a triangular shaped ligament, with its apex passing to the interosseous membrane, making it a continuation of the latter. The ligament runs from about 4-5 cm to 1-1.5 cm above the ankle joint line. Distally, the IOL is separated from the AITFL anteriorly with a gap. Posteriorly, the IOL passes directly to the PTFL, making it hard to tell these ligaments apart (20). The PITFL is like the AITFL, trapezoid in shape. From its broad attachment at the posterior tibial tubercle (Volkmann's tubercle), the PITFL runs horizontally to the posterior fibular tubercle (20). The TTFL is a transverse ligament located below the tibial margin. It fills the gap between the posterior ridge of the tibia and the lateral malleolus, creating a posterior labrum or reinforcement of the posterior joint capsule. With its horizontal bands it is by some considered as a part of the PITFL (20,21). Several mechanical studies have been conducted to analyze the contributions of the syndesmotic ligaments to rotational stability of the syndesmosis. Ogilvie- Harris studied the force required to achieve 2 mm diastasis in the syndesmosis after successive sectioning of the syndesmotic ligaments. AITFL was described to provide 35% of the stability, TTFL 33%, IOL 22% and the PITFL 9%(22). The AITFL is particular important to provide resistance to external rotation and posterior translation of the fibula. The PITFL is important for controlling internal fibular rotation (23).

Epidemiology of ankle fractures

Ankle fractures are common injuries, making up 10-17% of all fractures (24,25), with a reported incidence of 0,7-1.7 per 1000-person years (25-28). The age distribution of ankle fractures is described to be bimodal, with peak incidences in adolescents and middle-aged, with a mean age of 41- years (26), mean 45 years for men and 58 years for women (27). Women experience an increasing incidence with age, with the highest age-specific incidence between 75 and 85 years (24). This is in contrast to men, where there is a decline after teenage years (26).

The most common injury mechanism is fall from the same height, reported to cause 61-64% of all fractures (26,27), followed by sports which accounts for 10-22% (26,29). 42-57% of ankle fractures are treated operatively (28,30), out of which 15-37% has an associated syndesmotic injury (31,32). The majority of syndesmotic injuries occur alongside ankle fractures (11). An isolated ligamentous syndesmotic rupture is called a high ankle sprain and is described in 1-18% of ankle sprains (14,33,34). However, the true incidence of these injuries are believed to be higher (11). The incidence of PMF is not well defined, with the incidence varying from 7 to 44% when analyzing all ankle fractures (24,35,36). Isolated PMF are rare, with a reported incidence of < 1% (37). Before suspecting an isolated PMF, high fibula fractures and syndesmotic instability must be ruled out (38).

Pathomechanics and injury mechanism

Syndesmotic injury

The classical and most common injury mechanism for ligamentous rupture of the syndesmotic ligaments is external rotation with the ankle placed in dorsiflexion (39,40). The talus, which is broader anteriorly will put strain on the ankle mortise if it is rotated externally or laterally. If the rotational force is strong enough, the talus will push the fibula away from the tibia and rupture the syndesmotic ligaments (41-43). Several different injury mechanisms can produce a syndesmotic injury (43,44), eversion, inversion, plantar flexion, pronation, and internal rotation are all reported as causes for syndesmotic injury (45-47).

Posterior malleolar fracture

Mason et al. linked the PMF-morphology to injury mechanism and outcome. An extra-articular posterior malleolar fracture (Mason type 1, Haraguchi type III) would occur with a plantarflexed unloaded talus subjected to rotation. A Mason type 2A fracture occur in the case of a fractured posterolateral corner of the tibia (Volkmann area, Haraguchi type I), with a fracture line extending to the incisura. The mechanism of this injury is described to be a rotational force applied to a loaded talus in neutral or plantarflexion. If the rotation of the talus in the mortise continues, a posteromedial extension of the fracture is produced, making it a Mason type 2B fracture (Haraguchi type II). Lastly the Mason type 3 fracture, which is a coronal plane fracture line involving the whole posterior plafond. The mechanism behind this fracture is believed to be axial load on a plantarflexed talus (9). An isolated PMF may result from axial load with ankle in maximum plantar flexion, known as the paratrooper fracture (48).

Classification of ankle fractures and their history

The Causative Lauge-Hansen Classification

Niels Lauge-Hansen (1899-1976) was a Danish physician who studied ankle fractures in the 1940-ies and 50-ies. This was after radiographs were taken into clinical use for fracture diagnosis, hence the classification system was based on dissection. Lauge-Hansen constructed a classification system based on human cadaver models. His focus was the patho-mechanism behind the injury, not radiology, thus making his classification a causative system. Lauge-Hansen applied rotational force on freshly amputated limbs to produce a fracture. He used force by hand and found that specific injury mechanisms gave characteristic fracture patterns. The goal behind The Lauge-Hansen classification was to guide the physician to treat the fracture without surgery, restoring the anatomy by closed reduction. The theory was that by knowing the injury mechanism, you could restore the anatomy by reversing the mechanism of that specific injury. His research led to an intricate classification system where the ankle fracture was classified into 4 categories with 13 subgroups (41). This system has been criticized for lack of validity, and in 1997 Michelson failed to reproduce the findings of Lauge-Hansen (49). Despite this criticism, the classification is still in use today.

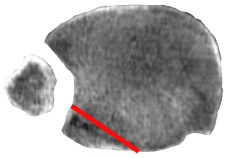
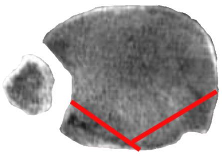
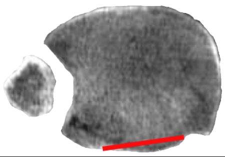
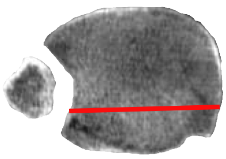
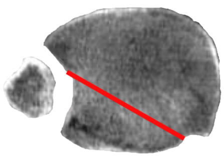
The descriptive Danis-Weber classification

The Belgian surgeon, Robert Danis (1880-1962) was one of the true pioneers among modern orthopaedic principals. Danis was a general surgeon, but he is first and foremost known for his contributions to the principles on fracture treatment. In 1932 Danis published *"La technique de l'ostéosynthèse Masson et Cie, Etudede quelques procédés"* ("The technique of osteosynthesis: Study of some procedures"), where strict aseptic principles were described. He was an advocate for dissecting as little as possible, fixing the fracture with absolute stability, to allow mobilization of the injured limb after surgery. In 1949 Danis published his results in his second book "Théorie et pratique de l'ostéosynthèse" (Theory and Practice of Osteosynthesis). In this book the first classification system based on radiographs for ankle fractures was described. Danis received several honorary degrees for his work, but his classification system was not widely used before Bernhard Georg Weber published a modified version in the paper Die Verletzungen des oberen Sprunggelenkes (*The injuries of the upper ankle*) (50) in 1972, 10 years after Danis' death. We know this classification as the Danis-Weber classification. This is a descriptive classification system categorizing fibula fractures according to their relations to the syndesmotic ligaments, based on plain radiographs.

CT and the classification systems of the posterior malleolar fracture

In 1973, Sir Godfrey Newbold Hounsfield published his first article on the CT technology (51), receiving the Nobel Price for Physiology or medicine in 1979. CT is now recommended for assessing complex ankle fractures with joint involvement (11). Currently there are 3 different classification systems for PMF based on CTs (Table 1).

Table 1: Overview of the different classification systems for PMF, based on morphology. The red lines represent fracture lines. Illustration by BW. Ræder.

Description	Illustration	Haraguchi type	Bartonicek type	Mason type
Posterolateral with incisura involvement		1	3	2a
Fracture extending to the medial malleolus		2	2	2b
Extra-incisural small shell type		3	1	1
Involvement of the whole posterior plafond				3
Large posterolateral triangular fragment			4	

Between 1999 and 2003, Haraguchi et al. categorized 57 ankle fractures of the posterior malleolus into 3 subtypes (Fig. 4). The posterolateral-oblique type (I) is a triangular fragment involving the posterolateral corner of the tibial plafond. The medial extension type (II) has a fracture line extending to the anterior part of the medial malleolus. The small-shell type (III) is characterized by one or more small shell-shaped fragments at the posterior tip of the tibial plafond (7). There is a continuum between the PMF and the posterior Pilon fracture. Haraguchi proposed the transmalleolar line to distinguish these fractures (7). In the work by Bartonicek and colleagues, they suggest fractures to be defined as “partial pilon” when the fracture line extends into the anterior colliculus of the medial malleolus or when it comprises > 50% of the incisura.

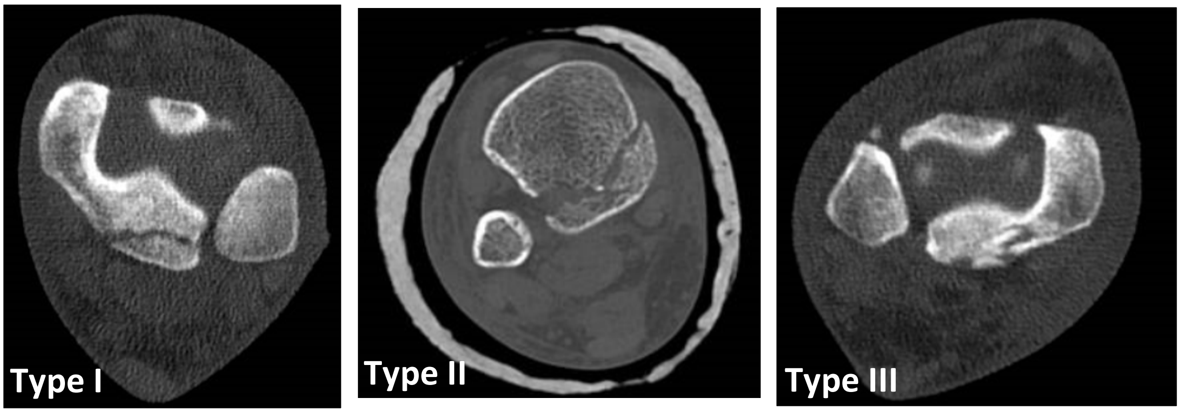


Figure 4: CTs from Paper III; Haraguchi type I, II and II fracture on axial CT scan. Department of Radiology, Bærum Hospital.

Bartonicek et al. published a different classification system, naming 4 subtypes (8) in 2015. In 2017, Mason incorporated patho-mechanisms as well as fracture morphology into a new classification of posterior malleolar fractures (9), in order to predict associated injuries and guide treatment. The Mason type 1 fracture (Haraguchi type III equivalent) is an avulsion injury by pull of the posterior inferior tibiofibular fragment (PITFL), where the PITFL was found ruptured in 100%. The theory was that the injury mechanism was injury with the ankle in plantarflexion with an unloaded talus and a rotational force applied to the foot. The Cohen's kappa coefficient for interobserver reliability with the Mason classification is 0.919 (9).

Diagnosis of syndesmotic injury

In the acute setting, clinical examination of a syndesmotic injury is often not tolerated by the patient. Patients will typically present with tenderness by palpation in the anterolateral aspect of the ankle joint, enhances by forced dorsiflexion or external rotation.

Clinical tests

Physical tests used for clinical examination of the syndesmosis is challenging in the acute setting, and rarely done in patients with a concomitant fracture. The tests are useful supplements to a thorough history, in patients with suspected subacute or chronic instability. A common complaint is pain anteriorly (over the AITFL) and posteromedially in the ankle, increasing with weight bearing or toe push of from the ground (52). Tenderness by palpation over the AITFL and the deltoid ligament is significantly associated with ligamentous injury found on MRI (53). How proximally the tenderness reach along the interosseous membrane reach is termed the “tenderness length”. The measured tenderness length is found to correlate with time to return to sports (54). Commonly used tests for subacute and chronic syndesmotic instability include the squeeze test, the ankle external rotational test, the cotton test and the fibular translation test (Fig. 5). A positive squeeze produces pain at the level of the distal tibiofibular syndesmosis when the tibia and fibula is compressed at a midcalf level. With the external rotational test, the leg is stabilized, and the foot is rotated with the ankle in neutral position, a positive test reproduces pain. Compared to MRI, the squeeze test and the external rotation test has a high specificity (94% and 85%, respectively) and low sensitivity of (30% and 20%, respectively). A Cotton test is performed by fixating the lower leg with one hand, pulling the talus laterally with the other. With the fibular translation test, the examiner pulls the fibula anteriorly and posteriorly relative to the talus. Pain and increased translation, compared with the contralateral side, makes the Cotton test and the fibular translation test positive (55,56).

Figure 5: The squeeze test, the talar exorotation test and the fibula translation test. Photo by BW. Ræder.

The stabilization test or the tape test is a non-validated test first described by Amendola (52). It is commonly used as a supplement to the previously mentioned tests, when examining a patient with subacute or chronic syndesmotic instability. The test is performed by tightly applying several layers of athletic tape, circumferentially, just above the ankle joint

(Fig. 6). The tape will compress the fibula and tibia together, stabilizing the syndesmosis and the ankle joint. Patients are asked to walk and do a single leg squat before and after the tape is applied. If the tape gives pain relief this is a good indication of syndesmotic instability.

Figure 6: Example of the stabilization test. Multiple layers of rigid athletic tape are applied tightly in multiple layers just above the ankle joint. The patient then does a single leg squat. Pain relief with the tape suggests syndesmosis instability. Photo by BW. Ræder.

Radiology

In a recent systematic review and meta-analysis by Chun et al., radiologic tests were compared to gold standard arthroscopic findings. The pooled sensitivity and specificity were respectively; 53% and 98% for radiographs, 67% and 87% for CT and 93% and 87% for MRI, (57). Standard radiographs include an AP-view, mortise view, and lateral view. Radiographs are described to be inaccurate, with a sensitivity and specificity of 40-53% and 95-100% (58,59). Parameters traditionally used in the assessment of syndesmotic integrity on plain radiographs are tibiofibular overlap (TFO), tibiofibular clear space (TFCS) and medial clear space (MCS) (Fig. 7). Findings of a TFO of ≥6 mm (or 42% of the fibular width) in the AP view or >1 mm in the mortise view, and a TFCS <6 mm are considered normal (60). These tests should be interpreted with knowledge of their low sensitivity and high specificity. Several studies have failed to find correlation between syndesmotic injuries and TFO and TCS measurements (61,62).

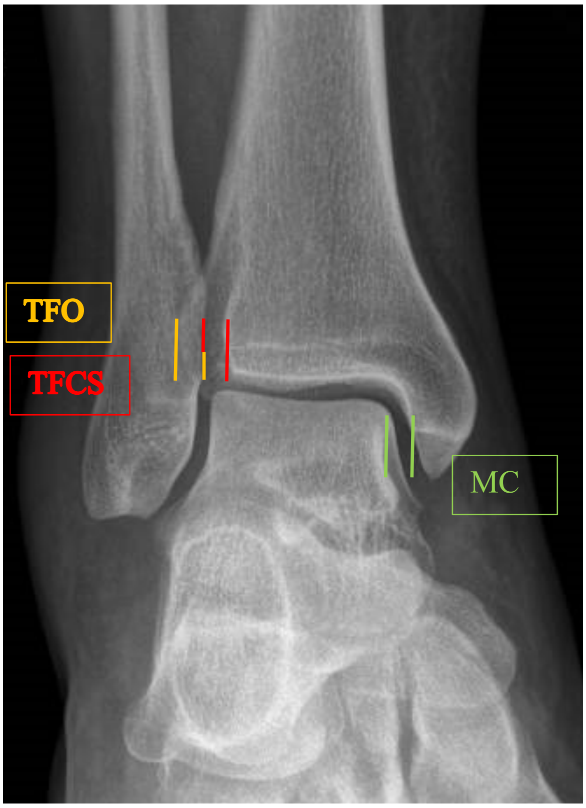


Figure 7: Landmarks on standard mortise radiographs where distance between the vertical lines represent: tibiofibular overlap (TFO), tibiofibular clear space (TFCS) and medial clear space (MCS). TCO and TFCS should be measured 1 cm proximal to the tibial plafond (63). Department of radiology, Bærum Hospital.

Weight-bearing radiographs have been used to assess the deltoid ligament and distinguish unstable from stable isolated lateral malleolar fractures (64). Amin et al. applied the principle of weight-bearing radiographs to assess the normal range for TFCS and TFO in ankles without known pathology. They established that a TFCS <5 mm or TFCS/FW <29% and TFO >9 mm or TFO/FW >57% in males and a TFCS <4 mm or TFCS/FW <30% and TFO >7 mm or TFO/FW >51% in females represented an intact syndesmosis (AP view).

A CT scan is used primary as a tool for assessing complex ankle fractures pre-operatively, since it does not assess soft tissue. A CT scan is recommended when a PMF is suspected (65). One study sought to predict syndesmotic instability measuring unilateral CT scans, finding significantly higher tibiofibular gap in ankles diagnosed with syndesmosis instability operatively, with the anterior tibiofibular distance being the most powerful parameter to predict operative instability (66). Since there is a great variability in the syndesmotic width between individuals, side to side comparison is advised (16,67).

The most common use of CT is for evaluation of postoperative results. To assess syndesmotic reduction, syndesmotic width, fibular rotation and translation has been described (68,69). To assess a syndesmotic injury, bilateral axial CT scans are compared, 1 cm above the joint line. A difference in anterior syndesmotic width >2 mm is found to predict poorer clinical outcome with an ICC of 0.5-0.7 (Landis and Koch scale) (70). Weight-bearing CT has the advantage of allowing functional assessment of the syndesmosis. Studies show that there is no side to side difference in weight-bearing CT and that the contralateral side is a valid internal control (71,72). There are presently no clinical trials where weight-bearing CT has been used on patients with syndesmotic injury. In addition, this is a costly examination, restricted to few hospitals, which limits the clinical use of this instrument.

MRI is the best non-invasive modality used for syndesmotic diagnosis: Takao et al compared MRI to arthroscopy. MRI had both high sensitivity and specificity for AITFL (100% and 93%, respectively) and PITFL rupture (100% sensitivity and specificity) (73). MRI is a static assessment of the syndesmosis, with the ability to identify ruptures. Dynamic function and true instability, however, cannot be assessed (74).

Ultrasonography (USG) is an inexpensive and quick examination. It is dynamic and can assess soft tissue pathology and ligamentous ruptures. The examination can be done during weight-bearing and testing. USG as a diagnostic tool has a steep learning curve and is highly operator dependent, limiting its availability. With a sensitivity of 89-100% and specificity of 0.95-100% it can be a valid diagnostic tool in experienced hands (75,76).

Intraoperative assessment

Intraoperative stress testing can be essential in the diagnosis and treatment of a rotational ankle fracture (74). When comparing the Cotton test (bone hook test) to the exorotation stress test, the Cotton test was found more reliable, because of greater displacement (77) when tested in a biomechanical cadaveric study. When assessing movement of the fibula, movement in the sagittal plane is described to be more sensitive than assessment in the AP view (42,78). In order to observe instability on AP view, the deltoid ligament or the interosseous membrane must be divided as well. To stress test the syndesmosis intraoperatively, Van den Bekerom et al. concludes that the surgeon should use the hook test with lateral views and sagittal directed force (74).

The gold standard for diagnosing a syndesmotic instability is ankle arthroscopy. An opening of 2 mm or more anteriorly is described as pathological (59,79,80). However arthroscopy is an invasive procedure and is primary a tool used to treat intraarticular and chronic syndesmotic pathology (81).

Diagnosis of posterior malleolar fractures

With radiographs, a PMF is best diagnosed from the lateral view. In cases with a PMF with an extension to the medial malleolus, a double contour of the medial malleolus is present ("flake fragment") in the AP view (82). Studies show that radiographs are unreliable when assessing presence and size of a PMF (83,84), therefore a preoperative CT is recommended when suspecting a PMF (6,85-87).

Treatment

Conservative treatment

For stable syndesmotic injuries, conservative management is advised. The medial deltoid ligament is found to function as a principal stabilizer in the ankle (88). If intact, the deltoid ligament will prevent external rotation of the talus and maintain stability (88). In a cadaver study, Boden et al. found that ankles with syndesmotic ruptures remained stable, given an intact deltoid ligament (89). In the ESSKA-AFAS consensus, Van Dijk et al recommends conservative treatment for isolated syndesmotic injuries with an intact deltoid ligament (90). In the ESSKA-AFAS consensus conservative treatment includes 3 weeks of non-weight bearing in a below knee cast, followed by proprioceptive exercises (90).

Syndesmotic fixation

When stabilizing the syndesmosis, the ankle should be in neutral position. Reduction of the syndesmosis is performed either manually or by used of a reduction clamp. A temporary guidewire is recommended (91). The syndesmotic reduction should be confirmed with radiographs, with the contralateral side as a control (92). The implant of choice is placed from the lateral side, 1-2 cm above the joint line, parallel to the tibial plafond, angled 30° from posterior to anterior (11,91). Direct inspection and open reduction of the syndesmosis can be achieved through an anterolateral or lateral approach. Sagi et al. found that the rate of malreduction of the syndesmosis was 44% with closed reduction, compared to 15% with open reduction, recommending open reduction and postoperative bilateral CT control (31).

Implant choice

For decades the SS has been used as the main fixation device for syndesmotic injuries. After Thornes first presented the suture button technique in 2003 (2), the use of SB has gained popularity amongst surgeons. Wikerøy et al. found similar functional results when comparing a quadricortical SS to two tricortical SS (93). Kortekangas found similar functional outcomes and malreduction rates when comparing SB to StSS (94). Since 2018, several meta-analyses have been published comparing SS to SB, reporting better outcomes for SB (95,96). The results are based on heterogenous studies with different numbers of implants, different diameters and cortices engaged for the screw fixation (95). A quadricortical SS is a rigid fixation, inhibiting tibiofibular movement throughout the gait cycle (97,98). The SB has a higher implant cost compared to SS (98), and may not be sufficient for maintaining fibular length in Maisonneuve fractures (97). The SB has an implant removal rate of 6%, mainly due to skin irritation from the lateral knot (99). Several knotless SBs are now available. Reports of fractures through the SB canal have raised concern whether SB should be used in osteoporotic bone (100). The single tricortical 3.5 mm SS (StSS) allows for some tibiofibular movement (23), making the StSS an inexpensive alternative, without need for routine implant removal.

Surgical fixation of the posterior malleolus

Indication

Previously, common practice was to stabilize a PMF that compromised more than 25% of the joint surface or had a >2 mm displacement (35). Several studies have failed to show correlation between fragment size and functional outcome (101-103). With increased use of CT, the focus has shifted towards fracture morphology, incisura involvement and syndesmotic stability. The aims of treatment are restoration of the incisura, fixation of PITFL avulsions and restoring talar containment with addressing intercalary fragments (7,10,82,104-106).

Restoration of a displaced fracture involving the incisura is essential to achieve appropriate fibular reduction in the tibiofibular joint with accompanied correct syndesmotic reduction (9,10). Fixing a PMF can restore syndesmotic stability (107). Miller et al. found that PMF fixation gave a more accurate syndesmotic reduction, and reduced the frequency of syndesmotic fixation (108,109). In patients with concomitant PMF it seems that stabilization of the PMF restores syndesmotic stability, making additional syndesmotic fixation redundant (106,109). In cases with impacted intercalary fragments, open reduced and fixation is recommended, to avoid malunion and possible talar subluxation (82).

Surgical approach

A PMF can be fixed indirectly with an anterior to posterior (AP) screw, direct posterolateral or a direct posteromedial approach (Fig. 8). Live fluoroscopy to assess fracture reduction, screw and plate placement is recommended with all approaches. Suggestions for approaches based on fracture morphology has been published (10,65). Mason et al. proposes syndesmotic fixation for smaller extraincisural fragments, posterolateral approach to an isolated posterolateral fracture involving the incisura (Volkmann triangle), posteromedial with or without posterolateral for fractures with a medial extension. For larger fractures involving the entire posterior margin of the tibia a posteromedial approach is recommended, this leaving the indirect fixation method out of the treatment algorithm (65). Baumbach et al recommends direct ORIF as supposed to indirect fixation, as it improved the reduction of the PMF compared to indirect AP screws (110).

Bartonicek et al. finds the indirect AP screw approach appropriate for isolated large fragments without intercalary fragments or impaction (10). With the patient in a supine or lateral decubitus position the posterior fragment is mobilized by dorsiflexion of the foot. Temporary reduction can be achieved with a reduction clamp. Final fixation with the compression principle is achieved by using partially threaded screws introduced parallel to the joint surface in the lateral view (111).

The direct posterolateral approach can be used for smaller fractures with impacted osteochondral fragments (10). With this approach, direct visualization and anatomic reduction is achieved. The posterolateral approach is practical, since a fibula fracture can be fixed through the same incision. With the patient in the prone position a longitudinal incision is made between the Achilles and fibula. The subcutaneous sural nerve runs parallel to the lateral margin of the Achilles tendon and will usually lie medial to the incision. Further blunt dissection creates an interval between FHL and the peroneal muscles where the posterolateral margin of the tibia is exposed. In this maneuver care should be taken not to injure the peroneal artery. Through mobilization of the main fragment, impacted joint fragments can be addressed. Final fracture fixation can be achieved with either screws or a posterior buttress or locking plate (112).

The direct posteromedial approach is used for posteromedial fractures, and impacted intercalary fragments (65,82). The incision runs longitudinally halfway between the Achilles tendon and the medial malleolus. Proximally the incision should be parallel to the posteromedial tibial border, and distally the incision should run parallel to the PTT. After dissecting through the fascia, care must be taken before entering the deep fascia. One should start proximally, to identify the neurovascular bundle, retracting it medially. Blunt dissection creates an interval between the FHL laterally and the neurovascular bundle, FDL, and PTT medially, before visualizing the posteromedial rim of the distal tibia where direct reduction and fixation can be performed (113).

Figure 8: Lateral radiograph of different approaches to the PMF. AP screw, PA screw and plate. Department of radiology, Bærum Hospital.

Postoperative treatment

The AO surgical reference recommends a postoperative CT control of both ankles if any syndesmotic incongruence is suspected, or if a positioning screw was inserted, in order to control and compare fibular placement in the incisura (91). Partial weight-bearing is recommended until removal of the positioning screw, advised after 8 to 10 weeks (114). Controversy exists on timing and indication for screw removal (115). Retention of tricortical screws, even with screw breakage, is described unproblematic (116). The timing of screw removal varies in the literature. Miller et al. and Song et al. removed screws after 4 months (117,118). A reason for late screw removal is to ensure ligamentous healing. Screw removal before 6 weeks is a potential risk for recurrent diastasis (119). A concept review suggests that routine removal of a tricortical screw is probably unwarranted, while a quadricortical screw should be removed after 6-8 weeks (115). In the case of suture button, implant removal is unwarranted (99). Few studies focus on weight-bearing after syndesmotic fixation. Schepers et al. could not detect any differences in functional outcomes comparing patients treated with immobilization to patients allowed partial unprotected weight-bearing first 6 weeks after surgery (120). When deciding postoperative care, with potential use of plaster cast and time until mobilization, patients should be evaluated individually, taking compliance, comorbidity, age and bone quality into consideration. In cases with poor bone healing potential (osteoporosis, diabetes, neuropathy) time until weight-bearing can be prolonged up to 12 weeks (10).

Complications

Malreduction of the syndesmosis

Syndesmotic malreduction is common (44-52%) (31,121). A malreduced ankle fracture or syndesmosis changes the biomechanics of the talocrural joint. Ramsey et al found that 1 mm lateral dislocation of the talus reduced the tibiotalar contact area with 42% (122), increasing the risk of OA (1). Left untreated, a chronic syndesmotic diastasis may be a cause of chronic pain, joint stiffness, and limited joint function (11). A syndesmotic malreduction should be corrected as early as possible to avoid instability and ankle OA (123). The most common indication for re-operation following ankle fracture surgery is syndesmotic malreduction (124). To evaluate the syndesmotic reduction CT scanning postoperatively with side-to-side comparison is advised (Fig. 9) (16,70). A cut-off point for acceptable syndesmotic width is proposed to be an anterior difference of maximum 2 mm when comparing sides, 1 cm proximal to the talocrural joint line (70).

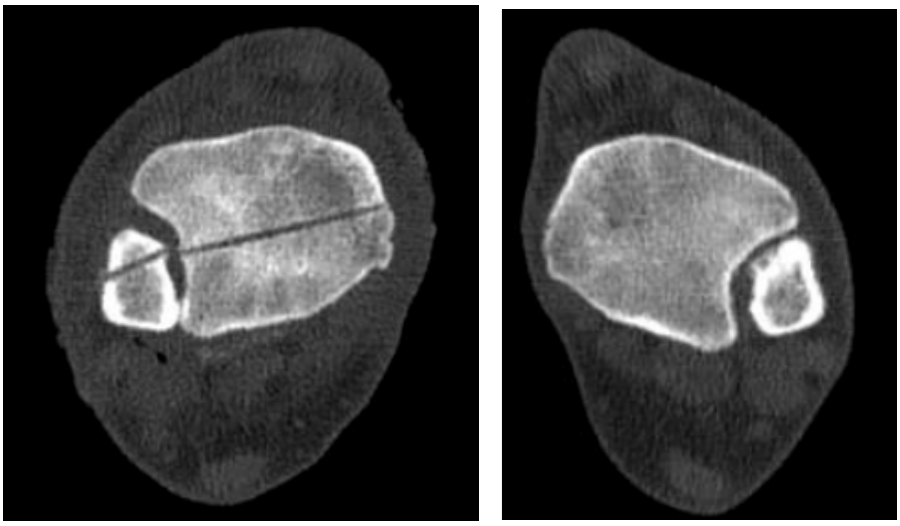


Figure 9: CT scan 1 cm proximal to the talocrural joint. Side to side comparison with unacceptable reduction with external rotation and misplacement of the fibula in the incisura on the right side. Department of radiology, Bærum Hospital.

Infection

Infection is the most common complication of operative treatment of ankle fractures, with rates ranging from 2 to 8% (125). Deep infections can have a devastating result: Zalavras reported an amputation rate of 17% after postoperative infection in patients treated for ankle fractures (126). Staphylococcus aureus is the most common pathogen found in implant-associated osteomyelitis (127). The formation of biofilm is key in the persistence of infection. Biofilm, which is colonies of microbes enclosed by an extracellular polysaccharide matrix (glycocalyx), adheres to implants, protecting the microbe from antibiotics and host defense mechanisms. Presence of implants promotes biofilm formation (128) and facilitates the infection. Risk factors of infection include diabetes mellitus, advanced age and high energy injuries (126). Flynn et al. reported a four times fold increased risk of infection comparing patients with and without diabetes (32% vs 8%) (129).

Nerve injury

The SPN originates at the lateral side of the neck of the fibula and runs between and supplies the peroneus longus and brevis muscles in the anterolateral compartment of the leg. Between the upper two thirds and lower two thirds, the nerve penetrates the deep fascia, and becomes a subcutaneous nerve. The nerve divides into a medial and a lateral cutaneous branch. It supplies the skin over the lower lateral side of the leg and dorsal skin of the first, second, third and medial side of the fourth toe (130). The nerve is known for its variable course and close relationship to the distal fibula, placing it at risk for iatrogenic injury and a cause of chronic ankle pain (131). The incidence of SPN injury is described to be 9% in ankle fractures treated with a cast, and 21% in patients treated with open reduction and internal fixation (131).

Osteoarthritis

Ankle trauma is described to cause 78% of cases with end stage OA, making it the most common cause of OA, where 39% of patients with ankle OA has a previous fracture (132). OA of the ankle gives a stiff and painful joint with ankle arthrodesis as end treatment. One study shows that patients with ankle OA report the same reduction in quality of life as patients with hip OA (133). Malreduction and increased age are independent risk factors for OA development (134).

Aim of the thesis

The general aims of the different studies were to increase the knowledge on treatment options for acute syndesmotic injuries and assess the implications of a posterior malleolar fracture in these patients.

Paper I

- Compare clinical and radiological outcomes of SB and SqSS five years after surgery.

Paper II

- Compare clinical and radiological outcomes for SB and StSS two years after surgery.

Paper III

- Assess incidence of PMF in patients treated for AO/OTA 44-C fracture.
- Classify PMF according to the Haraguchi classification.
- Assess intraobserver and interobserver reliability for the Haraguchi classification.
- Assess if presence and fracture morphology correlate with clinical outcome.

Patients

Paper I

97 patients were included at Bærum Hospital (34 patients) and Oslo University Hospital (63 Patients) from January 2011 to March 2013. Patients between 18 to 70 years with an acute syndesmotic injury, with or without an OTA/AO type 44-C ankle fracture, were assessed for study inclusion. Exclusion criteria were polytrauma, open fractures, prior injury to the ankle that could impair rehabilitation, neurologic impairment of the lower extremities, or inability to consent. Patients gave their written consent prior to block randomization, with a one to one ratio and a block length of ten. Sequentially numbered opaque, sealed envelopes were opened according to patient number prior to surgery, assigning each patient to either SB (48 patients) or SqSS (49 patients) (Table 2). The five-year overall follow-up rate was 84%, and the radiologic follow-up rate was 79% (Fig. 10).

Table 2: Patient characteristics of Paper I.

Patient characteristics at time of enrolment		
Characteristics	**SB group (n = 48)**	**SS group (n = 49)**
Mean age, years (SD)	46 (15)	43 (16)
Male sex	34	30
Right side	17	29
Mean body mass index, kg/m^2 (SD)	27 (5)	27 (5)
Maisonneuve fracture	15	14
Medial malleolar fracture	19	25
Posterior malleolar fracture	25	36
Medial and posterior malleolar fracture	12	21
Osteochondral lesions	5	11
Values are expressed as number of patients. Age and body mass index are given as mean with SD.		

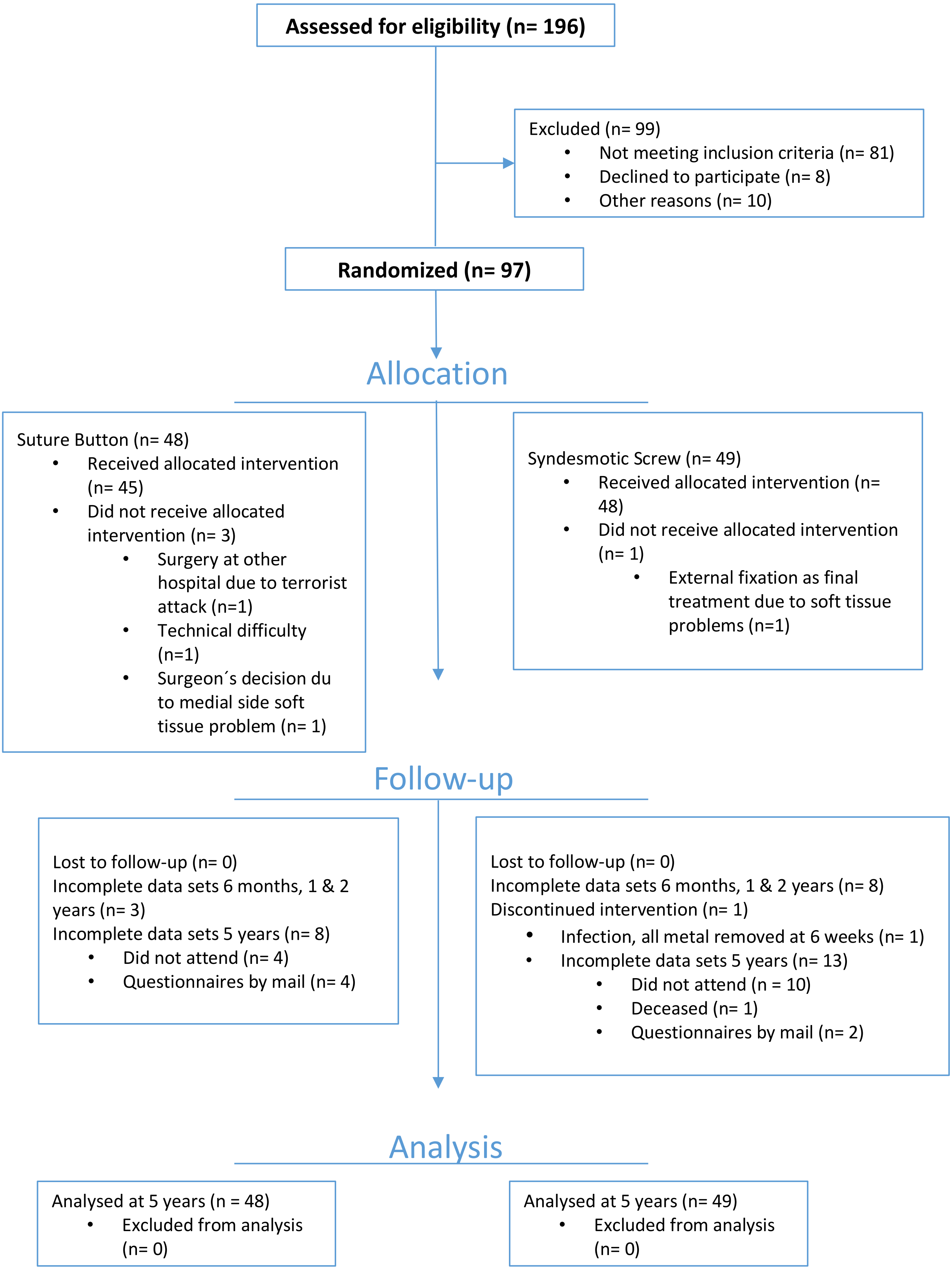


Figure 10: CONSORT FLOWCHART of the trial enrolment and analysis in paper I.

Paper II

113 patients were included at Bærum Hospital (34 patients), Kalnes Hospital (25 patients) and Ullevål Hospital, Oslo University Hospital (54 patients) from January 2016 to September 2017. Patients aged 18 to 69 who had suffered an acute OTA/AO type 44-C ankle fracture assessed by radiographs, were asked to participate. Exclusion criteria were polytrauma, open fractures, previous fracture or OA of the same ankle, neurologic impairment of the lower limbs, or inability to consent. Patients gave their written consent prior to randomization. A web-based randomization system was used, developed and administered by Clinical Research Unit Central Norway, Norwegian University of Science and Technology, Trondheim, Norway (Web reference 2009). The patients were randomized to fixation of the syndesmosis with either SB (58 patients) or StSS (55 patients) (Table 3). The two-year follow-up rate was 84%, the radiologic follow-up rate was 81% (Fig. 11).

Table 3: Patient characteristics of Paper II

Patient characteristics at time of enrolment		
Characteristics	**SB (n=55)**	**StSS (n=58)**
Age (years)	44 (15)	48 (14)
Male sex	35	30
Right side	32	26
BMI	27 (5)	26 (4)
Medial malleolar fracture	14	19
Posterior malleolar fracture	37	31
Medial and posterior malleolar fracture	10	15
Maisonneuve fracture	26	20
Osteochondral damage of the talus	2 (n=54)	4
Intra-articulate loose bodies	9 (n=54)	10
Temporary external fixator	7	2
Values are expressed as number of patients. Age and body mass index are given as mean with SD.		

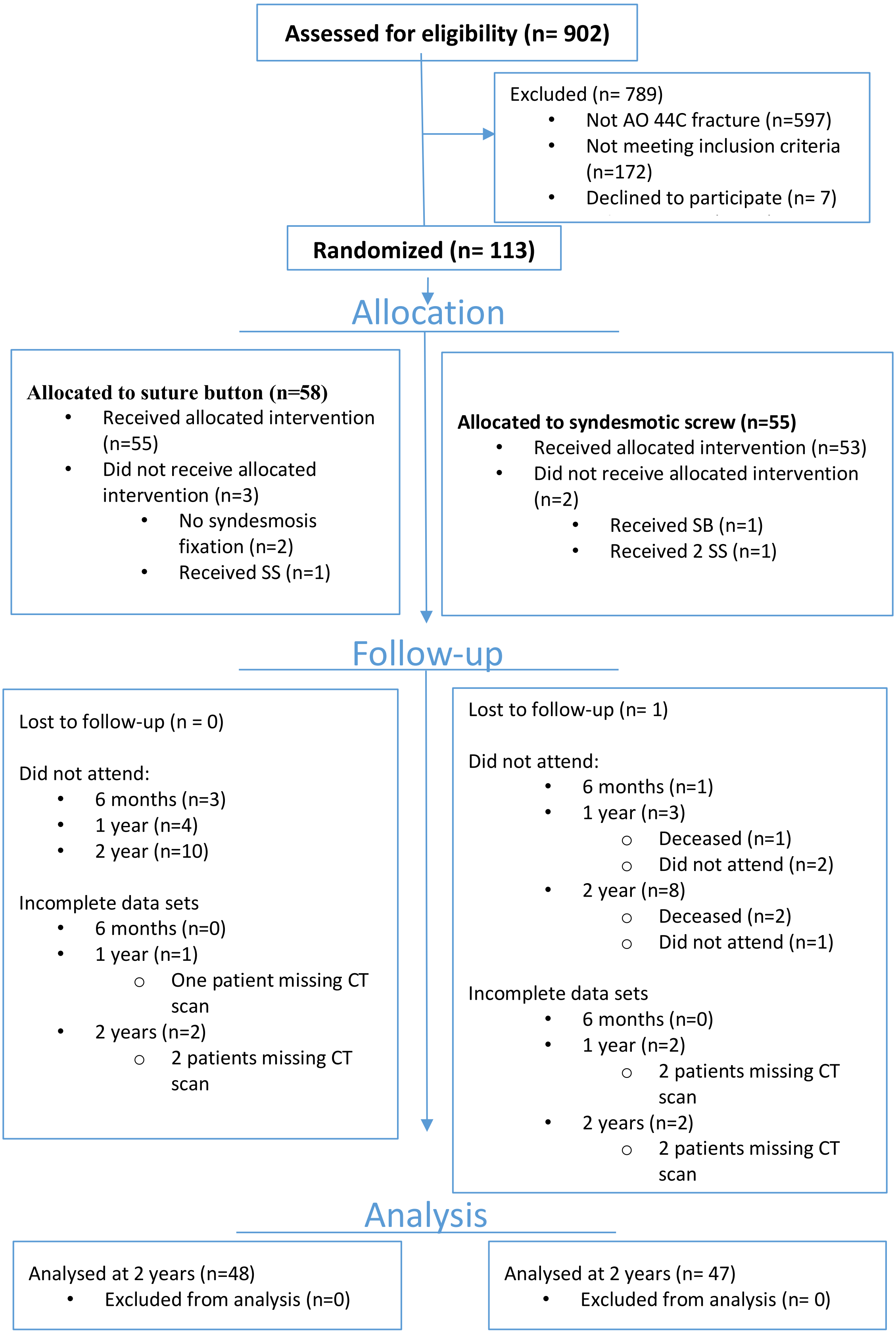


Figure 11: CONSORT flowchart of the trial enrolment and analysis in paper II.

Paper III

This study included all the patients from both study II and study III. 210 patients were divided into 4 groups, one for patients without a PMF (85 patients)(Table 4), and three groups according to Haraguchi type I-III (125 patients). The 2-year follow-up was 87%.

Table 4: Patient characteristics of Paper III

Patient characteristics, Haraguchi				
Characteristics	**No PMF N= (85)**	**Haraguchi=I (N=61)**	**Haraguchi=II (N=28)**	**Haraguchi=III (N=36)**
Age (years)	43 (14)	46 (15)	47 (14)	45 (16)
Male sex	62	34	9	25
Body Mass Index	27 (6)	28 (5)	26 (4)	27 (4)
Maisonneuve	29	18	8	20
Medial Malleolus fixation	18	33	15	10
Posterior malleolus fixation	0	5	12	0
Plate osteosynthesis of fibula	52	41	18	14
Values are expressed as number of patients, except for age and body mass index, which are presented as mean and SD.				

Methods

Paper I, II and III

Treatment

Surgery was performed by the on-call team, either by an experienced resident, or a less experienced resident accompanied by a consultant or senior resident. All patients received antibiotic prophylaxis, Cephalothin 2 grams was routine. Open reduction and internal fixation of malleolar fractures was preformed according to AO principles before reduction and fixation of the syndesmosis, guided by fluoroscopy. The manner of syndesmotic reduction was conducted in a closed manner, where the use of a reduction clamp was decided by the surgeon. Surgeons where recommended to fix the syndesmosis at a level just proximal to the inferior tibiofibular joint (91). All patients were allowed partial weight-bearing from 2-6 weeks and full weight-bearing as tolerated after six weeks.
Plaster cast was not routinely used.

Implants: Paper I

Patients randomized to SS were treated with a fully threaded, self-tapping 4.5 mm quadricortical screws (DePuy Synthes, Warsaw, Indiana, USA) (Fig. 12). A 3.2 canal was drilled just proximal to the tibiofibular joint, and with the ankle in neutral position the screw was placed through 4 cortices. This was the only implant which required routine removal, planned 10-12 weeks after primary surgery. Patients randomized to SB received a single Tightrope® (Arthrex, Naples, Florida, USA) (Fig. 13). First a guidewire was placed just proximal to the ankle joint guided by fluoroscopy. Then a 3.5 mm canal was drilled. The Tightrope® was introduced with a guide-needle and pull-through sutures, and an oblong button was pulled through and flipped at the cortex of the medial malleolus. The sutures were tightened until the lateral button fit firmly on the cortex, or on the plate when present. Three half-hitches secured the fixation.

Implants: Paper II

Patients randomized to StSS were treated with a fully threaded, self-tapping 3.5 mm tricortical screw (DePuy Synthes, Warsaw, Indiana, USA) (Fig. 14). A 2.5 mm canal was drilled just proximal to the tibiofibular joint with the ankle in neutral position, then the screw was placed through 3 cortices. This implant did not require routine removal. Patients randomized to SB in Paper II received a single ZipTight™ (Zimmer Biomet, Warsaw, Indiana, USA) (Fig. 15). First, a guidewire was placed just proximal to the ankle joint guided by fluoroscopy. Then a 3.2 mm canal was drilled. The ZipTight™ was then introduced with a guide-needle and pull-through sutures, and the ToggleLoc™ button was pulled through and flipped at the cortex of the medial malleolus. The sutures were tightened until the lateral button fit firmly on the cortex, or on the plate when present. This construct utilized ZipLoop Technology™, so there was no need for additional knots.

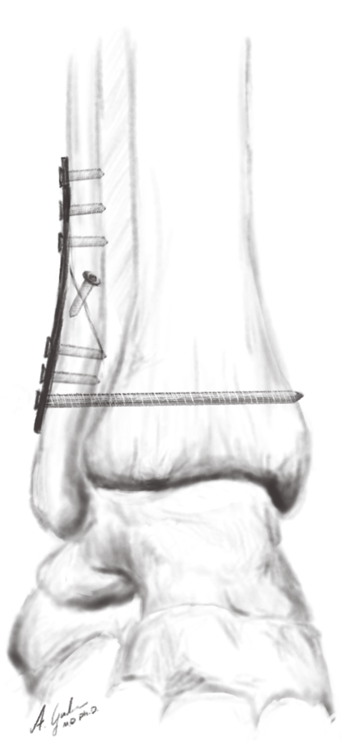


Figure 12: Illustration of ankle fracture with 4.5 quadricortical screw. Illustration by GA. Gundersen.

Figure 13: Illustration of ankle fracture with knotted SB. Illustration by GA. Gundersen.

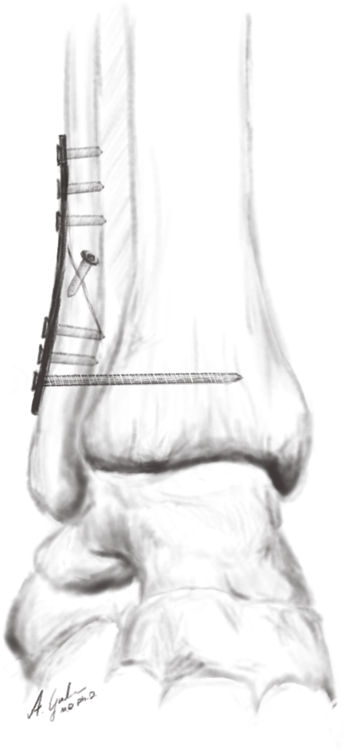


Figure 14: Illustration of ankle fracture with 3.5 tricortical screw fixation. Illustration by GA. Gundersen.

Figure 15: Illustration of ankle fracture with knotless suture button. Illustration by GA. Gundersen.

Outcome measures

The AOFAS (Appendix 1) (135) was the primary outcome score in Paper I, II and III. Secondary outcome measures in paper I and II included the OMA (Appendix 2), EuroQol-5D (EQ-5D) index, EQ-5D VAS (Appendix 3) and VAS scores (Appendix 4). For paper II the MOXFQ (Appendix 5) was added as a secondary outcome measure.

The American orthopaedic foot & ankle society ankle-hindfoot score:

The score is subdivided into two subjective parts; pain and function and one objective part; alignment. The subjective and objective categories are scored together, ranging from 0-100 points, 100 points being the best score. The AOFAS has been criticized for not being a patient-reported outcome measure, for not being validated, and for producing skewed data and ceiling effects (136). The scale was chosen due to its widespread use (137,138) and to enable comparison to related studies.

The Olerud-Molander ankle score

Secondary outcome measures in paper I and II included the (OMA). The OMA score is a self-administered patient questionnaire, ranging from 0 to 100, 100 being the best. This score is evaluated against a linear analogue scale, the ability of ankle dorsiflexion while weight-bearing, OA, and ankle displacement on radiographs (139).

The Manchester Oxford foot questionnaire

For paper II the MOXFQ (140,141) was added as a secondary outcome. This was mainly done because of the criticism to the AOFAS for lacking precision and validity. The MOQFQ This is a 16-item (each item scored 0-4) Patient Reported Outcome Measure (PROM), with three separate underlying dimensions: pain, activity, and social interaction. The raw score of maximum 64 can be converted to a metric index from 0 (best) to 100 (worst) (142). MOXFQ is validated in Norwegian and found to be highly responsive(141).

The visual analogue scale

Is a subjective measurement instrument where patients are asked to mark on a continuous pain scale from 0 (no pain) to 10 (worst possible pain) in 4 different situations: During rest, during walking, at nights, and during daily activities. The VAS is described as a simple, valid, and reliable measurement (143).

The EQ-5D-3L index and the EQ-5D VAS

EQ-5D is a validated generic self-reported health-related quality of life instrument. It was introduced by the EuroQol Group in 1990. It consists of two parts: a descriptive part, and the EQ-5D VAS for health status (144,145). The descriptive part consists of 5 dimensions; mobility; self-care; usual activities; pain/discomfort and anxiety/depression. Each dimension has three levels of response (3L) (1=no problems, 2=some problems, or 3= major problems). Digits from the 5 dimensions can be combined to give a 5-digit number describing the patients state. For example, a patient in health state 12231 would have no problems with mobility, some problems with self-care and usual activities, severe pain/discomfort, and no anxiety or depression. The EQ-5D index value can then be calculated based on the 5 digits scored from the 5 dimensions arriving on a value from 0 to 1 (1 indicates best possible health state, 0 indicates health state equivalent to death). The EQ-5D VAS provides a direct valuation of the respondent's current perception of health. The patient rates his/her heath on a visual scale, ranging from 0 to 100 (0=worst).

Range of motion

Range of motion was assessed by comparing injured to non-injured ankle. The measurements were conducted with the foot on a 25 cm high benchlet. The measurements were the angle between the lateral margin of the foot and the longitudinal axis of the fibula (from the lateral malleolus to the caput of the fibula). Active loaded dorsiflexion was measured with a goniometer, while the heel remained in contact with the benchlet, modified after the description by Lindsjø (30) (Fig. 16). Active plantarflexion was measured with the patient keeping the 1. MTP joint in contact with the benchlet (Fig. 16). This was done unblinded throughout Paper I, and at 6 weeks and 6 months in Paper II. For the 1- and 2-years follow-up in Paper II, measurements were conducted by a physiotherapist who were blinded to the treatment allocation. Testing the healthy ankle first, both feet were measured twice, with the highest range recorded. We propose to test and compare range of motion in this manner. We observed a learning curve in the patients, with a higher range of motion recorded in the second measurement.

Figure 16: Measurement of range of motion with loaded dorsiflexion and plantar flexion. Photo by BW. Ræder.

Radiological measurements

In Paper I, CT scans were obtained at the 5-year follow-up. In Paper II, mortise and lateral radiographs of the injured ankle were obtained prior to surgery, at 6 weeks and 6 months. CT scans of both ankles were obtained postoperatively, and after 1 and 2 years. In paper III, mortise and lateral radiographs before surgery and CT scans postoperatively and at 2 years were assessed. All radiographs and CT imaging were analyzed using digital imaging software Siemens Pacs Syngo Studio VB36E (Siemens, Munich, Germany) and Carestream Pacs v 12.1.5.1046 (Carestream Health, Rochester, New York, USA).

Assessment of the syndesmosis

CT Scans were standardized by placing the feet in a purpose made device, keeping the ankles in neutral position with 20° internal rotation of the legs. Radiologic measurements were performed by one senior musculoskeletal radiologist and one orthopedic surgeon. The syndesmosis was assessed postoperatively and after 1 and 2 years by measuring the tibiofibular distance on axial CT scans, 1 cm proximal to the midpoint of the tibial plafond (Fig. 17). The difference between injured and uninjured side was calculated. A criterion of <2 mm difference in tibiofibular distance was selected for acceptable syndesmotic reduction (70,71).

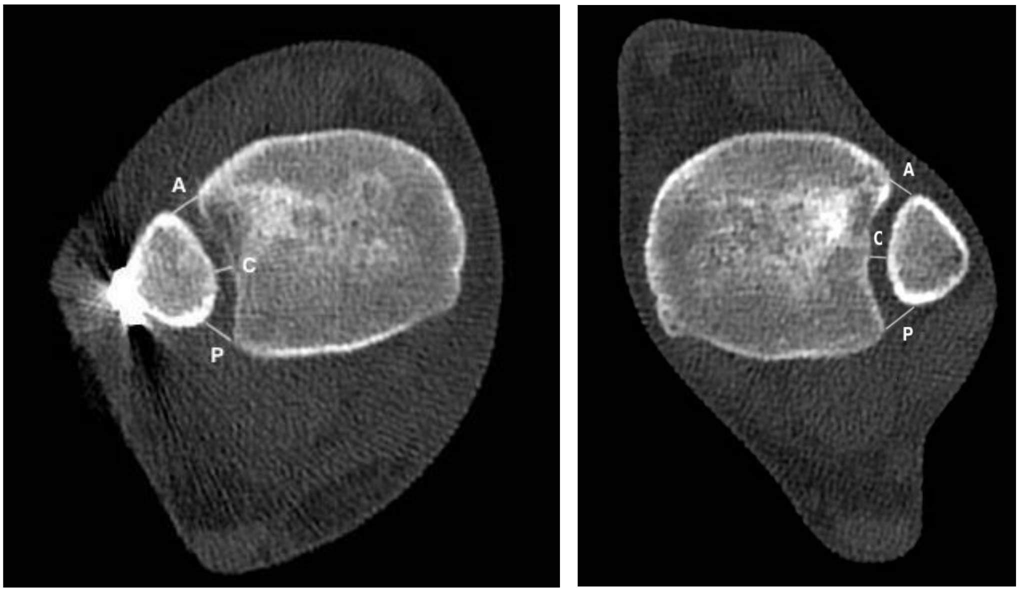


Figure 17: CT of injured ankle in a 20-year-old female, 2 years after injury. Tibiofibular distance is measured on axial CT 1 cm proximal to the ankle joint. Distance measured anterior (A); central (C); and posterior (P). Department of radiology, Bærum Hospital.

Classification of the posterior malleolar fracture

In Paper III, presence of a PMF was stated analyzing plain radiographs pre-operatively. Comparing this to postoperative CTs, the number of missed PMF on radiographs could be assessed. Then the PMF were then classified on postoperative CT scans according to the Haraguchi classification (7). Interobserver agreement for the Haraguchi classification was determined by three independent observers (first and second author, and one foot and ankle specialist). Disagreements between the observers were resolved by a plenary discussion between the raters. For the intraobserver (test-retest) agreement the first author (BWR) classified all CTs twice, with at least 6 months delay between the assessments.

Assessment of ankle OA

Assessed at five years for Paper I and at two years for Paper II and III. Presence of ankle OA was reported and classified according to the Kellgren-Lawrence grade system (146). This is not an ankle specific grading system, but widely used in describing ankle OA on radiographs (134,147). We applied the Kellgren-Lawrence grading system to assess our CT scans, defining mild OA as Kellgren-Lawrence grade 1-2 with the presence of osteophytes and advanced OA as Kellgren-Lawrence grade 3 and 4 with narrowing of the joint space and presence of sclerosis (Fig. 18).

Figure 18: Post traumatic OA in a 53-year-old male, 5 years after surgery. In this patient one can find subchondral cysts, sclerosis, narrowing of the joint space and a PMF heled in with a superior displacement. Department of radiology, Bærum Hospital.

Assessment of tibiofibular synostosis

Distal tibiofibular ossification was assessed in CT scans at 5 years in study I and at 2 years in study II. Patients were divided into three groups; no calcifications; calcifications present or; synostosis. Only patients with a complete ossification connecting the tibia to the fibula were registered with a synostosis (Fig. 19)

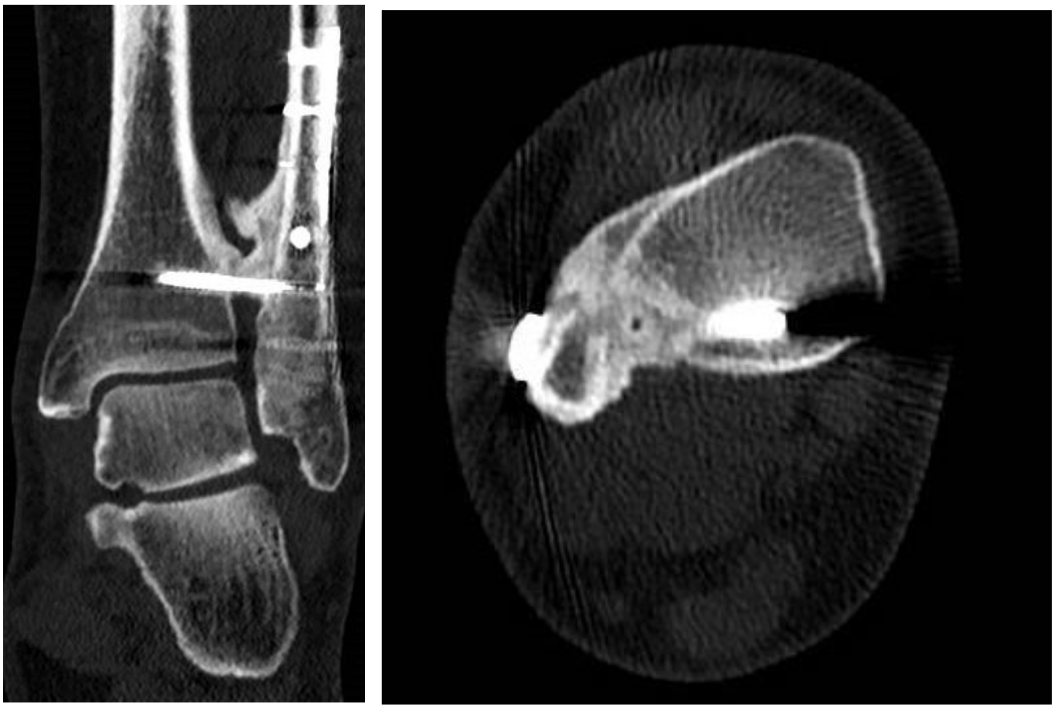


Figure 19: CT of 65-year-old-male, 2 years after injury. Coronal and Axial views of a complete tibiofibular synostosis. Department of radiology, Bærum Hospital.

Statistical methods

Study I and II:

Sample size was calculated according to the equivalence criterion and the extension of the CONSORT (Consolidated Standards of Reporting Trials) statement (148). Although the minimal clinically important difference (MCID) for the AOFAS is not defined specifically for ankle fractures, several authors have hypothesized it to be one half of the SD (147,149,150). Based on data from a previous trial with a similar population, the SD was estimated to 12 points (93), with a MCID of the AOFAS of 6 points. A between-group difference of 10 points (AOFAS) was used to ensure a sufficient inclusion of patients. 38 patients had to be included in each group to achieve a power of 0.95 and a significance level of 0.05. To strengthen the data and compensate for loss to follow-up, 50 patients in each group were planned for inclusion in study I and 60 patients in each group were planned for inclusion in study II. For study I and II, analyses were performed as both intention-to-treat and per-protocol. Patient baseline characteristics were analyzed using normality tests. 2-sided T-test was used to compare means of normally distributed data. The Mann-Whitney U-test was used in cases of skewed data. Fisher's Exact test was used for categorial data. For study I, multivariate regression analysis using the generalized estimation equation was used to compare outcome scores between the two groups, with adjustment for patient age, sex, PMF, medial malleolar fracture, Maisonneuve fracture type and osteochondral injury. Binary logistic regression was conducted to analyze our findings of OA at the 5-year-follow-up.

Study III

For study III we conducted inter- and intraobserver reliability tests. The Cohen's Kappa coefficient (κ) was used to determine the inter- and intrareliability for the fracture classification. The strength of examiner agreement was defined according to the guidelines of Landis and Koch as follows: poor, (κ)<0; slight, κ=0.0-0.20; fair, κ=0.21-0.40; moderate, κ=0.41-0.60; substantial, κ=0.61-0.80; almost perfect, κ=0.81-1.00 (151). The significance level was 0.05. Data analysis was conducted in IBM SPSS Statistics version 25 and 26. Due to the repeated data structure of the study design and incomplete dataset for the AOFAS (6 weeks: 94%, 6 months: 92%, 1 year 91% and 2 years: 81% follow-up) a linear mixed model analysis was performed. Adjustment for potential confounders (gender, age, BMI) was performed. The covariance structure autoregressive (1) (AR(1)) was chosen. Analysis was done with a random intercept model, comparing of the three different Haraguchi fracture types to no PMF at each control. Bonferroni adjustment was used for comparison of the main effect.

Ethics, approvals, conflicts of interest and funding

The study participants signed a written consent at inclusion after being informed by an orthopedic surgeon. Patients included received implants already in use on all departments. In addition to a 6-week follow-up, inclusion in study I and II lead to additional follow-ups and CT scans. Some might argue that additional controls were a benefit for the patients included, others might argue that the additional controls were time consuming. The radiation dose with a CT of an extremity is low. The group planning and conducting the studies do not find ethical problems with the studies in this thesis. Patients declining to participate in study I or study II received treatment according to the current guidelines of the participating hospitals.

Study I and II were approved by the regional Ethical Committee of South-Eastern Norway Health Authority (registration number 2010/2012 and 2015/1860) and the local Data Protection Official. Both RCTs were registered at www.clinicaltrials.gov (registration number NCT01275924 and NCT02930486). For study III, the regional Ethical Committee of South-Eastern Norway Health Authority approved the use and re-analysis of data from study I and II (registration number 2020/69005).

There was no external funding to conduct the studies of this thesis. The main author received a research grant of 50 000 NOK from the Norwegian Orthopaedic association (Norsk Ortopedisk Forening) in 2017. The co-authors of the studies have no conflict of interest to declare.

Main results

Paper I

The 5-year follow-up rate was 84%. Patients treated with SB had a higher median AOFAS score (100 (IQR 92 to 100) vs 90 (IQR 85 to 100); p=0.006), and higher median OMA score (100 (IQR 95 to 100) vs 95 (IQR 75 to 100); p=0.006) (Fig. 20 and Fig. 21). The SS group had a higher incidence of ankle OA at five years (24 (65%) vs 14 (35%), OR: 3.4 (95% CI: 1.3 to 8.8); p=0.009). On axial CT, we measured a significantly smaller mean difference in the anterior tibiofibular distance between injured and non-injured ankles in the SB group (-0.1 mm vs 1.2 mm; p=0.016). The ability to dorsiflex the ankle was better in the SB group, but only by 4 degrees, most likely not clinically significant. Between two- and five-years follow-up, only one reoperation was registered, an ankle arthroscopy due to anterior impingement.

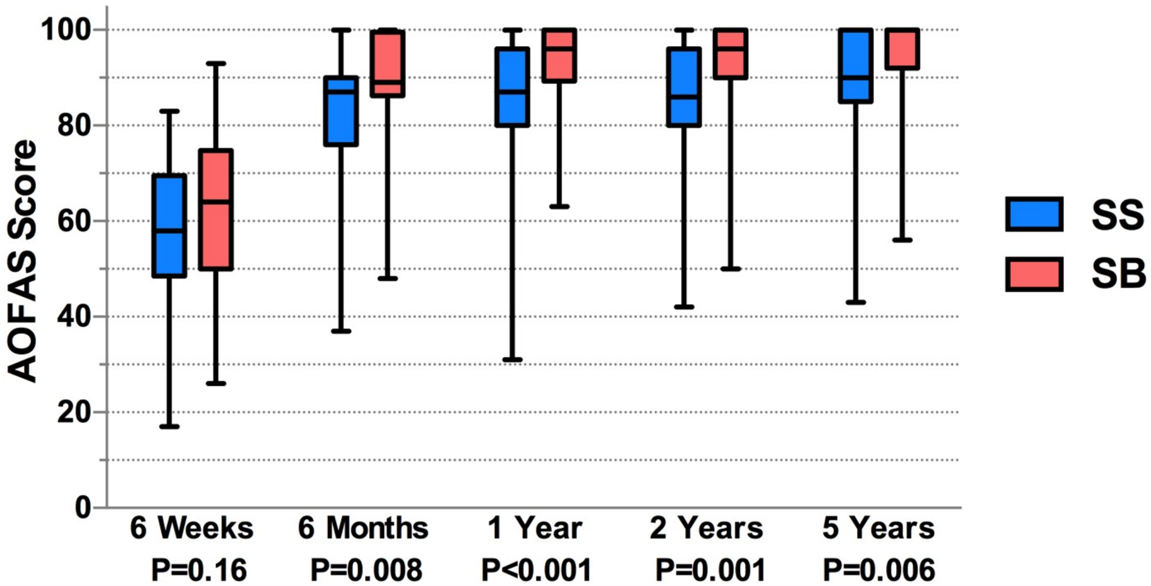


Figure 20: Results for paper I. Boxplots of the AOFAS score at all time intervals. The boxed represent the middle 50% of the data, with central bands representing the median. The whiskers represent the minimum and maximum recorded score. Analysis with Mann-Whitney U-test. SS= 4.5 mm quadricortical syndesmotic screw. SB= suture button (TightRope®, Arthrex).

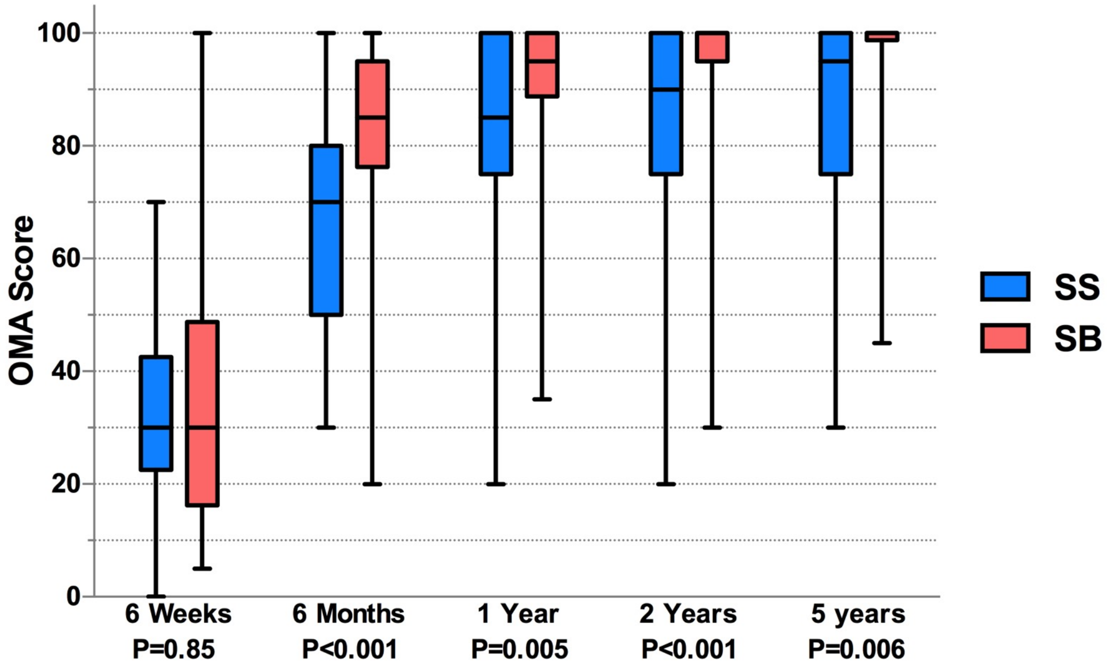


Figure 21: Results for paper I. Boxplots of the OMA score at all time intervals. The boxed represent the middle 50% of the data, with central bands representing the median. The whiskers represent the minimum and maximum recorded score. Analysis with Mann-Whitney U-test. SS= 4.5 mm quadricortical syndesmotic screw. SB= suture button (TightRope®, Arthrex).

Paper II

The two-year follow-up rate was 84%. At two years, median AOFAS was 97 in both groups (IQR SB: 87-100, IQR StSS: 90-100, p=0.7) (Fig. 22). The AOFAS results were equivalent when comparing the groups, with mean AOFAS difference between the groups overlapping and inside the margins of the 95% CI at all controls (Fig. 23). Median MOXFQ index was 5 in the SB group and 3 in the StSS group (IQR SB: 0-18, IQR StSS: 0-8, p=0.2) (Fig. 24), and median OMA score was 90 in the SB group and 100 in the StSS group (IQR SB: 75-100, IQR StSS: 83-100, p=0.2). The syndesmotic reduction was similar 2 years after surgery; 19 (35%) patients in the SB group and 13 (22%) in the StSS group had a difference in anterior syndesmotic width ≥ 2 mm (p=0.3). 0 patients in the SB group and 5 patients (11%) in the StSS group had complete tibiofibular synostosis (p=0.03). At 2 years, 10 StSS were broken. Complications and reoperations did not differ between the groups.

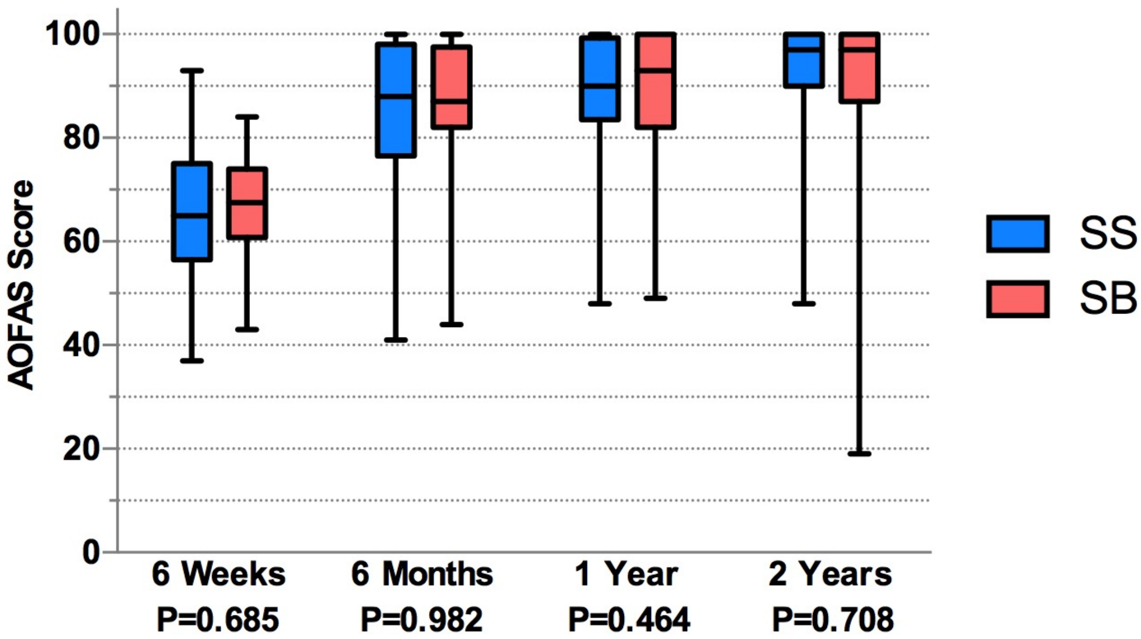


Figure 22: Results for paper II. Boxplots of the AOFAS score at all time intervals. The boxed represent the middle 50% of the data, with central bands representing the median. The whiskers represent the minimum and maximum recorded score. Analysis with Mann-Whitney U-test. SS = Single 3.5 mm Tricortical Syndesmotic screw. SB = Suture button (ZipTight™, Biomet).

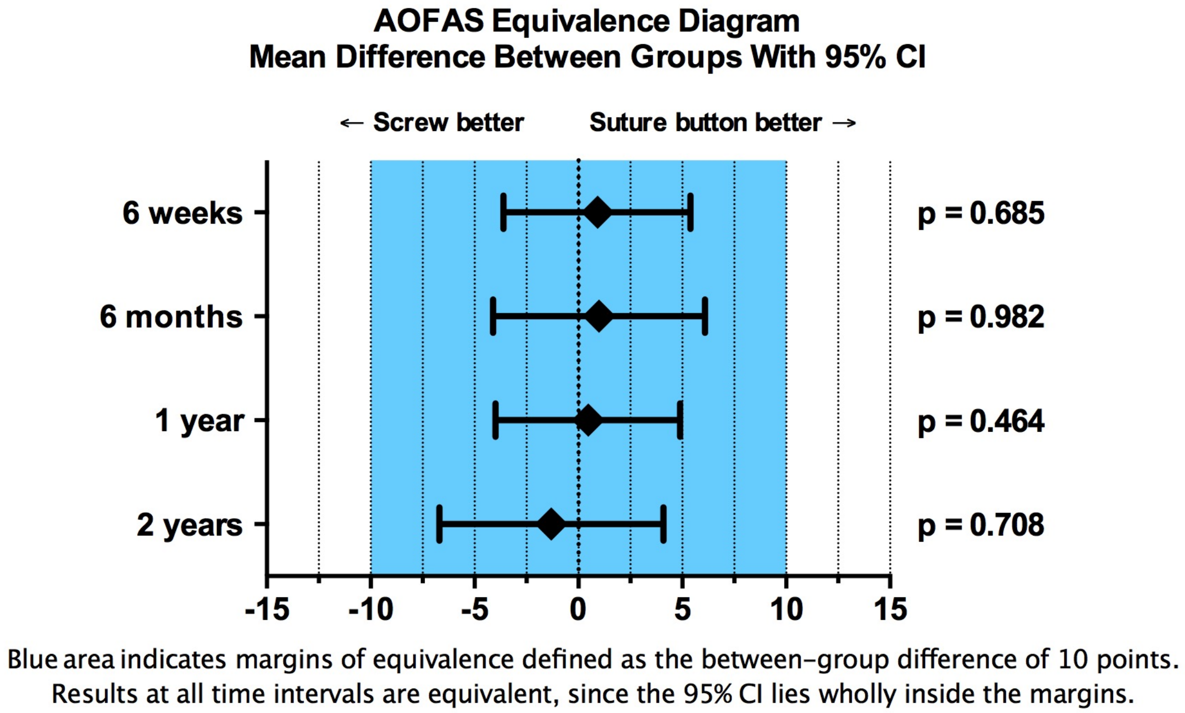


Figure 23: Results paper II. Equivalence Diagram for the AOFAS results.

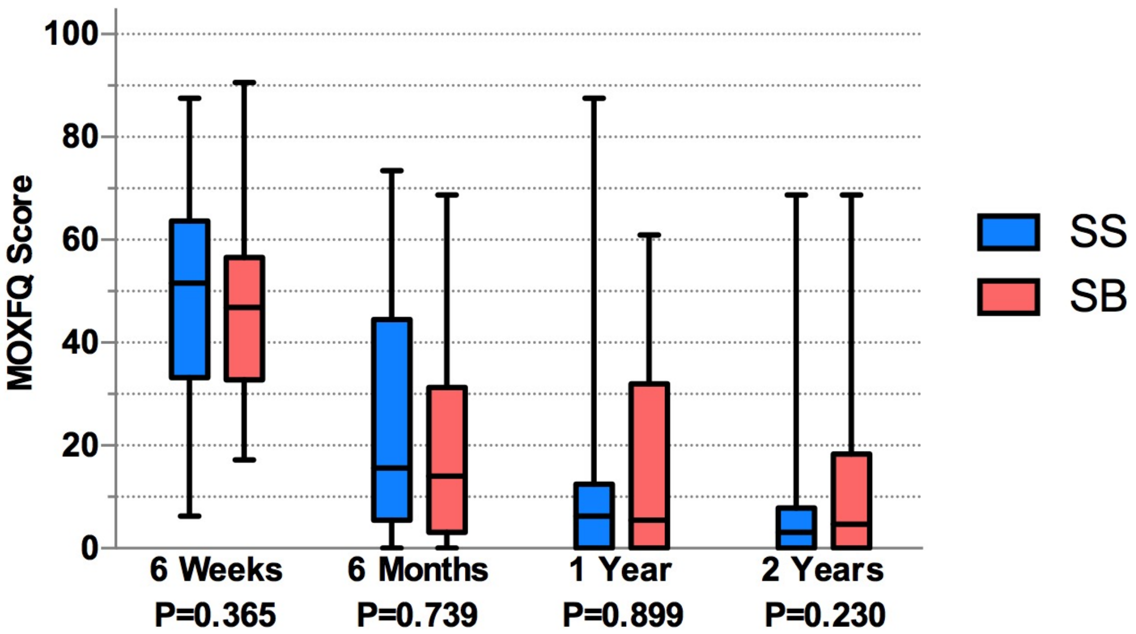


Figure 24: Results for paper II. Boxplots of the MOXFQ score at all time intervals. The boxed represent the middle 50% of the data, with central bands representing the median. The whiskers represent the minimum and maximum recorded score. Analysis with Mann-Whitney U-test. SS = Single 3.5 mm Tricortical Syndesmotic screw. SB = Suture button (ZipTight™, Biomet).

Paper III

The two-year follow-up rate was 87%. 210 patients were divided into 4 groups, one for patients without a PMF, and three groups according to Haraguchi type I-III. Gender distribution differed between the groups, with males dominating the group without PMF (73%) and Haraguchi type III (69%). In the Haraguchi type II group, 68% of the patients were female. Out of all PMFs, 17 (13%) had a PMF addressed surgically, with the highest number of fixed fractures in the Haraguchi II group. All PMFs were classified according to Haraguchi: We found 61 (49%) Type I, 28 (22%) type II and 36 (28%) type III fractures. The intraobserver agreement for the Haraguchi classification was 0.733, (95% CI: 0.629 to 0.884) p<0.001. The interobserver agreement for the Haraguchi classification was 0.797, (95% CI: 0.705 to 0.889) p<0.001. When comparing plain radiographs (AP, mortise and lateral view) to CTs, 42 (34%) of the PMFs (22 (36%) Haraguchi type I, 1 (4%) Haraguchi type II and 19 (53%) Haraguchi type III) were missed when assessing plain radiographs. Two patients were assessed to have a PMF on plain radiographs, when there was no fracture visible on CTs. The presence of OA ranged from 34.5 % in the Haraguchi III group to 64% in the Haraguchi II group. The difference between the groups was not significant.

In the mixed model analysis, the AOFAS between the four PMF groups had similar slopes and the group effect did not change significantly over time (Fig. 25) (p=0.234). When analyzing the differences in AOFAS between the four PMF groups at each time point with a mixed model analysis the Haraguchi type II fracture had a significantly lower AOFAS at 6 weeks (-7.5 (95% CI; -15.0, -0.2), p=0.04) and 6 months (-8.4 (95% CI; -15.3, -1.5), p= 0.01) compared to patients with no PMF.

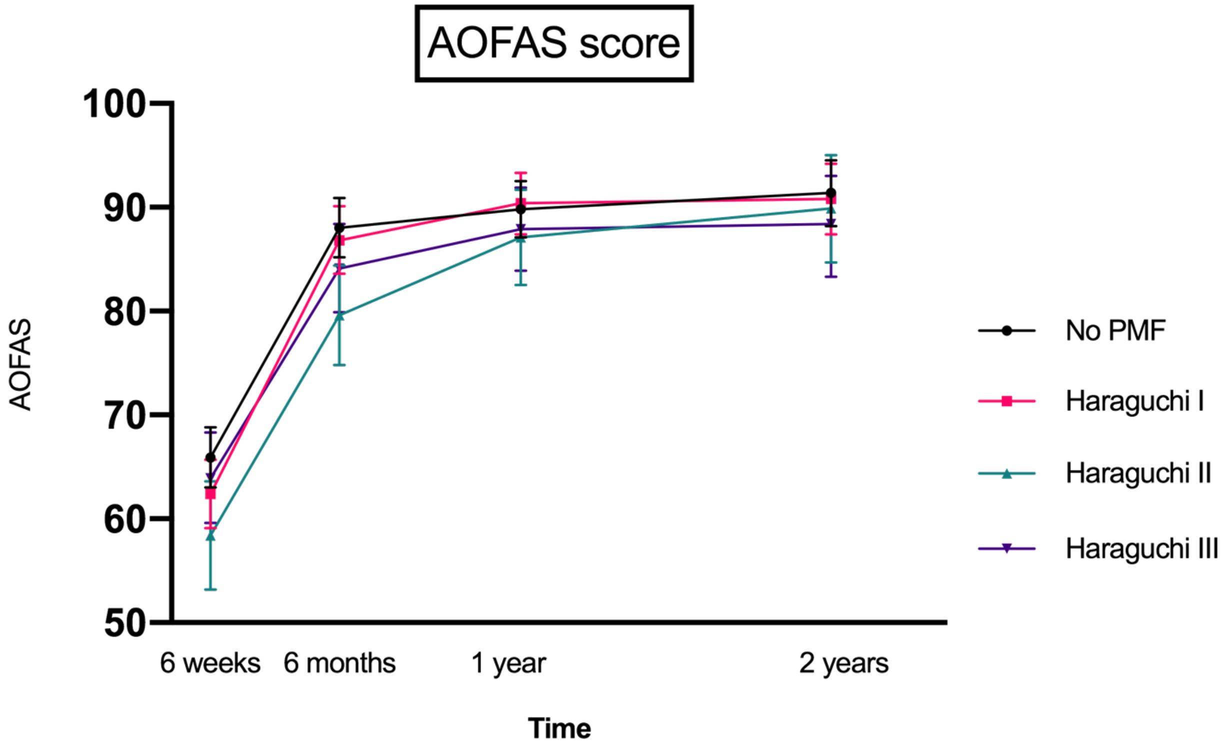


Figure 25: Results from paper III: Line graph illustrating the slope of the AOFAS for the four subgroups of patients with confidence intervals.

Discussion

Discussion of methods

Study design: Paper I & II

Study I and II are both RCTs with a 5- and 2-year follow-up period, respectively. An RCT is regarded as level 1 or 2 evidence for therapeutic studies (152). The studies were conducted as equivalence trials in accordance with the CONSORT statement of non-inferiority and equivalence trials (148). By conducting an RCT the goal is to achieve comparable groups with respect to known and unknown risk factors (153), reducing selection bias and confounding (154). In paper I, we did block randomization with sequentially numbered, concealed, opaque envelopes. Patients were randomized using a random number generator with permuted blocks of 10 (99). Block randomization avoids imbalance in the number of participants assigned to each group, which can occur with simple randomization (for example a coin toss). In addition, blocked randomization guarantees that the allocation is balanced throughout the randomization process (155). In the first study, three randomization envelopes went missing. In light of this and the fact that the study was conducted at three hospitals, we decided to do the block randomization by online means (156).

Blinding in an RCT can minimize bias and enhance validity of the results (157). In surgical trials, blinding of the patient and surgeon is particularly difficult (158). In Paper I we did not use blinding, which is a weakness in the results of Paper I. In paper II, a physiotherapist blinded to the intervention conducted the measurements for the AOFAS and the range of motion test at 1 and 2 years. This was done to reduce bias, type 1 error and enhance the validity of the results. For both studies, a non-inferiority design was chosen, to underline the open question on whether any method was better than the other.

Study design: Paper III

By selecting all patients from Paper I and II, we were able to increase the number of subjects with PMF for analysis. The study is a level 3 diagnostic cohort study (152) with enrolment over 7 years (2011-2017). The two studies we used to conduct our subgroup analysis has the same inclusion and exclusion criteria, which is a strength in Paper III, making the study populations comparable. The long duration of patient enrolment represents a weakness in paper III, since there has been an increasing trend in fixating PMF surgically. More patients in study II had their PMF fixed (5 patients in Paper I and 12 patients in Paper II).

Primary outcome measure

The choice of our primary outcome score, the AOFAS, has been subject to debate and criticism. The AOFAS has one patient reported part and an objective part consisting of measurements obtained by an examiner (Appendix 1). The AOFAS is criticized for producing skewed data and having a ceiling effect. The AOFAS is not validated for ankle fractures.
We choose to use of the AOFAS because of its frequent use in other studies. By applying this in both Paper I and II we could more easily compare the results. To compensate for the AOFAS limitations, we added VAS, Eq-5D, OMA and MOXFQ as secondary outcome measures.

Statistics

Sample size

Sample size was calculated according to the equivalence criterion (148). Sample size calculations are needed to determine the number of patients to be included in a clinical trial to represent the population. The MCID is a parameter used to determine the required sample size to reach the statistical power needed to conclude on statistically significant treatment effect when comparing groups (159). The AOFAS was the primary outcome measure in all the papers of this thesis, however, the MCID is not defined for ankle fractures (160,161). In order to conduct sample size calculations for Paper I and II and to interpret the results we needed to define the MCID for the AOFAS. A hypothesis is that ½ SD can be used as an indicative for the MCID (147,162). By using the ERES-method described by Sloan, the MCID would be 6, based on previous studies (93,163). The choice of MCID must be justified by both statistical and clinical ground. Using ½ a SD to define MCID will provide information on how difficult it would be to detect a difference, but it does not give information on the clinical relevance of this difference. We chose to use a 10-point difference in the AOFAS score in sample size calculations, to ensure a sufficient number of patients enrolled. 38

patients had to be included in each group to achieve a power of 95 and a significance level of 0.05.

Statistical analysis: Paper I & II

For continuous, normally distributed data, values were given as mean with SD and tested with the 2-sided T test. For continuous, not normally distributed data, values were given as median with IQR and tested with the Mann-Whitney U-test. Analysis of endpoint results were performed as both intention-to-treat and per-protocol. Statistical significance was set at a p-value of <0.05 and a 95% CI was used to describe uncertainty.

Statistical analysis: Paper III

Due to the repeated data structure of the study design and incomplete dataset for the AOFAS (6 weeks: 94%, 6 months: 92%, 1 year 91% and 2 years: 81% follow-up), a linear mixed model analysis with adjustment for potential confounders (gender, age, BMI) was performed. The advantage of using a mixed model is the handling of missing data. In cases with missing data at one timepoint, this time point is deleted and treated as random, while the subject owning the data is kept for further analysis at other timepoints (164). The covariance structure autoregressive (1) (AR(1)) was chosen. Analyses were conducted with a random intercept model, comparing the three different Haraguchi fracture types to no PMF at each control. Bonferroni correction was conducted for comparison of the main effect to protect for type-I error (incorrect rejection of the null- hypothesis). To assess the reliability of the Haraguchi classification the ICC was calculated. When a measurement is done by different observers (inter-rater) or the same observer repeatedly (intra-rater or test-retest), the ICC (κ) will be an assessment of reproducibility and agreement. The strength of examiner agreement was defined according to the guidelines of Landis and Koch(151) as follows: poor, (κ)<0; slight, κ=0.0-0.20; fair, κ=0.21-0.40; moderate, κ=0.41-0.60; substantial, κ=0.61-0.80; almost perfect, κ=0.81-1.00.

Syndesmotic width measurement

For all studies we measured and compared anterior, central and posterior tibiofibular distance to describe the tibiofibular relationship. Several studies have used these measurements and a 2 mm difference between sides has been proposed as a cut-off for malreduction (70, 166). When comparing the anterior, central and posterior tibiofibular distance, the anterior and central measurement has the highest ICC, with a moderate agreement on the Landis and Koch Scale (0.5-0.7) (151,165). In addition to tibiofibular distance, the placement of the fibula in the incisura can indicate correct reduction. Lepojärvi et al. found that the fibula was located anteriorly or centrally in 97% of the patients, and that malreduction should be suspected if the posterior translation is found postoperatively (166). In a study by Nault et al. a new method to measure the tibiofibular relationship was proposed, which incorporates fibular translation and rotation in addition to the tibiofibular distance. This method gave 6 measurements and 2 angles (167). Finding the translation and rotation of the fibula gives additional information, that might go unnoticed when only measuring anterior, central and posterior distance. Not applying this is a weakness in paper I and paper II.

Measurement of osteoarthritis

A weakness in all the studies is a lack of statistical power to conclude on the OA findings. In addition, we did not use a validated system to measure OA on CTs, challenging the reproducibility of our results. The Kellgren-Lawrence grading system is described for weight bearing radiographs (146). For all our studies, the same senior musculoskeletal radiologist conducted the analysis for OA. OA assessment was done by analyzing CTs. Presence of osteophytes, cysts and joint space narrowing were noted and classified as either no OA, signs of OA or advanced OA. Signs of OA were extrapolated to correspond to a KL of 1-2 and advanced OA to correspond to KL 3-4. In 2015, a CT atlas for grading ankle OA was validated. The atlas grades OA from 0 (no OA) to 3 (severe OA), based on osteophytes, subchondral cysts, sclerosis of the talus, tibiofibular alignment and potential joint space narrowing (168). The atlas is a valid tool that could benefit further studies.

Choice of classification system for PMFs

Of the three classification systems, we chose the Haraguchi classification where fractures are classified from I to III (fig 4). In the classification by Bartonicek, equivalent types to Haraguchi type I to III are described. In addition, Bartonicek describes a type 4, which includes larger posterolateral triangular fragments (involving more than one-third of the notch) (8). In the classification by Mason there are 3 types equivalent to the Haraguchi fractures (type 1, type 2a and type 2b). This classification also has a forth type (type 3), which is a coronal plane fracture line involving the whole posterior plafond, which is described to be a posterior pilon fracture (Table 1) (9). The AO/OTA C fracture, is in theory a rotational, not an impaction injury. Hence using the classification by Bartonicek or Haraguchi would be the most sensible, as we did not expect to find any posterior pilon fractures. We chose to use the Haraguchi since the Haraguchi fracture types are all described in the two other classification systems. In the one clinical trial assessing outcome according to fracture pattern, fractures are classified according to Haraguchi, which makes our results comparable (83). When applying the Bartonicek classification to our dataset, 5 PMFs would have been classified as a Bartonicek type 4.

Discussion of results

The aims of this thesis were to evaluate the outcomes of different implants when restoring syndesmotic integrity and investigating the clinical implications of a PMF in patients with OTA/AO C fracture.

Treatment and implant choice for syndesmotic injuries

In paper I, the SB had superior results compared to 4.5 mm quadricortical SS at 5 years. In paper II, SB and 3.5 mm tricortical SS gave the same outcome after 2 years. These trials are conducted at the same hospitals (OUS and Bærum for paper I, adding Kalnes for paper II). An explanation for the difference in the results could be the 4 different implants used in the two studies (4.5 mm quadricortical screw and TightRope®in the first study, 3.5 mm tricortical screw and ZipTight™ in the second study). Especially the use of two different SB implants can be a potential bias when comparing results between the two studies. Wikerøy et al. found no difference between a quadricortical screw and two tricortical screws (93). The dynamic properties of the screws in vivo are not known, but there are biomechanical studies looking into this issue. Clanton found that one tricortical screw had some dynamic properties (169). Fixing the syndesmosis with several tricortical screws or a quadricortical screw will lock the fibula to the incisura. One tricortical screw may be more dynamic, allowing some micromovement. Since the publication of paper I, Several meta- analyses have been published comparing SB to SS. The studies included in these meta-analyses use a variety of implants in a variety of numbers (95,170-172). The SB group contains 1 or 2 SBs. In the meta-analyses the SB group is compared to screw fixation, which can be one or two 3.5 mm, one 4.5 mm, one 6.5 mm, engaging 3 or 4 cortices (95). In paper II, we found a single tricortical screw to be sufficient for syndesmotic fixation. The loss of reduction was the same comparing StSS to SB (one patient in each group). Our similar results comparing StSS and SB agrees with Kortekangas' findings (94). Several metanalyses find the SB superior, with better reduction and lower implant removal rate. However, treatment heterogeneity, small samples, and lack of personnel blinding are limiting for the quality of the evidence (95,170-172).

Syndesmotic reduction

In study I and II, there was a significant number of patients with ≥2 mm difference in syndesmotic width between normal and injured ankle, which is suggested as a cut of value for malreduction (70, 165). In the first study, 15% of the patients treated with SB and 23% treated with quadricortical screw had with ≥2 mm difference measured anteriorly postoperatively (p= 0.4). In the second study 35% treated with SB and 28% treated with StSS had a ≥2 mm difference measured anteriorly (p= 0.5). Achieving a side to side similar syndesmotic reduction depends on surgical technique, implant choice and measurement technique. We did all our syndesmotic reductions in a closed manner. When compared, open reduction has given better results regarding syndesmotic reduction (67). In our 2 studies, a total of four different implants were used, presenting a weakness when comparing the reduction between studies. Our first study and several published meta- analyses does suggest that a SB has a better rate of adequate reduction (95,170). A reason for this could be that the fibula more easily will find its way to its position in the incisura with the more dynamic SB fixation, giving a better reduction. Our measurements were done manually. The measurements were rounded off to the nearest millimeter, this could be a source of inaccuracy.

Recurrent syndesmotic diastasis

For all patients seen in the two trials, seven patients treated with 4.5 mm quadricortical screw, one patient treated with 3.5 mm tricortical screw and one patient treated with ZipTight™ SB experienced recurrent diastasis. In five of the patients treated with 4.5 mm SS, the diastasis was suspected to occur after screw removal which was planned 10-12 weeks after surgery. The timing of screw removal is debated and advised from 6-12 weeks (115). Both loss of reduction and achievement of better reduction is found after screw removal (117,173). The finding of recurrent syndesmotic diastasis in the 4.5 mm quadricortical screw patients can be seen as another disadvantage for a thick screw requiring routine removal with a potential loss of reduction.

Fixing the PMF in cases with syndesmotic instability

At present there are no RCTs comparing fixation of a PMF to syndesmosis fixation. There are however, several retrospective trials looking into this issue (109,110,174). Li et al. concludes that fixing a sizable PMF reduces the need for additional syndesmotic fixation. A direct ORIF has a lower need for additional syndesmotic fixation compared to an indirect approach with AP screws (110,174). When a PMF fixation reduces the need for a SS will depend on the fracture morphology. Fixating a Volkmann fracture (Haraguchi type I) with a direct posterolateral approach would ensure an anatomical reduction, restoring the incisura, providing anatomic length and tension of the PITFL. Some PMF are shell-fragments and hard to fixate directly. Mason found syndesmotic disruption inn 100% of the extra incisural fragments (Haraguchi III) (9), which are rarely or never addressed by a PMF fixation (8). If one finds syndesmotic instability along with a Haraguchi III fracture, a syndesmotic fixation is advised (65). Further research is needed to conclude on whether a fixation should be directly addressing the PMF or indirectly with a SB or SS across the incisura.

Use of CT as a diagnostic tool and post- operative control

The use of CT in pre- and postoperative control is increasing in the clinical practice (175). The radiation of a cone beam CT of the foot and ankle is 0.0038 mSv, less than a chest radiograph (0.1mSv), equivalent to a few hours of background radiation present in the environment. This makes the radiation dose negligible with this examination (176). In Paper I and II, postoperative CT was used as a control for fracture and syndesmotic reduction. The postoperative CT lead to some early reoperations because of unacceptable screw placement, fracture- or syndesmotic- reduction (four patients in Paper I and six patients in Paper II). An unacceptable fracture reduction can be visible on plain radiographs, but for diagnosing malreduction of the syndesmosis, a postoperative CT control should be conducted.

In Paper III, 34% of PMF were missed on radiographs, compared to postoperative CTs. Most of the PMFs missed were Haraguchi type III fractures (53%). These fractures are rarely addressed surgically, hence diagnosing a Haraguchi type III will most likely not affect decision making regarding PMF fixation (8). Presence of this fracture type does, however, provide information on syndesmotic disruption (9) and potential syndesmotic instability. We missed 22 Haraguchi I and 1 Haraguchi II fracture. According to these data, we cannot conclude if catching these fractures preoperatively would have changed the treatment.

The AO surgical reference and several authors recommend a pre-operative CT when suspecting a PMF (65,87,177). By keeping a low threshold for performing a postoperative CT control, relevant malreduction can be detected (87). In a critical analysis review, Rammelt and Boszczyk propose a grade B recommendation for preoperative CT for malleolar fractures with an unstable syndesmosis and PMF, and a grade C recommendation for postoperative CT scan (87). Our results from Paper I, II and III supports these conclusions.

Outcome after a PMF fracture

In previous studies, presence of a PMF has been associated with worse outcome in terms of stiffness, OA and low PROMs (101,177,178). In our analysis, we found that the Haraguchi type II fractures was the only fracture type that had a worse outcome (lower AOFAS score) up until 6 months. A weakness in our results is the fact that when and how a PMF was fixed, was decided by the surgeon. In addition, all patients received a syndesmotic fixation, making it challenging to compare outcomes between fractures. Rammelt has in his critical review suggested treatment options for PMF. The suggestion is to treat extra-incisural fragments nonoperatively, displaced posterolateral fractures with direct fixation, medial extension fractures with direct fixation, and large triangular fragments with either direct or indirect fixation (177). Wang et al. found no significant difference in outcomes between AP, PA and plate fixation in PMF involving >15% of the joint space. They found higher AOFAS scores in patients with PMF involving <15% when fractures were fixed with screws (AP or PA) compared to direct plate fixation (179). This study was retrospective, did not describe fracture morphology and fixation method was according to surgeon's choice. Studies analyzing patient outcomes after treatment of a PMF with standardized fixation techniques randomized by fracture pattern could enhance the knowledge in this area further.

Relevant complications

The studies are conducted on patients aged 18-69 years, and exclusion criteria included peripheral neuropathy. Thus, the clinical implications of our results should be limited to patients younger than 69 years, without peripheral neuropathy. There are currently no studies published on SB done in the geriatric population, or in patients with known peripheral neuropathy or known poor bone quality. In Paper II, 2 patients (male, age 50 and female, age 52 years) suffered a low-energy tibia fracture through the SB canal. They both had a large PMF, both addressed surgically from a posterolateral approach. A dual energy x-ray absorptiometry (DEXA scan) showed osteoporosis in the female. There is one case report describing a low energy fracture through the SB canal (100). Further studies might answer if SB is suitable in the elderly.

Conclusions

- A suture button has better clinical and radiological results compared to a 4.5 mm quadricortical screw for acute syndesmotic injuries in patients followed for 5 years.
- A suture button is equivalent to a 3.5 mm tricortical screw when comparing clinical and radiological results in patients followed for 2 years after acute syndesmotic injury.
- Significantly more patients treated with a 4.5 mm quadricortical screw had a recurrent syndesmotic diastasis at 1 year compared to SB.
- Complications and unplanned reoperations do not differ when comparing a suture button to a 3.5 mm tricortical screw.
- To stabilize an acute syndesmotic injury in patients 18-69 years, either a suture button or one 3.5 mm StSS is recommended.
- A PMF is common in patients with an AO 44-C ankle fracture. In our patient cohort, 60% had a concomitant PMF.
- Plain radiographs underestimate the presence of a PMF, in particular the Haraguchi type III.
- The Haraguchi classification has a high inter- and intra rater reliability, providing orthopedic surgeons with a valid tool for describing PMFs.
- Fractures with a medial extension (Haraguchi II) result in a poorer outcome at 6 weeks and 6 months compared to AO 44- C ankle fractures without a PMF.

Suggestions for future research

All our patients with an AO/OTA C injury were treated with syndesmotic stabilization according to protocol. The medial deltoid ligament is found to be the primary stabilizer of the ankle, preventing external rotation of the talus (88). In a recent ESSKA-AFAS consensus, Van Dijk et al. proposes that isolated syndesmotic injuries with intact deltoid ligament can be managed conservatively (181). A new RCT is being planned as a multicenter study in Norway, where patients with a stable, isolated suprasyndesmotic (AO/OTA C) fracture, are randomized to surgical or non-operative intervention.

In our studies we found similar results comparing tricortical SS to SB and poorer results for quadricortical screw compared to SB. We conclude that the tricortical SS is less rigid, and acts similarly to the SB. Considering our findings, meta-analyses should stratify groups by the number of screws and how many cortices they engage, rather than placing them in one group.

Future studies could compare different methods of assessing the tibiofibular relationship and possibly find an efficient way to measure and conclude on malreduction, with incorporation of tibiofibular distance, fibular rotation and translation measured by CT. The conventional CT scan is a static modality. Weightbearing radiographs can be helpful in detecting ankle instability. Weight bearing CT scans provides new possibilities, in detecting dynamic instability of the syndesmosis. Clinical studies with weight bearing CTs should be conducted.

The stabilization test, or “tape test” is commonly used for assessing subacute or chronic syndesmotic instability. A study validating this test, comparing it to findings done by arthroscopy, would enhance knowledge on its usefulness as a tool in making a diagnosis of syndesmotic instability based on clinical findings.

Future studies assessing ankle OA, could benefit by using the validated CT for grading ankle OA by Cohen (169).

In our first study, there was an observed increase in the syndesmotic width with time. The reason for this is unknown. After ACL reconstruction, enlargement of the bone tunnel is a known phenomenon (182). We are currently planning a study to analyze the SB canal width by assessing CTs from Paper I to assess SB canal widening with time.

Several studies find that fixing a PMF directly can restore syndesmotic integrity, making a syndesmotic fixation redundant. Further research is needed to conclude on this matter, preferably an RCT. There is currently one study registered at Clinicaltrials.gov (NCT02599285), where patients are randomized to either fixation of the syndesmosis or ORIF of a PMF, then testing the syndesmotic stability and fixing it with a SS, if found unstable. The results from this study can contribute to the knowledge of syndesmotic stability and outcome after PMF fixation alone.

Authors have suggested treatment of a PMF according to fracture pattern (10,65). Studies analyzing patient outcomes after treatment of a PMF with standardized fixation techniques allocated by fracture pattern could enhance the knowledge in this area.

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Appendix

1 AOFAS
2 OMA
3 Eq5D
4 VAS
5 MOXFQ
6 Paper I
7 Paper II
8 Paper III

OTA Ankle-hindfoot Scale (total 100 points) Kitaoka et al. Foot & Ankle Int. Vol 15 No 7/July 1994

Pain (40 points)			
		None	40
		Mild, occasional	30
		Moderate, daily	20
		Severe, almost always present	0
Function (50 points)			
	Activity limitations	No limitations, no support	10
		No limitations of daily activities, limitations of recreational activities, no support	7
		Limited daily and recreational activities, cane	4
		Severe limitations of daily and recreational activities, walker, crutches, weelchair, brace	0
	Maximum walting distans, blocks	Greater than 6	5
		4-6	4
		1-3	2
		Less than 1	0
	Walking surfaces	No difficulty on any surface	5
		Some difficulty on uneven terrain, stairs, inclines, ladders	3
		Severe difficulty on uneven terrain, stairs, inclines, ladders	0
	Gait abnormality	None, slight	8
		Obvious	4
		Marked	0
	Saggital motion (Flexion plus extension)	Normal mild restriction (30°)	8
		Moderate restriction (15-29°)	4
		Severe restriction (less than 15°)	0
	Hindfoot motion (inversion + eversion)	Normal or mild restriction (75%-100%)	6
		Moderat restriction (25%-74% normal)	3
		Marked restriction (Less than 25% normal)	0
	Ankle-hindfoot stability (AP, varus/valgus)	Stable	8
		Definetly unstable	0
Alignment (10 points)			
		Good, plantigrade foot, ankle-hindfoot well alignet	10
		Fair, plantigrade foot, some degree of ankle-hindfoot malalignment observed, no symptoms	5
		Poor, non-plantigrade foot, severe malalignment, symptoms	0

Pasientnr. Dagens dato:

Sett ring: 6 uker 6 mndr 1 år 2 år 5 år

Olerud og Molander Ankel score

Utfylles av lege/fysioterapeut Sett ring omkring ett av valgene for hvert spørsmål

Parameter	Grad	Score
1. Smerte	Ingen	25
	Gange på ulendt terreng	20
	Gange på jevnt underlag utendørs	10
	Gange innendørs	5
	Konstante og sterke	0
2. Stivhet	Ingen	10
	Stiv	0
3. Hevelse	Ingen	10
	Bare om kvelden	5
	Konstant	0
4. Trappe-gang	Ingen problemer	10
	Noe vanskeligheter	5
	Umulig	0
5. Løping	Mulig	5
	Umulig	0
6. Hopping	Mulig	5
	Umulig	0
7. Sitte på huk	Ingen problemer	5
	Umulig	0
8. Bruk av støtte	Ingen	10
	Taping, støttebandasje	5
	Stokk, krykke	0
9. Arbeid, daglige gjøremål	Samme som før skaden	20
	Redusert tempo	15
	Byttet til lettere jobb/deltid jobb	10
	Alvorlig redusert arbeidskapasitet	0
		Total:

Dårlig (poor)= 0-30 Middels (fair)= 31-60 God (good)= 61-90 Veldig god (excellent)= 91-100

Signatur:

EQ - 5D

Vis hvilke utsagn som passer best på din helsetilstand i dag ved å sette et kryss i en av rutene utenfor hver av gruppene nedenfor.

Gange

Jeg har ingen problemer med å gå omkring. ☐

Jeg har litt problemer med å gå omkring. ☐

Jeg er sengeliggende. ☐

Personlig stell

Jeg har ingen problemer med personlig stell. ☐

Jeg har litt problemer med å vaske meg eller kle meg. ☐

Jeg er ute av stand til å vaske meg eller kle meg. ☐

Vanlige gjøremål *(f.eks. arbeid, studier, husarbeid, familie- eller fritidsaktiviteter).*

Jeg har ingen problemer med å utføre mine vanlige gjøremål ☐

Jeg har litt problemer med å utføre mine vanlige gjøremål. ☐

Jeg er ute av stand til å utføre mine vanlige gjøremål. ☐

Smerte/ubehag

Jeg har verken smerte eller ubehag. ☐

Jeg har moderat smerte eller ubehag. ☐

Jeg har sterk smerte eller ubehag. ☐

Angst/depresjon

Jeg er verken engstelig eller deprimert. ☐

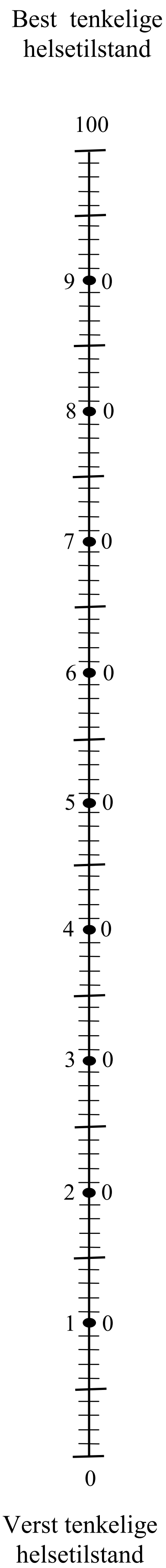
Jeg er noe engstelig eller deprimert. ☐

Jeg er svært engstelig eller deprimert. ☐

For å hjelpe folk til å si hvor god eller dårlig en helsetilstand er, har vi laget en skala (omtrent som et termometer) hvor den beste tilstanden du kan tenke deg er merket 100 og den verste tilstanden du kan tenke deg er merket 0.

Vi vil gjerne at du viser på denne skalaen hvor god eller dårlig helsetilstanden din er i dag, etter din oppfatning. Vær vennlig å gjøre dette ved å trekke en linje fra boksen nedenfor til det punktet på skalaen som viser hvor god eller dårlig din helsetilstand er i dag.

Din egen helsetilstand i dag



Visuell score (pasienten skal selv avmerke)

Smerter i hvile:

Ingen 0........1........2.........3........4........5........6.........7........8........9........10 Utålelige

Smerter ved gange:

Ingen 0........1........2.........3........4........5........6.........7........8........9........10 Uutholdelige

Smerter om natten:

Ingen 0........1........2.........3........4........5........6.........7........8........9........10 Intensive

Daglige aktiviteter:

Normale 0........1........2.........3........4........5........6.........7........8........9........10 Meget reduserte

	J	Delvis	Nei
Hvis hemmet, skyldes hemming ankelskaden?	☐	☐	☐

Manchester-Oxford Foot Questionnaire (MOxFQ)

Norsk versjon (Bokmål) for Norge

Fyll ut følgende før du fyller ut spørreskjemaet:

Dagens dato:

				2	0		
D	D	M	M	Å	Å	Å	Å

På hvilken side av kroppen har du det leddet som du **får eller har fått behandling for**:

Venstre ❑

Høyre ❑

Begge ❑

Hvis du svarte "begge", fyller du ut det <u>første</u> skjemaet med tanke på <u>høyre side</u>. Deretter følger et nytt spørreskjema for venstre side.

Sett ring rundt riktig side **Høyre / Venstre**

Sett et kryss (✓) for hvert utsagn

1. <u>I løpet av de 4 siste ukene</u> har jeg opplevd følgende:
Jeg har smerter i foten/ ankelen min.

Aldri	Sjelden	Noen ganger	Det meste av tiden	Hele tiden
☐	☐	☐	☐	☐

2. <u>I løpet av de 4 siste ukene</u> har jeg opplevd følgende:
Jeg unngår å gå lange distanser på grunn smerter i foten/ankelen

Aldri	Sjelden	Noen ganger	Det meste av tiden	Hele tiden
☐	☐	☐	☐	☐

3. <u>I løpet av de 4 siste ukene</u> har jeg opplevd følgende:
Jeg endrer måten å gå på, på grunn av smerter i foten/ ankelen

Aldri	Sjelden	Noen ganger	Det meste av tiden	Hele tiden
☐	☐	☐	☐	☐

4. <u>I løpet av de 4 siste ukene</u> har jeg opplevd følgende:
Jeg går sakte på grunn av smerter i foten/ ankelen

Aldri	Sjelden	Noen ganger	Det meste av tiden	Hele tiden
☐	☐	☐	☐	☐

5. <u>I løpet av de 4 siste ukene</u> har jeg opplevd følgende:
Jeg må stoppe og hvile foten/ankelen på grunn av smerter

Aldri	Sjelden	Noen ganger	Det meste av tiden	Hele tiden
☐	☐	☐	☐	☐

6. <u>I løpet av de 4 siste ukene</u> har jeg opplevd følgende:
Jeg unngår enkelte harde og ujevne underlag på grunn av smerter i foten/ankelen

Aldri	Sjelden	Noen ganger	Det meste av tiden	Hele tiden
☐	☐	☐	☐	☐

7. <u>I løpet av de 4 siste ukene</u> har jeg opplevd følgende:
Jeg unngår å stå lenge på grunn av smerter i foten/ankelen

Aldri	Sjelden	Noen ganger	Det meste av tiden	Hele tiden
☐	☐	☐	☐	☐

8. <u>I løpet av de 4 siste ukene</u> har jeg opplevd følgende:
Jeg bruker buss eller bil i stedet for å gå på grunn av smerter i foten/ankelen

Aldri	Sjelden	Noen ganger	Det meste av tiden	Hele tiden
☐	☐	☐	☐	☐

9. <u>I løpet av de 4 siste ukene</u> har jeg opplevd følgende:
Jeg bekymrer meg for hva andre tenker om min fot/ankel.

Aldri	Sjelden	Noen ganger	Det meste av tiden	Hele tiden
☐	☐	☐	☐	☐

10. <u>I løpet av de 4 siste ukene</u> har jeg opplevd følgende:
Jeg bekymrer meg for hva andre tenker om fottøyet jeg er nødt til å bruke.

Aldri	Sjelden	Noen ganger	Det meste av tiden	Hele tiden
☐	☐	☐	☐	☐

11. <u>I løpet av de 4 siste ukene</u> har jeg opplevd følgende:
Smerten i foten/ankelen min er verre om kvelden

Aldri	Sjelden	Noen ganger	Det meste av tiden	Hele tiden
☐	☐	☐	☐	☐

12. <u>I løpet av de 4 siste ukene</u> har jeg opplevd følgende:
Jeg får lynende smerter i foten/ ankelen min

Aldri	Sjelden	Noen ganger	Det meste av tiden	Hele tiden
☐	☐	☐	☐	☐

13. <u>I løpet av de 4 siste ukene</u> har jeg opplevd følgende:
Smertene i foten/ ankelen min forhindrer meg fra å utføre jobben min/ daglige gjøremål

Aldri	Sjelden	Noen ganger	Det meste av tiden	Hele tiden
☐	☐	☐	☐	☐

14. <u>I løpet av de 4 siste ukene</u> har jeg opplevd følgende:
Jeg er <u>ikke</u> i stand til å gjennomføre alle mine sosiale aktiviteter eller fritidsaktiviteter på grunn av smerter i foten/ankelen min.

Aldri	Sjelden	Noen ganger	Det meste av tiden	Hele tiden
☐	☐	☐	☐	☐

15. **<u>I løpet av de 4 siste ukene..</u>**
Hvordan vil du beskrive smerten du <u>vanligvis</u> kjenner i foten/ ankelen?

Ingen	Svært mild	Mild	Moderat	Sterk
☐	☐	☐	☐	☐

16. **<u>I løpet av de 4 siste ukene..</u>**
Har du blitt forstyrret av smerte fra foten/ ankelen etter at du har lagt deg om kvelden?

Ingen netter	Bare 1 eller 2 netter	Noen netter	De fleste nettene	Hver natt
☐	☐	☐	☐	☐

Til slutt, sjekk at du har svart på <u>alle spørsmålene.</u>
Tusen takk!

II

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Randomized trial comparing suture button with single 3.5 mm syndesmotic screw for ankle syndesmosis injury: similar results at 2 years

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Background and purpose — Better outcomes are reported for suture button (SB) compared with syndesmotic screws (SS) in patients treated for an acute ankle syndesmotic injury. One reason could be that screws are more rigid than an SB. A single tricortical 3.5 mm syndesmotic screw (TS) is the most dynamic screw option. Our hypothesis is that 1 SB and 1 TS provide similar results. Therefore, in randomized controlled trial, we compared the results between SB and TS for syndesmotic stabilization in patients with acute syndesmosis injury.

Patients and methods — 113 patients with acute syndesmotic injury were randomized to SB (n = 55) or TS (n = 58). The American Orthopedic Foot & Ankle Society (AOFAS) Ankle–Hindfoot Score was the primary outcome measure. Secondary outcome measures included Manchester Oxford Foot Questionnaire (MOXFQ), Olerud–Molander Ankle score (OMA), visual analogue scale (VAS), EuroQol- 5D (EQ-5D), radiologic results, range of motion, complications, and reoperations (no implants were routinely removed). CT scans of both ankles were obtained after surgery, and after 1 and 2 years.

Results — The 2-year follow-up rate was 84%. At 2 years, median AOFAS score was 97 in both groups (IQR SB 87–100, IQR TS 90–100, p = 0.7), median MOXFQ index was 5 in the SB group and 3 in the TS group (IQR 0–18 vs. 0–8, p = 0.2), and median OMA score was 90 in the SB group and 100 in the TS group (IQR 75–100 vs. 83–100, p = 0.2). The syndesmotic reduction was similar 2 years after surgery; 19/55 patients in the SB group and 13/58 in the TS group had a difference in anterior syndesmotic width ≥ 2 mm (p = 0.3). 0 patients in the SB group and 5 patients in the TS group had complete tibiofibular synostosis (p = 0.03). At 2 years, 10 TS were broken. Complications and reoperations were similar between the groups.

Interpretation — We found no clinically relevant differences regarding outcome scores between the groups. TS is an inexpensive alternative to SB.

Since 2018, several meta-analyses have been published evaluating treatment of acute ankle syndesmotic injury, reporting better outcomes for suture button (SB) fixation compared with syndesmotic screw (SS) (Shimozono et al. 2018, McKenzie et al. 2019). Shimozono concluded that the SB technique resulted in improved outcome and lower rates of joint malreduction. These results are based on heterogenous studies: different fracture types were compared; different numbers of implants were used and different diameters and cortices were engaged for SS fixation (Shimozono et al. 2018). Andersen et al. (2018) reported superior results for SB compared with a quadricortical 4.5 mm SS. A quadricortical SS necessitates routine screw removal, with a 5–9% reported risk of wound infection (Schepers et al. 2011, Andersen et al. 2015) and potential loss of reduction after implant removal (Laflamme et al. 2015). A quadricortical SS is a rigid fixation, inhibiting tibiofibular movement throughout the gait cycle (Riedel et al. 2017, Ramsey et al. 2018). The SB has a higher implant cost compared with SS (Ramsey et al. 2018), may not be sufficient to maintain fibular length in Maisonneuve fractures (Riedel et al. 2017), and has an implant removal rate of 6%, mainly due to irritation from the lateral knot (Andersen et al. 2018). The single tricortical 3.5 mm syndesmotic screw (TS) allows for some tibiofibular movement (Clanton et al. 2017), making the TS an inexpensive alternative, without need for routine implant removal. In this study we compare outcomes between a knotless SB and TS. Our hypothesis was that there is no difference in outcomes in patients treated with SB and a 3.5 mm TS.

Patients and methods

Patients and procedures

3 hospitals participated in recruiting and treating patients. Surgery was conducted by 45 different surgeons. Patients were included by the orthopedic resident on call, from January 2016

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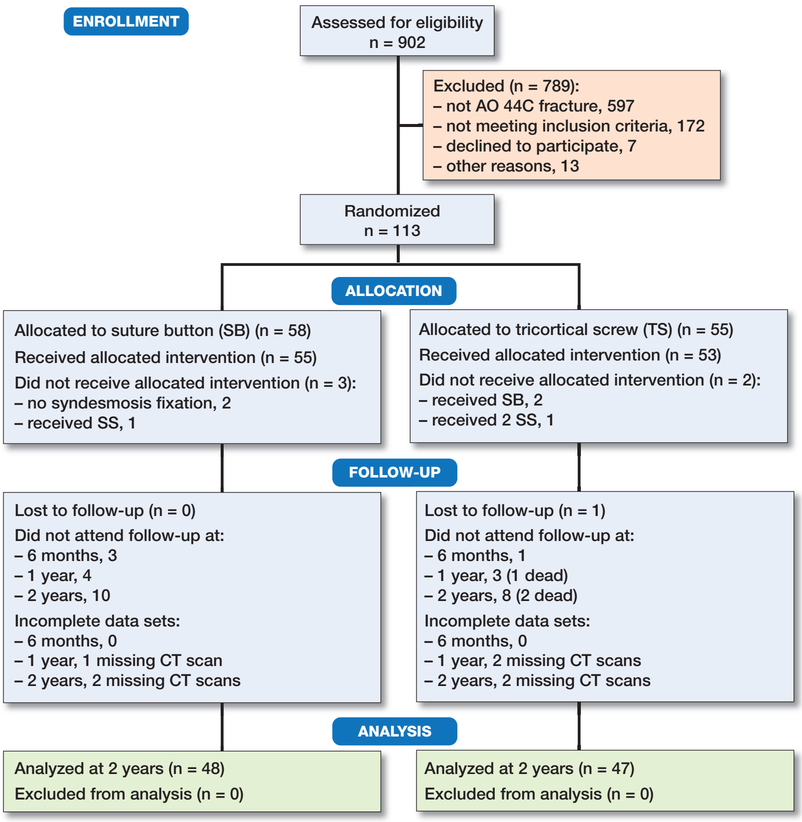

Figure 1. CONSORT flowchart of the trial enrollment and analysis.

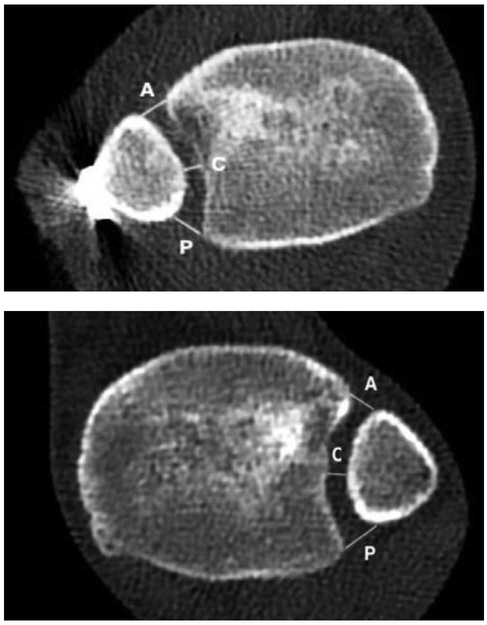

Figure 2. CT of injured ankle (upper panel) and uninjured ankle (lower panel) in a 20-year-old woman, 2 years after injury. Tibiofibular distance is measured on axial CT 1 cm proximal to the ankle joint. Distance measured anterior (A); central (C); and posterior (P).

to September 2017. Patients aged 18 to 69 who had suffered an acute AO type 44-C ankle fracture assessed by radiographs were asked to participate (Figure 1). Exclusion criteria were polytrauma, open fractures, previous fracture or arthritis of the same ankle, or neurologic impairment of the lower limbs. A web-based randomization system was used, developed and administered by Clinical Research Unit Central Norway, Norwegian University of Science and Technology, Trondheim, Norway.

Surgery was performed according to AO principles. The syndesmosis was reduced and fixed in a closed manner, guided by fluoroscopy. Surgeons were recommended to fix the syndesmosis at a level just proximal to the inferior tibiofibular joint (Barbosa et al. 2020), the use of temporary fixators (K-wire or reduction clamp) was decided by the surgeon. Patients allocated to SB were treated with a single knotless SB (Ziptight, Zimmer Biomet, Warsaw, IN, USA). Patients allocated to TS were treated with a fully threaded self-tapping, 3.5 mm tricortical screw (DePuy Synthes, West Chester, PA, USA). The screw length was not specified, but standardized to engage 3 cortices. Surgery was performed by the on-call team, either by an experienced resident, or a less experienced resident accompanied by a consultant or senior resident. Antibiotic prophylaxis was given as a single dose peroperatively. All patients followed the same protocol postoperatively: implants were not routinely removed; plaster casts and thrombosis prophylaxis were not used routinely. Patients were advised partial weight-bearing (20–30 kg) directly after surgery (Barbosa et al. 2020), then weight-bearing as tolerated after 6 weeks.

Outcome measures

Patients were assessed by an orthopedic surgeon and a physiotherapist at 6 weeks, 6 months, 1 and 2 years. The physiotherapists who conducted the physical examinations were blinded to the treatment allocation. The main outcome measure was the American Orthopedic Foot & Ankle Society (AOFAS) Ankle–Hindfoot scale. AOFAS incorporates subjective and objective factors into a numerical scale of 0 to 100, 100 being the best. Secondary outcome measures included the Manchester Oxford Foot Questionnaire (Dawson et al. 2007, 2011) (MOXFQ), a 16-item (each item scored 0–4) patient reported outcome measure (PROM). MOXFQ has 3 separate underlying dimensions: pain, activity, and social interaction. The raw score of maximum 64 was converted to a metric index from 0 (best) to 100 (worst) (Morley et al. 2013). MOXFQ is available in Norwegian and is not validated for ankle fractures. The MOXFQ is validated for hallux valgus surgery and has been found to be highly responsive (Dawson et al. 2007). Other secondary measures were the Olerud–Molander Ankle (OMA) score (Olerud and

Molander 1984), EuroQol-5D (EQ-5D) index, EQ-5D visual analogue scale (VAS), and VAS scores for pain during rest, during walking, at night, and during daily activities. OMA is a self-reported scale validated for ankle fractures, ranging from 0 (worst) to 100 (best). EQ-5D is a well-validated generic health-related quality-of-life instrument. Ankle range of motion was measured, comparing injured with non-injured ankle. The examination was standardized by a blinded physiotherapist, measuring dorsal and plantar flexion with a goniometer, with the foot placed on a 25 cm high foot stool with the knee in flexion.

Radiological measurements

Plain radiographs of the injured ankle were obtained after surgery, and at 6 weeks and 6 months. CT scans of both ankles were obtained postoperatively, and after 1 and 2 years. CT scans were standardized with the patient in a supine position, placing the feet in a purpose-made device, keeping the ankles in neutral position with 20° internal rotation of the legs. Radiological measurements were performed by 1 senior musculoskeletal radiologist (SBJ) and one orthopedic surgeon (BWR). The syndesmosis was assessed postoperatively and after 1 and 2 years by measuring the tibiofibular distance on axial CT scans, 1 cm proximal to the midpoint of the tibial plafond (Figure 2). The difference between injured and uninjured side was calculated. A criterion of < 2 mm difference in tibiofibular distance was selected for acceptable syndesmotic reduction (Andersen et al 2019, Patel et al. 2019). Signs of ankle osteoarthritis (OA), synostosis, talar exostoses, broken screws, and osteochondral lesions were reported. When assessing OA on CT scans, we defined mild OA as presence of osteophytes, and advanced OA as narrowing of the joint space and presence of cysts and sclerosis (Ray et al. 2019).

Statistics

Sample size was calculated according to the equivalence criterion (Piaggio et al. 2012). The minimal clinically important difference (MCID) for ankle fracture patients is not defined for the AOFAS score but has been suggested to be half of the standard deviation (SD) (Norman et al. 2003). Based on data from previous trials with a similar population, the SD was estimated to 12 points (Wikeroy et al. 2010, Andersen et al. 2018), giving an MCID of the AOFAS score of 6 points. A between-group difference of 10 points (AOFAS) was used to ensure a sufficient inclusion of patients. 38 patients had to be included in each group to achieve a power of 0.95 and a significance level of 0.05. To strengthen the data and compensate for loss to follow-up, we planned to include 60 patients in each group. Analyses of endpoint results were performed as both intention-to-treat and per-protocol. Student's T-test was used to compare means of normally distributed data. The Mann–Whitney U-test was used in cases of skewed data. Fisher's exact test was used for categorial data. Data is reported as numbers, mean with SD, or median with interquartile range (IQR). We considered a probability of less than 5% as statistically significant and used 95% confidence intervals (CI) to describe uncertainty. Data analysis was conducted in IBM SPSS Statistics for Mac version 26 (IBM Corp, Armonk, NY, USA).

Table 1. Patient characteristics at time of enrolment. Values are number of patients unless otherwise specified

Characteristic	SB (n = 55)	TS (n = 58)
Mean age (SD)	44 (15)	48 (14)
Male sex	35	30
Right side	32	26
Mean BMI (SD)	27 (5)	26 (4)
Medial malleolar fracture	14	19
Posterior malleolar fracture	37	31
Medial and posterior malleolar fracture	10	15
Maisonneuve fracture	26	20
Osteochondral damage of the talus	2 [a]	4
Intra-articular loose bodies	9 [a]	10
Temporary external fixator	7	2

[a] n = 54

Ethics, registration, funding, and potential conflicts of interest

Patients gave their written consent prior to randomization. The trial was conducted in accordance with the Declaration of Helsinki, approved by the National Committees for Research Ethics in Norway 2015/1860 and registered at ClinicalTrials.gov (NCT02930486). The study did not receive external funding. The authors have no conflicts of interest to declare.

Results

Results are reported according to the CONSORT guidelines.

113 patients were randomized and allocated to SB (= 58) or TS (= 55) (Figure 1). The 2-year follow-up rate was 84%; the radiological follow-up rate was 81%. The baseline demographic patient characteristics and fracture treatment were reported (Table I).

Clinical outcomes

The groups did not differ statistically regarding clinical outcome: at 2 years, the median AOFAS score was 97 in both groups (IQR SB 87–100 vs. TS 90–100, p = 0.7) (Table 2). The difference in mean AOFAS was < 2, equivalent at all controls (Figure 3). Median MOXFQ was 5 in the SB group and 3 in the TS group (IQR SB 0–18 vs. TS 0–8, p = 0.2) (Table 2), and median OMA score was 90 in the SB group and 100 in the TS group (IQR SB 75–100 vs. TS 83–100, p = 0.2). Similarly, no statistically significant difference was detected in VAS, EQ-5D VAS, or EQ-5D (Table 2). Fracture pattern affected clinical outcome when we stratified the groups according to fracture pattern: after 2 years, patients with a Maisonneuve fracture

Table 2. Primary and secondary outcome measures

Outcome measure	SB [a] n	SB [a] score	TS [a] n	TS [a] score	p-value
AOFAS					
6 weeks	54	67 (10)	52	66 (13)	0.7 [c]
6 months	53	87 (82–98)	54	88 (77–98)	1.0 [b]
1 years	53	93 (82–100)	52	90 (84–99)	0.5 [b]
2 years	48	97 (87–100)	47	97 (90–100)	0.7 [b]
MOXFQ					
6 weeks	52	29 ((11)	48	31 (13)	0.4 [c]
6 months	55	14 (3–31)	53	14 (3–36)	0.7 [b]
1 year	52	5 (0–32)	51	6 (0–13)	0.9 [b]
2 years	48	5 (0–18)	47	3 (0–8)	0.2 [b]
OMA					
1 year	53	90 (73–100)	52	90 (76–100)	0.4 [b]
2 years	47	90 (75–100)	45	100 (83–100)	0.2 [b]
VAS for pain during rest					
6 weeks	53	1.0 (0–2)	49	1.0 (0–2)	0.9 [b]
6 months	54	0.0 (0–1)	54	0.0 (0–2)	0.1 [b]
1 year	53	0.0 (0–1)	52	0.0 (0–1)	0.5 [b]
2 years	48	0.0 (0–1)	47	0.0 (0–0)	0.6 [b]
VAS for pain during walking					
6 weeks	53	2.0 (1–4)	49	3.0 (2–4)	0.3 [b]
6 months	54	1.0 (0–3)	54	1.0 (0–2)	0.8 [b]
1 year	53	1.0 (0–2)	52	1.0 (0–2)	0.9 [b]
2 years	48	0.0 (0–1)	47	0.0 (0–1)	0.2 [b]
VAS for pain at night					
6 weeks	53	1.0 (0–2)	49	1.0 (0–3)	0.6 [b]
6 months	54	0.0 (0–0)	54	0.0 (0–1)	0.01 [b]
1 year	53	0.0 (0–0)	52	0.0 (0–0)	1.0 [b]
2 years	48	0.0 (0–1)	47	0.0 (0–0)	0.2 [b]
VAS for pain during daily activity					
6 weeks	53	3.0 (2–6)	49	4.0 (2–7)	0.4 [b]
6 months	54	1.0 (0–3)	54	1.0 (0–2)	0.9 [b]
1 year	53	0.0 (0–2)	52	1.0 (0–2)	0.6 [b]
2 years	48	0.0 (0–29	47	0.0 (0–0)	0.03 [b]
EQ-5D index					
6 weeks	53	0.7 (0.6–0.8)	53	0.7 (0.3–0.7)	0.1 [b]
6 months	54	0.8 (0.7–1.0)	54	0.8 (0.7–1.0)	0.9 [b]
1 year	53	1.0 (0.8–1.0)	52	1.0 (0.8–1.0)	1.0 [b]
2 years	48	1.0 (0.8–1.0)	47	1.0 (0.9–1.0)	0.3 [b]
EQ-5D VAS					
6 weeks	52	73 (15)	51	63 (18)	0.004 [c]
6 months	53	89 (70–95)	54	80 (74–90)	0.2 [b]
1 year	52	85 (71–95)	52	88 (76–90)	0.6 [b]
2 year	48	85 (70–95)	45	90 (77–95)	0.6 [b]

[a] For not normally distributed data values are given as median (IQR) in parentheses and for normally distributed data as mean (SD).
[b] Nonparametric (Mann–Whitney U) test.
[c] 2-sided t-test for independent samples.

pattern had better outcome scores with a median AOFAS at 100 in the Maisonneuve patients group compared with 95 in all other injuries (IQR 95–100 vs. 85–100, p = 0.001), while patients with trimalleolar fractures did worse, with a median AOFAS at 92 compared with 99 in other injuries (IQR 85–97 vs. 90–100, p = 0.03) (Table 3, see Supplementary data). The ability to plantar- and dorsiflex the ankle was similar between the groups. At 2 years, the mean difference between injured and uninjured ankle in plantar and dorsiflexion was ≤ 5° (Table 4, see Supplementary data). Per-protocol analyses supported the intention-to-treat findings.

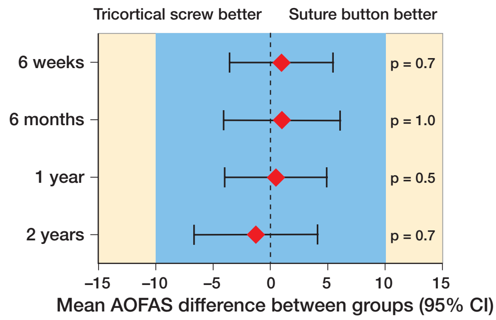

Figure 3. AOFAS equivalence diagram. Blue area indicates margins of equivalence defined as the between-group difference of 10 points. Results at all time intervals are equivalent since the 95% CI lies wholly inside the margins.

Radiological results

At 2 years, 30 patients in the SB group and 27 patients in the TS group had radiological signs of ankle OA (RR 1.1, CI 0.7–1.7). When analyzing for advanced OA, there was a difference between the groups at 2 years: 8 patients in the SB group and 1 patient in the TS group had advanced OA (RR 8, CI 1–60). The groups displayed similar results when analyzing presence of talar osteophytes at 2 years: 12 in the SB group and 7 in the TS group (p = 0.3). At 2 years, 0 patients in the SB group and 5 patients in the TS group had complete synostosis (p = 0.03) (Figure 4, see Supplementary data). When stratifying the complete cohort at 2 years according to fracture pattern, patients with a Maisonneuve fracture had less OA (15 vs. 42, RR 0.7, CI 0.4–1.0), patients with a trimalleolar fracture had more OA (19 vs. 38, RR 1.6, CI 1.2–2.1).

The tibiofibular distance measured on CT scans postoperatively and after 1 and 2 years was similar between the groups. At 2 years, the mean difference in tibiofibular distance was ≤ 1 mm for anterior, central, and posterior measurement in both groups (Table 5). When applying a tibiofibular difference of < 2 mm between injured and uninjured ankle as a criterion for acceptable reduction the groups had similar results at all controls; 19 patients in the SB group and 16 patients in the TS group had an anterior difference > 2 mm postoperatively (RR 1.2, CI 0.7–2.1) (Table 6, see Supplementary data). After 2 years, 35 of 45 patients still had their TS implanted; 10 screws were broken.

Complications and reoperations

10 patients in the SB group and 17 patients in the TS group had ≥ 1 reoperation (p = 0.2) (Table 7, see Supplementary data). 5 patients in the SB group and 11 patients in the TS group had their implants removed because of local irritation alone (p = 0.2). 3 patients in the SB group and 3 patients in the SS group required early reoperation (< 3 weeks) after CT postoperatively revealed unacceptable reduction of the fracture or of the syndesmosis (3 syndesmosis malreductions, 1 fibula malreduction, 2 medial malleolus malreduction). 2 patients (male, age 50 and female, age 52 years) suffered a low-energy tibia fracture through the suture button canal (Fig-

Table 5. Radiological results: difference measured in mm in tibiofibular distance at level of syndesmosis (1 cm proximal to the ankle joint) between injured and uninjured side. Values are mean (SD) or median (IQR) unless otherwise specified

Factor	n	SB difference	n	TS difference	Mean between-group difference (95% CI)	p-value [a]
Difference in anterior distance						
≤ 2 weeks	54	0.1 (1.9)	56	0.7 (1.8)	–0.5 (–1.2 to 0.2)	0.1
1 year	54	1.1 (2.0)	50	0.7 (1.8)	0.3 (–0.4 to 1.1)	0.4
2 years	46	0.9 (1.9)	45	0.7 (1.6)	0.2 (–0.5 to 1.0)	0.5
Difference in central distance						
≤ 2 weeks	54	0.1 (1.2)	56	–0.7 (1.1)	0.2 (–0.2 to 0.6)	0.3
1 year	54	1.2 (1.9)	50	0.9 (1.4)	0.3 (–0.3 to 1.0)	0.3
2 years	46	1.4 (0.0–2.0)	45	1.0 (0.0–1.0)	0.7 (0.0 to 1.4)	0.2 [b]
Difference in posterior distance						
≤ 2 weeks	54	–0.4 (2.2)	56	–0.6 (2.1)	0.2 (–0.6 to 1.0)	0.7
1 year	54	0.1 (1.8)	50	0.4 (1.8)	–0.3 (–1.0 to 0.4)	0.5
2 years	46	0.0 (2.3)	45	0.3 (2.0)	–0.4 (–1.2 to 0.5)	0.4

[a] Levene's test was used to assess equality of the variances. Statistical analysis was conducted using the 2-sided t-test for independent samples in normally distributed data; otherwise the Mann–Whitney U-test was used.
[b] The Mann–Whitney U-test was used.

ures 5, 6, see Supplementary data). The male patient presented 6 months postoperatively with a healed tibia fracture with 13° varus deformity. Since this patient had no complaints the fracture was not addressed surgically. The female patient presented initially with a large posterior malleolar fracture. She presented with pain while walking 4 months after her initial injury. She had suffered a tibia fracture and was reoperated on with open reduction and internal fixation. A dual energy X-ray absorptiometry (DEXA scan) showed osteoporosis.

Discussion

The main findings in this study are equivalent clinical results in patients treated with either an SB or an TS 2 years after acute syndesmotic injury. The mean AOFAS difference between the groups was overlapping and inside the margins of the 95% CI at all controls. The rate of appropriate syndesmotic reduction, reoperations, and rate of OA was similar between our groups. In the SB group, 2 patients experienced fractures through the suture button canal. 5 patients in the TS group had synostosis after 2 years. Fracture pattern affected clinical outcome.

The clinical results are in contrast to earlier studies reporting better results for SB fixation (Shimozono et al. 2018). An explanation for this discrepancy could be the different mechanical properties between the screw options for fixation. The dynamic properties of syndesmotic implants in vivo are unknown, but there are mechanical studies on the subject. Fixation of the syndesmosis with several 3.5 mm tricortical SS or a 4.5 mm quadricortical SS locks the fibula in the incisura, while the TS has in a cadaver study displayed more dynamic properties (Clanton et al. 2017). This may explain why Andersen et al. (2018) found a quadricortical SS to be inferior to an SB, while Kortekangas et al. (2015) found no difference when comparing an TS with an SB.

The first SBs available required a suture knot on the lateral side, with irritation and a reported removal rate of 6% (Andersen et al. 2018). We used a knotless SB to potentially lower this rate. Despite this, our removal rate was 9%. Changing to a knotless SB did not affect the removal rate. This could be due to other factors, such as irritation from the fibula plate, present in almost half of the SB patients. 6 patients required early reoperation, based on postoperative CT scans. We advocate a low threshold for obtaining postoperative CT scans after syndesmotic reduction (Garner et al. 2015, Barbosa et al. 2020).

Trauma is the most common cause of ankle OA (Saltzman et al. 2005). The rate of radiologic OA after 2 years was high in this study. The reason for this could be the use of CT, which is more sensitive than radiographs when assessing OA. Most of the patients (48 of 57) displayed only minor signs of OA. The rate of advanced OA in 9 patients is in line with previous studies (Lübbeke et al. 2012, Ray et al. 2019). The observation period of 2 years is short and the study population is underpowered to conclude on the differences in advanced OA between the groups. More patients had complete synostosis in the TS group, supporting the findings by Hinds et al. (2014) that SS fixation is a risk factor for synostosis development. 2 patients treated with SB suffered a non-traumatic fracture through the suture button canal. This specific complication and its incidence have not been reported in the literature. We suggest a syndesmotic screw as a better alternative in patients with poor bone quality.

A weakness in the study is our choice of outcome score. The ideal outcome score should be validated for the injury in question, have high reliability, and be available in the language of the patients examined. Our primary outcome, the AOFAS, is not validated; it is criticized for low precision, and for producing skewed data due to ceiling effects (Veltman et al. 2017). Even so, the AOFAS was chosen because of its widespread use. We decided to add the MOXFQ, since it was available in Norwegian. It is validated for hallux valgus surgery, not ankle fractures, hence its properties for ankle fractures are not known. After initiation of our trial, a comparison of 3 different PROMs available in Norwegian were published, recommending the Self-Reported Foot and Ankle Score (SEFAS) for evaluating patients with ankle fractures (Garratt et al. 2018). Another weakness is the lack of standardization in the syndesmosis fixation and several surgeons treating the patients. This could be a source of uncontrolled variability between the groups. On the other hand, it makes our results transferable to the day-to-day practice of fracture surgery.

The primary strengths of this study are the randomized prospective design with blinded scoring of clinical outcome measures, comparable groups at baseline, a high follow-up rate, and CT evaluation 2 years after treatment. In addition, all hospitals participating in the study used both implants as standard treatments before initiation of the trial, minimizing problems with the learning curve associated with new treatments. The procedure was performed by the on-call team, providing generalizability. Our outcome scores after 2 years are in line with scores from similar studies (Wikeroy et al. 2010, Laflamme et al. 2015, Andersen et al. 2018), supporting previous data on outcomes after syndesmotic injury.

Interpretation

In this RCT comparing a knotless SB and an TS we found no clinically relevant differences regarding outcome scores between the groups. TS is an inexpensive alternative to SB when treating acute syndesmotic injury.

Supplementary data

Tables 3, 4, 6, 7 and Figures 4–6 are available as supplementary data in the online version of this article, http://dx.doi.org/10.1080/17453674.2020.1818175

BWR, JEM, MRA, and WF planned and designed the study. BWR, IKS, JEM, FF, MRA, and WF were active in inclusion, treatment, and follow-up. SBJ and BWR did analysis of the radiologic examinations. BWR and MRA did statistical analysis with feedback from IKS, JEM, FF, and WF. BWR designed the tables and wrote the first draft of the paper; all authors revised the paper and tables.

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III

Incidence and clinical significance of posterior malleolar fractures in patients with AO/OTA C type ankle fractures. Results from two randomized controlled trials at 2 years.

Abstract

Objectives The incidence of posterior malleolar fractures (PMFs) associated with ankle fractures is historically based on plain radiographs. The aim of this study was to assess incidence, fracture pattern and clinical outcome of concomitant PMF in patients with AO/OTA C fractures with CT.

Design Diagnostic cohort study

Setting Three orthopedic departments in Norway.

Patients/Participants 210 patients treated for an AO/OTA C type fracture with syndesmotic fixation between 2011 and 2017 were included. The 2 year- follow up rate was 86%.

Allocation According to presence and morphology of PMF. PMFs were classified by the Haraguchi classification.

Main outcome measurements Patient assessment at 6 weeks, 6 months, 1 and 2 years. The American Orthopaedic Foot & Ankle Society Ankle-Hindfoot Score (AOFAS) was the primary outcome measure. A secondary outcome measures was presence of osteoarthritis. Intraobserver reproducibility and interobserver agreement for the Haraguchi classification were evaluated.

Results 125 of 210 patients (60%) had a PMF. 34% of the PMFs were missed on plain radiographs. Haraguchi type II fractures had a lower AOFAS compared to the no-fracture group at 6 weeks (-7.5 (95% CI; -15.0 to -0.2), p=0.04) and 6 months (-8.4 (95% CI; -15.3 to -1.5), p= 0.01). The intraobserver agreement was 0.733, (95% CI: 0.629 to 0.884, p<0.001), and interobserver agreement was 0.797, (95% CI: 0.705 to 0.889) p<0.001.

Conclusions Plain radiographs underestimated PMF. Patients with a Haraguchi type II fracture had a poorer outcome measured by the AOFAS score compared to no PMF up until 6 months. Classification of PMF according to the Haraguchi classification was found reliable.

Level of evidence Level III diagnostic cohort study

Introduction

The true incidence of Posterior malleolar fractures (PMF) is not well established, and occurs in 7 to 44 % of all ankle fractures (1-3). Patients with a PMF have a worse clinical outcome (4,5). There is no current consensus on when a PMF should be fixed. With the increased use of CT as a diagnostic tool, several classification systems for PMF have been developed (6-8).

Previously, common practice was to operatively stabilize a PMF that compromised more than 25% of the joint surface on a true lateral radiograph(9). The articular surface involvement of a PMF may, however, be less important for ankle stability (10-12), and several studies have failed to show correlation between fragment size and functional outcome(4,13,14). This has shifted the focus towards assessing fracture pattern rather than fragment size(15). Plain radiographs are known to be inaccurate when judging the presence, size and extension to the medial malleolus(16,17). Sheikh et al found that a preoperative computer tomography (CT) altered both the decision making and surgical approach to fix a PMF(18), and CT has been recommended by some authors before deciding final fracture treatment(9-11).

To assess the PMF pattern, several classification systems have been developed(6-8). The first classification system, based on axial CT scans, was developed by Haraguchi in 2006(6). PMFs were categorized into three types: the posterolateral-oblique type, the medial extension type and the small-shell type (figure 1). Blom et al. described inferior functional results in fractures extending to the medial malleolus (Haraguchi II), to our knowledge this study was the first to analyze differences in clinical outcome according to PMF pattern(16).

A PMF is closely connected to the Posterior Inferior tibiofibular ligament (PITFL) and syndesmotic stability. In an AO/OTA C type injury, an intact PITFL may be attached to the PMF and fixation of the PMF is reported to restore syndesmotic stability(19). Miller found equivalent results when comparing PMF stabilization to screw fixation in the event of syndesmotic injuries (20).

Studies on ankle fractures have usually extracted their results from mixed series of fracture types (AO/OTA A,B and C), which may impact their result on PMF´s potential effect on clinical outcome. Our present study is the first to assess AO/OTA C type fractures only with regards to PMF.

The hypothesis of the study is that radiographs underestimate the incidence of PMF in AO/OTA C fracture and by conducting CTs the true incidence can be found. In addition, we hypothesize that the presence and morphology of a PMF affects clinical outcome. The aims of the study were to assess presence, fracture pattern and clinical outcome of concomitant PMFs in patients with AO/OTA C type ankle fractures. With validation of the Haraguchi classification system, and assessment of clinical outcome according to fracture group, we seek to increase the knowledge on PMF, to assist surgeons in diagnosing and treating this fracture.

Materials & Methods

The National Committees for Research Ethics in Norway approved the reevaluation of the CT images and outcome scores from two previous randomized controlled trials, both approved by REK (2010/2012 and 2015/1860), registered at ClinicalTrials.gov (NCT01275924 and NCT02930486) (21,22) .

Subjects

Between January 2011 and March 2013, 97 patients were included in a randomized controlled trial (RCT) at 2 hospitals(23). Between January 2016 and September 2017, 113 patients were included in another RCT at 3 hospitals(22). Both trials included patients between 18 and 70 years with an acute injury to the syndesmosis, and an AO/OTA C type ankle fracture. Exclusion criteria were polytrauma, open fracture, inability to consent, previous injury or symptomatic ankle osteoarthritis or neurologic impairment of the injured leg. Both RCTs compared implants to stabilize a syndesmosis injury as the primary point of interest. The current study included 210 patients from the two RCTs, of which 125 patients had a PMF.

Surgical procedures and rehabilitation

Surgery was performed according to AO principles (24) by the orthopaedic surgeon on call. The surgeon decided if and how a PMF was addressed. The syndesmosis was fixed in all patients, according to randomization in the RCTs (number randomized to each implant; 25 4.5 mm quadricortical syndesmotic screw; 29 3.5 tricortical syndesmotic screw; 71 suture button (34 Tightrope®, Arthrex; 37 Ziptight™, Zimmer Biomet)(Table 2)). Postoperative plaster casts were not used routinely. Partial weight- bearing was instituted for 6 weeks, and the patients were encouraged to start full-weight bearing thereafter.

Radiographic Measurements

Presence of a PMF was stated analyzing plain radiographs preoperatively. Comparing this to post-operative CTs, the number of missed PMF on radiographs could be assessed. The PMF was classified on post-operative CT scans according to the Haraguchi classification (6). Interobserver agreement for the Haraguchi classification was determined by three independent observers (MRA and MRA), and one independent foot and ankle specialist). Disagreements between the observers were resolved by a plenary discussion between the raters. For the intraobserver (test-retest) agreement the first author (BWR) classified all CTs twice, with at least 6 months delay between assessments. CT scans were assessed for osteoarthritis (OA). Osteophytes, joint space narrowing, subchondral cysts or sclerosis was interpreted as an OA finding. All radiographs and CT images were analyzed using digital imaging software (Siemens Pacs Syngo Studio VB36E (Erlangen, Germany) and Carestream Pacs v 12.1.5.1046 (NY, USA).

Outcome Measures

The main outcome measure was the American Orthopaedic Foot & Ankle Society (AOFAS) ankle- hindfoot score. The AOFAS consists of 3 parts (pain, function and alignment), where subjective and objective measures make up a scale from 0-100, 100 being the best result (25). Patients were evaluated at 6 weeks, 6 months, 1 and 2 years.

Statistical Analyses

For our primary endpoint, the AOFAS, a minimal clinically important difference (MCID) for ankle fracture patients is not defined. In earlier studies, MCID has been hypothesised to be one half of the standard deviation (SD) (26,27), and was set to 12 points based on previous studies.

Due to the repeated data structure of the study design and incomplete dataset for the AOFAS (6 weeks: 94%, 6 months: 92%, 1 year 91% and 2 years: 86% follow up) a linear mixed model analysis with adjustment for potential confounders (gender, age, BMI) was performed. The covariance structure autoregressive(1) (AR(1)) was chosen. Analyses were conducted with a random intercept model, comparing the three different Haraguchi fracture types to no PMF at each control. Bonferroni correction was conducted for comparison of the main effect to protect for type-I error.

To determine the inter- and intrarater- reliability for fracture classification Cohen's Kappa coefficient (κ) was used. The strength of examiner agreement was defined according to the guidelines of Landis and Koch (28) as follows: poor, (κ)<0; slight, κ=0.0-0.20; fair, κ=0.21-0.40; moderate, κ=0.41-0.60; substantial, κ=0.61-0.80; almost perfect, κ=0.81-1.00. SPSS version 26.0 (SPSS Inc. Chicago, Illinois) was used for all data analyses. Statistical significance was set at 5% level (ρ<0.05).

Results

The 210 included patients were divided into 4 groups, one for patients without a PMF, and three groups according to Haraguchi type I-III. The 2-year follow up rate was 86%. The 4 groups were comparable according to age and BMI. Gender distribution differed between the groups, with males dominating the group without PMF (73%) and Haraguchi type III (69%). In the Haraguchi type II group, 68% of the patients were female (Table 1). 17 of 125 (13%) of the PMFs were addressed surgically, with the highest number of fixed fractures in the Haraguchi II group (Table 2).

Radiological results:

All 125 patients with a PMF were classified according to Haraguchi: We found 61 (49%) Type I, 28 (22%) type II and 36 (28%) type III fractures. The intraobserver agreement for the Haraguchi classification was 0.733, (95% CI: 0.629 to 0.884) p<0.001. The interobserver agreement for the Haraguchi classification was 0.797, (95% CI: 0.705 to 0.889) p<0.001. When comparing plain radiographs (AP, mortise and lateral view) to CTs, 42 (34%) of the PMFs (22 (36%) Haraguchi type I, 1 (4%) Haraguchi type II and 19 (53%) Haraguchi type III) were missed when assessing plain radiographs only. Two patients were assessed to have a PMF on plain radiographs, but no fracture was visible on the CTs. The presence of OA after two years ranged from 34.5 % in the Haraguchi III group to 64% in the Haraguchi II group. This difference between was not statistically significant (table 5).

Clinical results:

In the mixed model analysis, the AOFAS score showed similar slopes in the four groups (figure 2), and the group effect did not change significantly over time (p= 0.234). When analyzing the differences in AOFAS between the four groups at each time point with a mixed model analysis the Haraguchi type II fracture had a significantly lower AOFAS score at 6 weeks (-7.5 (95% CI; -15.0 to -0.2), p=0.04) and 6 months (-8.4 (95% CI; -15.3 to -1.5), p= 0.01) compared to patients with no PMF (table 3 and 4). There was no statistically significant difference between the other groups.

Discussion

In this study, 60% of the C type ankle fracture patients had a PMF, and 34% of these were missed on plain radiographs. We found classification of PMF according to the Haraguchi classification to be reliable, with substantial agreement between raters. Also, patients with the Haraguchi II fracture type (medial extension) had a lower AOFAS score at 6 weeks and 6 months compared to no PMF. At 1 and 2 years, we found no statistically significant difference for our end points based on presence, or fracture pattern, of a PMF.

Our reported incidence of PMF is high compared to earlier findings (9,29,30). This could be due to the fact that our patient series consisted of AO/OTA C fractures only, following a pronation- external rotation injury, where a rupture of the posterior tibiofibular ligament or avulsion fracture is known to commonly coexist in the fracture complex (19). We missed 34% of PMFs when analyzing plain radiographs only. This underestimation supports the use of preoperative CT in the case of an AO/OTA -C type fracture, to visualize the complete fracture complex before planning final fracture fixation (14,32).

As in previous reports, the Haraguchi type I fracture was the most common type in our dataset(6-8). This fracture involves the incisura (the Volkmann’s triangle). The Haraguchi system does not distinguish between size of the triangular fractures and type I includes both small and large posterolateral fractures. This may represent a weakness with the system, as type I fractures include both fractures caused by a combination of ligamentous avulsions and compressive forces with the ankle in neutral position or plantarflexed.

We observed twice as many patients with the extra-incisural fracture (type III) in our series, compared to Haraguchis findings (28% vs 14%) (6). The Haraguchi type III injury is described to be an avulsion from the distal posterior tibial cortex, by the pull of the posterior inferior tibiofibular ligament (PITFL), with a partial or full syndesmotic rupture (8). This correspond with the Mason type I and Bartonicek type I and occurs in theory when a rotational force is applied to a plantarflexed unloaded ankle(7,8). 77% of the patients in Haraguchis study were supination exorotation stage II-IV injuries and the difference in injury mechanism might explain why we observed more type III fractures in our series of patients.

To our knowledge, this is the first trial exclusively studying AO/OTA C fracture with respect to PMFs and outcome. The C type fracture is a more serious injury compared to the A and B-types, with frequent osteochondral lesions found on arthroscopy(31). Blom found poorer functional outcome in patients with a Haraguchi type II fracture compared to Haraguchi type I and III when assessing patients with the Foot and Ankle Score 2 years after injury (16). In our study, Haraguchi type II fracture did worse up until 6 months compared to no PMF. We could not, however, detect differences according to fracture pattern at 2 years, in agreement with Tejwani at al from 2010 (5). In Bloms study, 77% of the PMFs were treated surgically, but only 10% received an additional syndesmotic screw. In our data set, 13% were treated surgically, but all received a syndesmotic fixation. The absolute use of syndesmotic stabilization, regardless of PMF fixation, might explain our equal results between groups at 2 years. An additional syndesmotic fixation might gain stability and better functional outcomes, especially in the unstable Haraguchi type II fracture group, where the deep posteromedial corner is involved. However, studies show that fixing a PMF can restore the syndesmotic stability(32), making additional syndesmotic fixation unneeded(19,33). In the case of syndesmotic rupture treated with PMF fixation alone, the AITFL is not addressed. The AITFL is the strongest of the syndesmotic ligaments(34). Clanton found that an isolated AITFL injury could result in syndesmotic instability(35), but few clinical trials address this topic, and in light of Ogilvie Harris’ and Clanton’s findings one may question the ability to restore syndesmotic stability with a PMF fixation alone.

There were no statistically significant differences between the groups when assessing presence of OA at 2 years. When studying risk factors for OA, Lübekke et al. did not find an association between PMF and OA. They noted, however, that Weber C fractures, medial malleolar fractures and fracture dislocations were significant risk factors for OA development (36).

The difference in AOFAS comparing Haraguchi II fractures to no PMF at 6 weeks and 6 months was small, and the clinical significance of this finding is questionable. Other studies have reported that a PMF does not affect clinical outcome (29), but these findings may also reflect the fact that there is no consensus on when fixation of a PMF gains a more favorable outcome. RCTs comparing conservative and operative treatment of PMFs stratified by fracture pattern could potentially answer this question.

There are some inherent weaknesses in our present study. Classification of the PMFs was, in the majority of patients, conducted on CT after surgery, with metal artefacts making some of the fractures difficult to classify. We believe this could explain why our inter- and intra-rater reliabilities were lower than a previous study (8). Even so, our rating agreements are substantial, making the Haraguchi classification system reliable for orthopedic surgeons.

4 different implants were used for syndesmotic fixation (table 2). The quadricortical screw gained poorer results compared to suture button in the first RCT (23), and this represents a baseline difference between the groups, even though only 2 patients with a Haraguchi type II PMF received the less favorable quadricortical screw (Table 2).

Also, our patients were enrolled over a long period of time, from 2011-2017. In this period, assessment and treatment of PMF received increased attention and may explain the increase in patients treated with a PMF fixation during the study period (5 patients in the study by Andersen et al. 12 patients in the study by Ræder et al). Since only a small proportion of our patients were treated operatively for their PMF, giving advice on the treatment of PMF would be beyond the scope of this study.

The choice of outcome scores in this study is debatable, as it has previously been criticized for lack of validation, low precision and ceiling effects(37). The AOFAS was still chosen since it was the primary outcome in both RCTs contributing to the data in this study.

There is a lack of blinding in this cohort study. Neither the patient or examiner was blinded to fracture pattern or treatment. However, during patient follow up, the primary focus was syndesmotic stabilization, not presence of PMF.

There are several strengths to this study. It entails a high number of patients, with a high 2-year follow-up rate of 86%. Previous studies on the PMF have included all ankle fractures, with a predominance of B type fractures (6,8). Our inclusion of C type fractures only increases the homogeneity of the injury mechanism, and may thus increase our knowledge on PMFs in OA/OTA C type ankle fractures.

Conclusion

60% of patients with AO/OTA -C fractures have a PMF. 34% of PMFs where missed on plain radiographs compared to CT findings. PMFs with a medial extension (Haraguchi II), gives a poorer outcome at 6 weeks and 6 months. The Haraguchi classification can be used as a valid tool for describing PMFs with substantial agreement between raters.

Table 1: Patient & Fracture Characteristics at Time of Enrollment

	No PMF (n=85)	Haraguchi Type I (n=61)	Haraguchi Type II (n=28)	Haraguchi Type III (n=36)
Age (years)	43 ± 14	46 ± 15	47 ± 14	45 ± 16
Male sex	62 (73%)	34 (56%)	9 (32%)	25 (69%)
Body Mass Index	27 ± 6	28 ± 5	26 ± 4	27 ± 4
Maisonneuve	29 (34%)	18 (30%)	8 (29%)	20 (56%)
Medial Malleolus fixation	18 (21%)	33 (54%)	15 (54%)	10 (28%)
Posterior malleolus fixation	0	5 (8%)	12 (43%)	0 (0%)
Plate osteosynthesis of fibula	52 (61%)	41 (67%)	18 (64%)	14(39%)

Values are number of patients with the percentage in parenthesis, except for age and body mass index, given as mean ± standard deviation.
PMF = Posterior malleolar fracture

Table 2: Surgical Technique for ankle fracture fixation

	No PMF (n= 85)	Haraguchi Type I (n= 61)	Haraguchi Type II (n= 28)	Haraguchi Type III (n= 36)
PMF fixation anterior to posterior screw	0	2 (3%)	4 (14%)	0
PMF fixation posterior to anterior screw	0	1 (2%)	2 (7%)	0
PMF buttress plate fixation	0	2 (3%)	6 (21%)	0
4.5 mm quadricortical syndesmotic screw	23 (27%)	15 (25%)	2 (7%)	8 (22%)
3.5 mm tricortical syndesmotic screw	29 (34%)	15 (25%)	7 (25%)	7 (19%)
Suture button	33 (39%)	31 (51%)	19 (68%)	21 (58%)
Fibula plate fixation	52 (61%)	41 (67%)	18 (64%)	14 (39%)
Medial malleolar fracture fixation	18 (21%)	33 (54%)	15 (54%)	10 (28%)

Values are expressed as the number of patients with the percentage in parenthesis.
PMF = Posterior malleolar fracture

Table 3: Primary outcome measure
The American Orthopaedic Foot & Ankle Society Ankle-Hindfoot Score

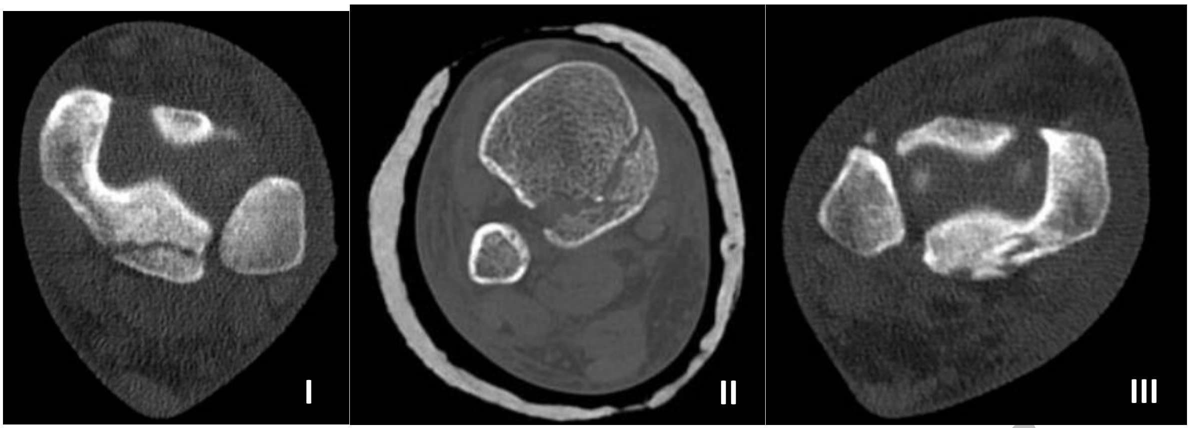
	No PMF (n=85)	Haraguchi Type I (n=61)	Haraguchi Type II (n=28)	Haraguchi Type III (n=36)
6 weeks	65.9 (63.0 to 68.8)	62.4 (59.1 to 65.7)	58.4 (53.2 to 63.6)	63.9 (59.6 to 68.3)

	(n=79)	(n=59)	(n=25)	(n=34)
6 months	88.0 (85.2 to 90.9) (n=76)	86.8 (83.6 to 90.1) (n=58)	79.6 (74.8 to 84.4) (n=28)	84.1 (79.7 to 88.4) (n=32)
1 year	89.8 (87.1 to 92.5) (n=72)	90.4 (87.4 to 93.3) (n=62)	87.1 (82.5 to 91.7) (n=26)	87.9 (83.9 to 91.9) (n=32)
2 years	91.4 (88.2 to 94.5) (n=68)	90.8 (87.4 to 94.2) (n=56)	89.9 (84.7 to 95.0) (n=26)	88.4 (83.8 to 93.0) n=31)
Values are expressed as mean with 95% confidence interval.				

Table 4: Pairwise comparisons at different time points for The American Orthopaedic Foot & Ankle Society Ankle-Hindfoot Score				
follow up time	Haraguchi	Haraguchi	Mean difference	p-value*
6 weeks	I	0	-3.5 (-8.9 to 1.9)	0.36
	II	0	-7.5 (-15.0 to -0.2)	0.04
	IIII	0	-2.0 (-8.4 to 4.4)	1.00
6 months	I	0	-1.2 (-6.5 to 4.1)	1.00
	II	0	-8.4 (-15.3 to -1.5)	0.01
	III	0	-4.0 (-10.3 to 2.4)	0.41
1 year	I	0	0.6 (-4.3 to 5.5)	1.00
	II	0	-2,7 (-9.3 to 3.9)	0.99
	III	0	-1.9 (-7.8 to 4.0)	1.00
2 years	I	0	-0.6 (-6.3 to 5.2)	1.00
	II	0	-1,5 (-9.0 to 6.0)	1.00
	III	0	-3.0 (-9.8 to 3.9)	0.88
Values are expressed as mean with 95% Confidence interval * Mixed Model Test of fracture group as fixed effect. Adjusted for age, BMI, gender.				

Table 5: Presence of ankle osteoarthritis (OA)				
	No PMF (n= 65)	Haraguchi type I (n= 53)	Haraguchi type II (n= 25)	Haraguchi type III (n= 29)
OA	26 (40%)	25 (47%)	16 (64%)	10 (34%)
Number of patients with osteoarthritis assessed by CT at 2 years. Pearson's Chi- Square p= 0.127				

Figure 1:



Legend figure 1: Axial CT images of the three different fracture patterns according to the Haraguchi Classification: Type I (the posterolateral-oblique type), type II (the medial extension type) and type III (the small-shell type).

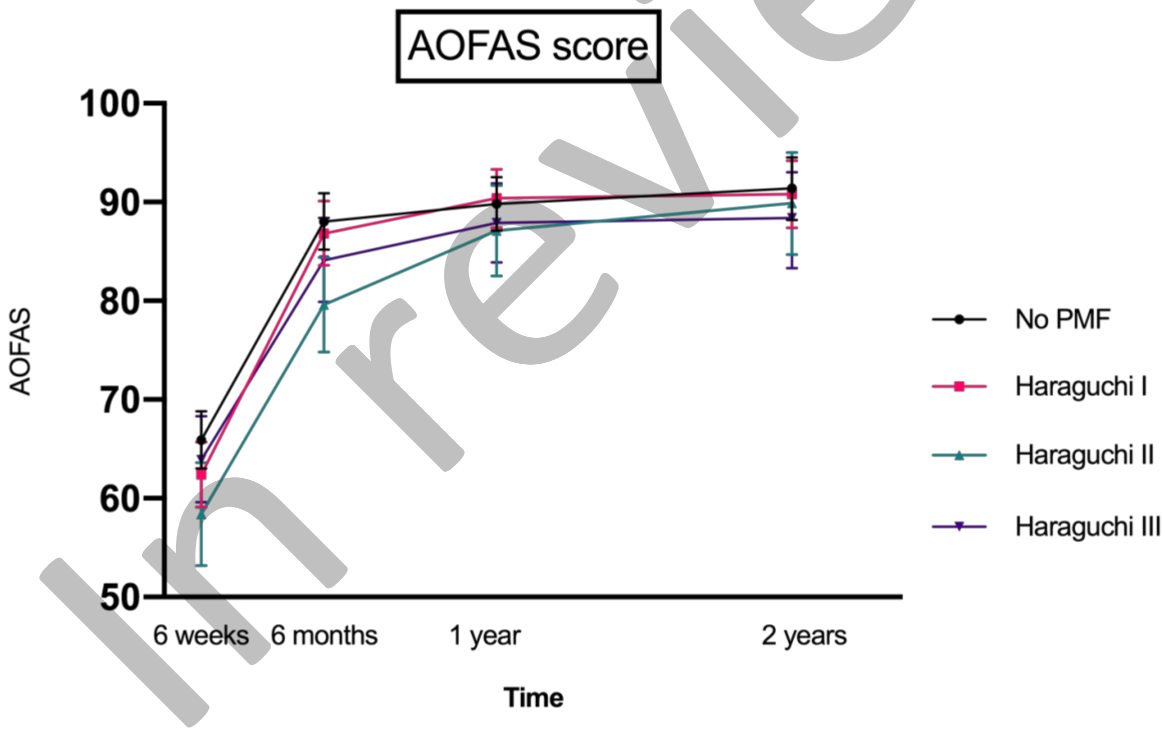


Figure 2:

Legend figure 2: Line graph illustrating slope for the American Orthopaedic Foot & Ankle Society Ankle-Hindfoot Score (AOFAS) for the four subgroups of patients with mean and 95% confidence intervals at the four different time points.

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