Tero Kortekangas

THE NON-OPERATIVE TREATMENT OF WEBER B-TYPE ANKLE FRACTURES AND THE CLINICAL RELEVANCE AND TREATMENT OF SYNDESMOSIS INJURY
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Abstract

Despite numerous biomechanical and clinical studies on ankle fractures, the optimal treatment method for a stable fibula fracture is poorly known. Additionally, the clinical relevance and optimal fixation method of syndesmosis injury for different ankle fracture types is unclear.

This thesis aimed: (I) to compare six weeks of cast immobilization with three weeks of immobilization (cast or orthosis) in a randomized controlled trial (RCT) of 247 patients with stable Weber B-type fibular fracture; (II) to compare mid-term outcome of syndesmosis transfixation with no fixation in an RCT of 24 patients with supination external rotation (SER) ankle fractures and syndesmosis injury; (III) to evaluate the significance of the syndesmosis injury on clinical outcome in a case-control study of 48 patients with SER ankle fractures; and (IV) to compare the syndesmosis fixation with a screw versus a suture-button device in terms of the accuracy and the maintenance of syndesmosis reduction in an RCT of 43 patients with pronation external rotation (PER) ankle fractures.

Three weeks of immobilization in either a cast or an orthosis resulted in non-inferior outcomes compared to traditional six weeks’ immobilization in patients with stable Weber B-type fibula fracture. In patients with SER ankle fracture and unstable syndesmosis after fixation of bone fractures, leaving unstable syndesmosis unfixed resulted in similar outcomes compared to syndesmosis transfixation at mid-term follow-up. Patients with SER ankle fractures with or without an associated syndesmosis injury had similar clinical outcomes after a minimum of four years of follow-up. The syndesmotic screw and the suture-button fixation in patients with PER ankle fracture and unstable syndesmosis resulted in a low malreduction rate and both methods maintained reduction well.

In conclusion, stable Weber B-type fibula fractures can safely be treated with only three weeks of cast immobilization or even with a simple orthosis. A syndesmosis injury in SER ankle fractures seems to be of minor therapeutic or prognostic importance and syndesmosis screw fixation has no effect on patient’s recovery compared to no syndesmosis fixation. An associated syndesmosis injury in PER ankle fractures can be fixed with a syndesmotic screw or a suture-button device with comparable outcomes.

Keywords: ankle fracture, non-operative treatment, PER, SER, stable fibula fracture, suture-button fixation, syndesmosis injury, syndesmosis malreduction, syndesmotic screw, Weber B
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"By knowing things that exist, you can know that which does not exist."
(Miyamoto Musashi 1645)

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Abbreviations

AITFL  Anterior inferior tibiofibular ligament
AO     Arbeitsgemeinschaft für Osteosynthesefragen
AO/ASIF Association for Osteosynthesis/Association for the Study of Internal Fixation
AP     Anterior posterior
CBCT   Cone beam computed tomography
CI     Confidence interval
CT     Computed tomography
DVT    Deep vein thrombosis
ER     External rotation
FAOS   Foot and Ankle Outcome Score
ITT    Intention-to-treat
LMM    Linear mixed model
MCS    Medial clear space
MCID   Minimal clinically important difference
MRI    Magnetic resonance imaging
OA     Osteoarthritis
OMAS   Olerud-Molander Ankle Score
ORIF   Open reduction and internal fixation
PA     Pronation adduction
PER    Pronation external rotation
PITFL  Posterior inferior tibiofibular ligament
RAND 36 RAND 36-Item Health Survey
RCT    Randomised controlled trial
ROM    Range-of-motion
SA     Supination adduction
SD     Standard deviation
SER    Supination external rotation
TTCS   Tibiotalar clear space
TFCS   Tibiofibular clear space
VAS    Visual Analogue Scale
List of original publications

This thesis is based on the following publications, which are referred throughout the text by their Roman numerals:


# Table of contents

**Abstract**

**Tiivistelmä**

**Acknowledgements**

**Abbreviations**

**List of original publications**

**Table of contents**

1 Introduction

2 Review of the literature

  2.1 Anatomy and biomechanics of the ankle .............................................. 25
  2.2 Classification of ankle fractures (Lauge-Hansen, Weber) ...................... 26
  2.3 Ankle mortise stability ........................................................................ 27
  2.4 SER/Weber B-type ankle fracture stability assessment .......................... 28
  2.5 Treatment of isolated Weber B-type fibula fractures ............................ 29
      2.5.1 Operative versus non-operative treatment ................................ 29
      2.5.2 Cast treatment ....................................................................... 30
      2.5.3 Functional treatment ................................................................ 30
  2.6 Syndesmosis injury ............................................................................ 31
      2.6.1 Diagnosis of the syndesmosis injury associated to ankle fracture 31
      2.6.2 Clinical relevance of the syndesmosis injury .............................. 32
  2.7 Treatment of the syndesmosis injury in connection with ankle fracture 33
      2.7.1 Conservative treatment of syndesmosis injury ............................ 34
      2.7.2 Indications for syndesmosis transfixation ................................. 34
      2.7.3 Syndesmosis screw fixation ...................................................... 36
      2.7.4 Flexible syndesmosis fixation .................................................... 37
      2.7.5 Syndesmosis malreduction ....................................................... 37
  2.8 Posttraumatic OA of the ankle joint ................................................... 39

3 Aims of the present study

4 Materials and methods

  4.1 RCT of non-operative treatment of stable Weber B-type ankle fractures (I) .................................................................................. 43
      4.1.1 Patients .................................................................................. 43
      4.1.2 Interventions and control ....................................................... 44
      4.1.3 Follow-up .............................................................................. 44
4.1.4 Outcome measures ........................................................................ 46

4.2 RCT mid-term results of syndesmotic transfixation versus no fixation in patients with SER IV-type ankle fractures (II) ....................... 46
4.2.1 Patients .......................................................................................... 46
4.2.2 Intervention and control ............................................................... 47
4.2.3 Follow-up ..................................................................................... 47
4.2.4 Outcome measures ....................................................................... 47

4.3 Clinical relevance of syndesmosis injury in SER IV/Weber B-type ankle fractures (III) ................................................................. 48
4.3.1 Patients .......................................................................................... 48
4.3.2 Matching .............................................................. 48
4.3.3 Follow-up ..................................................................................... 49
4.3.4 Outcome measures ....................................................................... 49

4.4 RCT Suture-button versus screw for fixation of syndesmosis injury (IV) ....................................................................................... 49
4.4.1 Patients .......................................................................................... 50
4.4.2 Intervention and control ............................................................... 50
4.4.3 Syndesmosis reduction assessment .............................................. 51
4.4.4 Follow-up ..................................................................................... 52
4.4.5 Outcome measures ....................................................................... 53

4.5 Ethics ....................................................................................................... 54

4.6 Statistical methods .................................................................................. 54
4.6.1 Sample size calculations ............................................................... 54
4.6.2 Randomisation and masking .......................................................... 55

5 Results 57
5.1 RCT of non-operative treatment of stable Weber B-type ankle fractures (I) ...................................................................................... 57
5.1.1 The Olerud-Molander Ankle Score (OMAS) ............................... 58
5.1.2 Secondary Outcomes (FAOS, VAS, RAND 36, ROM and fracture union) ....................................................................................... 59
5.1.3 Adverse effects ............................................................................. 62
5.1.4 Protocol violations ......................................................................... 62

5.2 Syndesmosis screw fixation versus no syndesmosis fixation (II) ............ 63
5.2.1 Functional results ........................................................................ 63
5.2.2 Radiological results ...................................................................... 64
5.2.3 Reoperations ................................................................................ 66
5.3 Clinical relevance of syndesmosis injury in SER IV/Weber B -
type ankle fractures (III) ........................................................................ 66
  5.3.1 Functional results .......................................................................... 66
  5.3.2 Radiological results ........................................................................ 67
5.4 Suture-button fixation versus screw fixation (IV) ............................... 68
  5.4.1 Syndesmosis reduction .................................................................... 69
  5.4.2 Functional results .......................................................................... 70
  5.4.3 Posttraumatic OA according to CBCT-scans................................. 72
6 Discussion 75
  6.1 General considerations ....................................................................... 75
  6.2 Non-operative treatment of stable Weber B-type fibula fracture ........ 76
  6.3 Indications for syndesmosis fixation in SER -type ankle fractures........ 78
  6.4 Clinical relevance of the syndesmosis injury in SER-type ankle
      fractures .............................................................................................. 80
  6.5 Dynamic or static syndesmosis fixation? ............................................ 81
  6.6 Clinical implications and future studies ............................................ 83
7 Conclusions 85
References 87
Original publications 103
1 Introduction

Maisonneuve (1840) was the first to describe the mechanism of external rotation injuries, the ruling trauma mechanism of the ankle fractures. Fractures about the ankle caused by indirect trauma account for 9% of all fractures, with increasing incidence, and represent a significant portion of the trauma workload (Court-Brown et al. 1998, Court-Brown & Caesar 2006). Only proximal femoral fractures are more frequent in the lower limb (Court-Brown et al. 1998, Court-Brown & Caesar 2006). By far, the most common ankle fracture type is supination-external rotation SER/Weber B-type, which comprises 80 to 90 per cent of all fractures about the ankle (Lauge-Hansen 1950, Danis 1949, Weber 1972, Müller et al. 1979, Lindsjö 1985, Michelson 1995). Ankle fractures can be treated either operatively or non-operatively, depending on the stability of the ankle mortise; therefore, stability assessment is considered crucial in terms of successful treatment of these fractures (Yde & Kristensen 1980a, Yde & Kristensen 1980b, Bauer et al. 1985b, Kristensen & Hansen 1985, Phillips et al. 1985, Tile 1987, Michelson 1995, Michelson et al. 2001, McConnell et al. 2004, Michelson et al. 2007, Gill et al. 2007, Gougoulias et al. 2010).

or high-quality prospective studies, together with heterogeneity in the study design for the published material, provides an inadequate evidence base with which to reach decisions for the optimal non-operative treatment method for stable SER/Weber B-type fibula fractures (Lin et al. 2012).


Apart from the indications for syndesmosis transfixation, accurate reduction of the ankle syndesmosis is also challenging for several reasons. Malreduction of the syndesmosis that alters tibiofibular joint kinematics may lead to degenerative changes of the upper ankle joint and poor clinical outcome (Klossner 1962, Pettrone et al. 1983, Leeds & Erclich 1984, De Souza et al. 1985, Lindsjö 1985, Weening & Bhandari 2005, Naqvi et al. 2012b, Sagi et al. 2012). Therefore, accuracy and maintenance of reduction of the syndesmosis are considered essential when treating

The metallic screw is currently considered the “gold standard” for syndesmotic transfixation (van den Bekerom & Raven 2007, Schepers 2012, Van Heest & Lafferty 2014). However, syndesmosis malreduction is reported to occur in 16% to more than 50% of patients following syndesmotic screw fixation (Weening & Bhandari 2005, Gardner et al. 2006, Miller et al. 2009, Naqvi et al. 2012b, Sagi et al. 2012). Furthermore, syndesmotic screw fixation alters the normal biomechanics of the distal tibiofibular joint (Needelman et al. 1989, Pereira et al. 1996, Miller et al. 1999). Hence, the effectiveness and feasibility of syndesmotic screw fixation is now brought increasingly into question, with a concomitant and rapid increase in the use of the more dynamic suture-button syndesmotic fixation systems (Bava et al. 2010, Van Heest & Lafferty 2014). Theoretically, suture-button devices allow physiologic motion of the syndesmosis without need for implant removal, and lowers the possibility of fixation breakage when normal weight-bearing is started; therefore, it may reduce the risk of recurrent syndesmotic diastasis (Thornes et al. 2005, Cottom et al. 2008 & 2009, DeGroot et al. 2011, Schepers 2012, Van Heest & Lafferty 2014). No clinical studies have yet compared the syndesmotic screw and suture-button fixation methods using bilateral CT-scans for syndesmosis reduction assessment both intraoperatively and after a reasonably long follow-up.

This doctoral thesis was initiated to find the optimal non-operative treatment method for isolated stable Weber B-type fibular fractures. In addition, the clinical relevance of syndesmotic injury and the influence of the syndesmotic screw fixation to the ankle functional and radiological results in patients with SER/Weber B-type ankle fractures were evaluated in two studies. Lastly, syndesmosis screw and suture-button fixation methods were compared primarily in terms of the accuracy and maintenance of syndesmosis reduction, and secondarily for the functional outcome and the rate of posttraumatic OA.
2 Review of the literature

2.1 Anatomy and biomechanics of the ankle

The ankle joint is composed of the articulation of three bones: the talus, the distal aspect of tibia and the distal aspect of the fibula. The primary articulation of this joint complex is between the dome of talus and the tibial plafond, with 80 to 90% of the load transmitted through the tibial plafond to the dome of the talus (Calhoun et al. 1994). Under normal weight-bearing conditions, the fibula transmits 17% of the total load proximally (Lambert 1971). However, the mechanism by which the load is transferred to the fibula via syndesmosis is not fully understood (Michelson 1995). A syndesmosis (from the Greek syndesmos, meaning “ligament”, and -osis, meaning “condition”) is a fibrous articulation in which the opposing surfaces are combined by ligaments. This ligamentous complex consists of four main ligaments: the anterior and posterior tibiofibular ligaments, the transverse ligament and the interosseous ligament (Lutz 1942, Hermans et al. 2010). The syndesmosis complex acts as a secondary stabiliser of the ankle mortise by fixing the fibula in the fibular notch (Rasmussen et al. 1982, Sarrafian 1993, Michelson 1995). According to biomechanical study the posterior inferior tibiofibular ligament (PITFL) complex is the strongest part of the syndesmosis, and together with the associated transverse ligament provides 42% of the overall syndesmosis resistance strength (Ogilvie-Harris et al. 1994). The distal aspect of the fibula is also attached to the hind foot by three separate ligaments. The medial side of the ankle joint is stabilised by the deltoid ligament. The deltoid ligament complex consists of two layers; a superficial and a deep layer. While the deep posterior tibiotalar ligament is the strongest ligament of the deltoid complex, it is also responsible for preventing the external rotation (ER) of the talus and is therefore the main stabiliser of the ankle mortise (Rasmussen et al. 1983, Rasmussen 1985, Burns et al. 1993, Michelson 1995, Michelson et al. 1996).

The normal ankle joint mechanics consists of a combination of sliding and rolling, as the joint moves through the sagittal range of motion (Sammarco et al. 1973, Michelson 1995). When the foot is brought from plantarflexion to dorsiflexion, the talus also externally rotates (Michelson et al. 1994, Siegler et al. 1988). The dome of the talus is wider anteriorly than posteriorly; therefore, the intermalleolar distance increases by approximately 1.5 mm as the ankle dorsiflexes and the fibula moves posterior to lateral direction and rotates externally 2–4 degrees.
through the tibiofibular syndesmosis (Close 1956, Lundberg 1989, Burns et al. 1993, Peter et al. 1994, Bragonzoni et al. 2006, Clanton et al. 2017). Under physiologic conditions, the intact ankle syndesmosis allows 3.3 mm of fibular translation in the sagittal plane (i.e. AP direction) (Clanton et al. 2017). Normal ankle movements under axially loaded ankle specimens have been reported to limit to 32 degrees of dorsiflexion and 45 degrees of plantarflexion (Lindsjö et al. 1985).

### 2.2 Classification of ankle fractures (Lauge-Hansen, Weber)

The rational treatment of ankle fractures requires a knowledge of the extent of bone and soft tissue injury. For this reason, different classification systems for ankle fractures have been developed to provide diagnostic information and prognostic guidance in clinical decision making (Michelson et al. 1997). The two most widely used ankle fracture classification systems are the Lauge-Hansen (Lauge-Hansen 1950) and AO/Danis-Weber (Danis 1949, Weber 1972, Müller et al. 1979) systems. The Lauge-Hansen classification system classifies ankle fractures based on the foot position (supination or pronation) and the force applied (external-rotation, abduction or adduction) at the time of injury (Lauge-Hansen 1950). This classification system divides ankle fractures into four types: supination-external rotation (SER), pronation-external rotation (PER), supination-adduction (SA) and pronation-adduction (PA), and further into four stages (I-IV) depending on the extent of the deforming force. For each stage from I to IV, another stabilising structure of the ankle mortise (bone or ligament structure) is injured. In SER fractures, the deforming force starts from the lateral side, generating first a rupture of the anterior-inferior tibiofibular ligament (AITFL) (SER type I) and continued deforming force then causes progression around the ankle posteriorly, as a lateral short oblique fibular fracture (anteroinferior to posterosuperior) (SER type II), a posterior malleolus fracture or posterior-inferior tibiofibular ligament (PITFL) rupture (SER type III), and finally as a medial malleolus fracture or the deltoid ligament rupture (SER type IV). In PER fractures, the medial structures are tensioned at first, and the injury starts with a disruption of the deltoid ligament or the transverse fracture of the medial malleolus (PER type I) and progresses around the ankle anteriorly as the AITFL ruptures (PER type II), as a lateral short oblique or spiral fracture of fibula (anterosuperior to posteroinferior) above the level of the upper ankle joint (PER type III), and finally as the PITFL rupture or avulsion of posterior malleolus (PER type IV) (Lauge-Hansen 1950).
While the Lauge-Hansen classification system could help to guide closed treatment of ankle fractures, it tends to be complicated and difficult to apply in clinical work (Michelson 1995). The Danis-Weber classification (Danis 1949, Weber 1966) was developed based on the view that the fibular fracture is the most important component in an ankle injury (Danis 1949, Weber 1966, Cedell 1967). This concept was shared by many authors, who considered that the medial structures of the ankle joint are unimportant, as far as stability is concerned (Picaud 1953, Iselin & de Vellis 1961, Weber 1966). This classification, today best known as Weber classification, was modified by Weber in 1972. The Weber classification system divides ankle fractures into three types (A–C) based on the level of the fracture of the lateral malleolus relative to the upper ankle joint line. The Weber system was developed to indicate the necessary amount of operative correction (Weber 1972, Michelson 1995). The lateral malleolus fracture starts distal to the tibial plafond in type A, at the level of tibial plafond and spiral/oblique morphology in type B, and proximal to the tibial plafond involving injury to the syndesmosis in type C (Weber 1972, Müller et al. 1979). Unlike the Lauge-Hansen classification system, the Weber classification does not consider medial side injuries.

2.3 Ankle mortise stability

The ankle mortise is defined as unstable if the injury pattern of the fractured ankle allows ER of the talus, which displays as a lateral shift of the talus on a two-dimensional plain radiograph (Yablon et al. 1977, McCullough & Burge 1980, Harper 1983, Michelson 1995). In conjunction with lateral side injury (e.g. syndesmosis injury), sectioning of the deep deltoid ligament leads to an unstable ankle mortise by allowing ER of the talus (Harper 1983, Michelson 1995, Michelson & Waldman 1996). Several investigators have demonstrated that the medial malleolus and deltoid ligament are the primary sources of ankle stability (Petrone et al. 1983, Phillips et al. 1985, Michelson et al. 1992, Harper 1995, Earll et al. 1996, Sasse et al. 1999, Michelson et al. 2002). Previous studies have also shown that even 1 mm of talar displacement decreases the contact area in the tibiotalar joint by 42% (Ramsey & Hamilton 1976, Clarke et al. 1991, Harris & Fallat 2004). Abnormal movement of the talus and widening of the ankle mortise, if not corrected, is considered to result in early osteoarthritis and to poor clinical outcome (Wilson & Skilbred 1966, Brodie & Denham 1974, Joy et al. 1974, Michelson 1995). Therefore, the stability of the ankle mortise is widely regarded as the most crucial factor when treating ankle fractures (Yde & Kristensen 1980a,

2.4 SER/Weber B-type ankle fracture stability assessment

2.5 Treatment of isolated Weber B-type fibula fractures

2.5.1 Operative versus non-operative treatment


In the 1970s, biomechanical studies by Ramsey & Hamilton and by Yablon et al. suggested that the amount of displacement of the lateral malleolus is the most important factor when choosing a treatment method (Ramsey & Hamilton 1976, Yablon et al. 1977). They based their views on an assumption that the talus follows the lateral malleolus; therefore, the fracture of the fibula should be anatomically reduced (Ramsey & Hamilton 1976, Yablon et al. 1977). Treatment recommendations returned to non-operative treatment when Kristensen & Hansen and Bauer et al. published their results from long-term (20–30 years) outcome studies about the non-operative treatment of SER II/Weber B-type fibula fractures and showed no appreciable signs of posttraumatic OA development (Bauer et al. 1985, Kristensen & Hansen 1985). Since then, clinical studies on the non-operative treatment of these fractures with both short (Yde & Kristensen 1980a, Stuart et al. 1989, Zeegers et al. 1989, Ryd & Bengtsson 1992, Brink et al. 1996, Port et al. 1996) and long (Donken et al. 2012) follow-up have reported good clinical outcomes. Studies reporting failures in the non-operative treatment of SER/Weber B-type fibula fractures have also found their stability

2.5.2 Cast treatment


2.5.3 Functional treatment

Problems associated with cast treatment might be avoided by an equally effective treatment of stable ankle fractures with simple, more functional measures (Hutchinson & Barrie 2015), such as braces or orthoses (Stuart et al. 1989, Brink et al. 1996), strapping (Ryd & Bengtson 1992, Port et al. 1996), high top shoes (Zeegers et al. 1989) or even without any immobilisation (Lapidus & Guidotti 1968). These functional treatment methods are suggested to result in more rapid
rehabilitation and better short-term functional outcome when compared to traditional cast immobilisation (Stuart et al. 1989, Port et al. 1996). However, only two randomised clinical trials with a relatively small patient numbers and follow-up limited to three to six months, have compared cast and functional ankle fracture treatments. (Stuart et al. 1989, Port et al. 1996). A Cochrane review by Lin et al. concluded that insufficient evidence is available to determine the benefits of using an air-stirrup over a cast or orthosis in the non-operative treatment of ankle fractures (Lin et al. 2012). Thus, the lack of RCTs or high-quality prospective studies, together with heterogeneity in the study design for the published material, provides an inadequate evidence base from which to reach decisions for the optimal non-operative treatment of stable ankle fractures.

2.6 Syndesmosis injury


2.6.1 Diagnosis of the syndesmosis injury associated to ankle fracture

Syndesmosis injury maybe apparent in static ankle radiographs of cases of PER/Weber C-type ankle fracture with a widened ankle mortise or distal tibiofibular joint (Lauge-Hansen 1950, Boden et al. 1989, Yamaguchi et al. 1994, Chissell and Jones 1995, van den Bekerom et al. 2010). However, plain radiographs are viewed as poor instruments for assessing the distal tibiofibular joint congruence and syndesmosis injury (Kaye et al. 1989, Ebraheim et al. 1997, Takao et al. 2001,
Nielson et al. 2004). Therefore, intraoperative syndesmosis stress tests (Colton 1982, Leeds & Ehrlich 1984, Jenkinson et al. 2005, Weening and Bhandari 2005, Stark et al. 2007, Pakarinen 2011b&c), ankle arthroscopy (Ogilvie-Harris & Reed 1994, Takao et al. 2001), magnetic resonance imaging (MRI) (Takao et al. 2001, Nielson et al. 2004) or computed tomography (CT) scans (Ebraheim et al. 2003) of the fractured ankle have been recommended instead. These methods have revealed unsuspected disruption of the syndesmosis also in low (SER/Weber B -type) fibular fractures, with reported incidences of the syndesmosis injuries in these fractures of around 30% (Takao et al. 2001, Nielson et al. 2004, Jenkinson et al. 2005, Weening and Bhandari 2005, Stark et al. 2007, Pakarinen 2011c) However, static CT or MRI scans seldom reveal syndesmotic instability; therefore, most authors have recommended intraoperative syndesmosis stress testing (Pankovich 1976, Pankovich 1978, Stiehl & Schwartz 1990, Amendola 1992, Ogilvie-Harris & Reed 1994, Wuest 1997, Beumer et al. 2004, Candal-Couto et al. 2004, Nielson et al. 2004, van den Bekerom et al. 2010). A variety of clinical tests are available for diagnosing instability of the distal tibiofibular joint intraoperatively, including the hook test (Candal-Couto et al. 2004), fibular translation or rotation tests (Ogilvie-Harris & Reed 1994, Candal-Couto et al. 2004), and the external rotation stress test (Boytim et al. 1991, Xenos et al. 1995, Jenkinson et al. 2005, Stoffel et al. 2009, Pakarinen et al. 2011b&c). However, the data regarding the validity and reliability of these tests are limited, and the interpretation of these tests can be very subjective (Jenkinson et al. 2005, Pakarinen et al. 2011b). Biomechanical studies have shown that instability of the syndesmosis can be detected by using a 7.5 Nm external rotation stress (Xenos et al. 1995, Beumer et al. 2003). Jenkinson et al. described a standardised technique to perform intraoperative external rotation test using 7.5-Nm torque under fluoroscopy, after fixation of the bone fragments (Jenkinson et al. 2005). This standardised method increases the accuracy and reliability of detection of distal tibiofibular joint instability (Jenkinson et al. 2005, Pakarinen et al. 2011b&c). Thresholds of 1 to 2 mm of side-to-side (injured vs. uninjured ankle) difference in either the tibio-talar clear space (TTCS) or the tibio-fibular clear space (TFCS) in a stress examination is defined as indicative of syndesmosis injury (Jenkinson et al. 2005, Pakarinen et al. 2011b&c).

2.6.2 Clinical relevance of the syndesmosis injury

The distal tibiofibular syndesmosis is regarded as essential for stability of the ankle mortise (Close 1956, Grath 1960, Cedell 1967, Rasmussen et al. 1982). Disruption
of the ligaments of the syndesmosis, and especially the interosseous membrane, decreases the weight transmission from the tibia to the fibula from 30% to 100% (Vukićević et al. 1980, Skraba & Greenwald 1984). Widening of the distal tibiofibular joint (i.e. syndesmosis instability) in connection with ankle fracture is regarded as resulting in poor clinical outcome, pain and early OA, especially in high fibular (PER/Weber C-type) fractures (Leeds & Ehrlich 1984, Lindsjö 1985, Chissell & Jones 1995). However, the clinical relevance of the syndesmosis instability, diagnosed with intraoperative syndesmosis stress tests, to the ankle function or to the incidence of osteoarthritis is not well known (Leeds & Ehrlich 1984, Boden et al. 1989, Clarke et al. 1991, Amendola 1992, Kennedy et al. 2000, Miller 2000, Ebraheim et al. 2003, Pakarinen et al. 2011c). This situation is especially evident in cases of SER/Weber B-type ankle fractures – the most common type of ankle fracture (Burwell & Charnley 1965, Michelson 1995, Court-Brown & Caesar 2006, Gougoulias et al. 2010).

Leeds and Ehrlich, in their retrospective study of 34 patients with SER/PD/SA-type ankle fractures, found a substantial correlation between the primary reduction of the syndesmosis, the late stability of the syndesmosis, and the ankle functional and radiological results (Leeds & Ehrlich 1984). They treated all SER-type ankle fractures, without syndesmosis transfixation, by rigid internal fixation of the bone fractures and toe-to-thigh cast immobilisation for six weeks (Leeds & Ehrlich 1984). Egol et al. reported worse ankle functional scores after 1-year of follow-up in patients with Weber A, B or C type ankle fractures who had a syndesmotic injury fixed with a transfixation screw, compared to those with a normal syndesmosis (Egol et al. 2010). However, no studies comparing functional or radiological outcome in SER IV/Weber B-type ankle fracture patients with or without syndesmosis disruption exist.

2.7 Treatment of the syndesmosis injury in connection with ankle fracture

The fibula should remain free to separate slightly from the tibia, which is the normal state (Close 1956), and it should also be able to rotate along its long axis as stated by Grath (Grath 1960).

2.7.1 Conservative treatment of syndesmosis injury

Leeds and Ehrlich concluded that if adequate reduction of the medial and lateral malleolus is achieved and restored with a toe-to-thigh cast for six weeks, the torn syndesmotic ligaments will heal with their appropriate lengths (Leeds & Ehrlich 1984). A prospective study with 21 Weber C-type ankle fracture patients and syndesmotic injury by Yamaguchi et al. recommended 8 weeks cast immobilisation and full weight-bearing started at 4 weeks (Yamaguchi et al. 1994). Pakarinen et al., in their RCT study, used only four weeks of immobilisation in a below-the-knee cast, with weight-bearing allowed as tolerated, in patients with SER-type ankle fractures and intraoperatively confirmed syndesmosis injury and no syndesmotic transfixation (Pakarinen et al. 2011c). In addition, Pankovich in his retrospective studies of patients with fibula fractures proximal to the distal tibiofibular syndesmosis (Maisonneuve and Dupuytren fracture), recommended that, if stress roentgenograms reveal only a slight motion of the fibula in relation to tibia after fixation of bone fractures, only the anterior tibiofibular ligament should be repaired, followed by immobilisation for three to four weeks in a long cast and then three to four weeks in a short walking cast (Pankovich 1976 & 1978). However, the clinical relevance of repairing the AITFL injury was later questioned in a comparative retrospective study of 288 patients with Lauge-Hansen SE4 ankle fractures (Pakarinen 2012). The study results suggested that AITFL exploration and repair may not offer any benefit against syndesmosis widening or favour a better functional outcome (Pakarinen 2012).

2.7.2 Indications for syndesmosis transfixation

Despite the numerous biomechanical and clinical studies concerning ankle fractures and the syndesmosis injury, no clear recommendations have emerged regarding the use of the syndesmotic screw for specific fracture types and injury patterns (van den Bekerom 2007, van den Bekerom et al. 2008, Pakarinen et al. 2011c). In 1965, Burwell and Charnley concluded that, although instability of the syndesmosis maybe present in SER-type ankle fractures, rigid syndesmosis transfixation from the fibula to the tibia is contra-indicated because it involves
unnecessary interference with the syndesmosis (Burwell & Charnley 1965). A landmark biomechanical study by Boden et al. concluded that syndesmosis transfixation is indicated only when fibula fracture is 4.5 cm proximal to the tibiotalar interface (PER/Weber C) and rigid medial fixation is not possible (Boden et al. 1989). These guidelines were confirmed in two small clinical series (Yamaguchi et al. 1994, Chissell & Jones 1995). Furthermore, Kennedy et al., in their RCT, found similar results in patients with low Weber C/SER-type ankle fractures (within 5 cm from TC-joint) and associated syndesmosis injury diagnosed from plain radiographs, when treated with or without syndesmosis screws (Kennedy et al. 2000). Van den Bekerom et al., in their review article, also concluded that low fibula fractures (<5 cm proximal to the tibiotalar interface) do not require syndesmotic transfixation when the lateral and medial malleolar fractures are fixed anatomically and the deltoid ligament is intact (van de Bekerom et al. 2007). A biomechanical study by Burns et al. revealed no significant change in the tibiotalar contact area or the peak pressure, even with complete disruption of the syndesmosis, when medial structures are intact (Burns et al. 1993). Unstable medial side after malleolar fixation is the most important factor leading to unstable syndesmosis in SER-type ankle fractures (Tornetta 2000, Jenkinson et al. 2005, Pakarinen et al. 2011c).

Despite published biomechanical data, several clinical studies recommend syndesmosis transfixation if an intraoperative syndesmosis stress test suggests an unstable syndesmosis after malleolar fixation, regardless the level of the fibula fracture (Miller 2000, Nielson et al. 2004, Jenkinson et al. 2005, Weening & Bhandari 2005, Egol et al. 2006, Stark et al. 2007, Tornetta et al. 2012). However, only one study has evaluated the clinical relevance of syndesmosis transfixation with screw in patients whose syndesmosis instability appeared in the intraoperative syndesmosis stress test performed after malleolar fixation (Pakarinen et al. 2011c). This RCT by Pakarinen et al. found similar functional results at 1 year in patients with SER IV-type ankle fractures and unstable syndesmosis following treatment either with syndesmosis transfixation or no syndesmosis fixation. A review article by van den Bekerom et al. stated that syndesmotic transfixation is indicated in cases of combined talar shift without fibula fracture (tibiotalar diastasis, i.e. medial clear space widening), syndesmotic disruption and medial ligamentous injury, and in the treatment of high fibular fractures (i.e. Maisonneuve fractures) where the ankle mortise is clearly widened (van den Bekerom et al. 2008). Apart from these two cases, no general agreement has been reached regarding the indications for syndesmotic transfixation.
2.7.3 Syndesmosis screw fixation

The metallic screw is currently considered as the “gold standard” for syndesmotic transfixation (van den Bekerom & Raven 2007, Monga et al. 2008, Schepers et al. 2012, Van Heest & Lafferty 2014). A syndesmotic screw is placed across the syndesmosis from the lateral aspect of the fibula into the tibia. The AO/ASIF-group advises that the syndesmotic screw should be angled approximately 30 degrees from posterolateral to anteromedial to engage the tibia (Müller et al. 1991). Apart from that recommendation, no clear consensus has been reached regarding the number of screws needed, the optimal number of cortices, the screw size, the position of the ankle during trans-syndesmotic fixation, the use of bioabsorbable screws or routine screw removal (van den Bekerom et al. 2007, Tucker et al. 2013, Boyle et al. 2014, Van Heest & Lafferty 2014). However, the effect of these technical aspects of syndesmosis fixation on the ultimate clinically important outcomes, such as patient function and quality of life, remains unclear (Weening & Bhandari 2005). One 3.5 mm three-cortical syndesmotic screw – placed with the ankle in a neutral position, approximately 2 cm proximal to the tibiotalar joint and parallel to joint line, and removed only if local irritation occurs – is sufficient in most cases (van de Bekerom et al. 2007, Pakarinen et al. 2011c, Schepers et al. 2014, Van Heest & Lafferty 2014).

Rigid transfixation of the syndesmosis with a screw can have negative side effects. The elastic syndesmosis ligament complex connects the fibula to the tibia, and in the normal ankle joint, it allows external rotation of the fibula relative to the tibia and widening of the ankle mortise. In summary, then, fibular motion in three planes is critical to normal ankle function, and a trans-syndesmotic screw fixation will adversely affect the kinematics and congruity of the ankle joint, thereby possibly leading to increased abnormal contact stresses during weight bearing and gaiting (Needleman et al. 1989, Pereira et al. 1996, Miller et al. 1999). In addition, problems or adverse effects associated with syndesmosis screw fixation can occur, including screw loosening or breakage, ankle joint stiffness, a requirement for prolonged periods of protected weight bearing, a possible need for a second operation for screw removal and the risk of late diastasis after early removal or breakage of the screw (Needleman et al. 1989, Heim et al. 1993, Bell & Wong 2006).
2.7.4 Flexible syndesmosis fixation

Flexible syndesmosis fixation methods, like the suture-button devices, were developed for physiologic stabilisation of the ankle mortise (Thornes et al. 2005, Cottom et al. 2008 & 2009, DeGroot et al. 2011, Schepers 2012). The popularity of these fixation devices has increased rapidly in the last few years (Thornes et al. 2005, Bava et al. 2010). Theoretically, this suture-button device allows physiologic motion of the syndesmosis without a need for implant removal, which may lower the risk of recurrent syndesmotic diastasis, as described after syndesmosis screw removal (Thornes et al. 2005, Cottom et al. 2008 & 2009, DeGroot et al. 2011, Schepers 2012, Van Heest & Lafferty 2014). Biomechanical studies have demonstrated the strength of the suture-button device as comparable to a tricortical 3.5 mm syndesmotic screw (Soin et al. 2009, Klitzman et al. 2010, Teramoto et al. 2011). Clinical studies assessing syndesmosis stabilisation with a suture-button device (Cottom et al. 2009, DeGroot et al. 2011, Qamar et al. 2011, Naqvi et al. 2012a, Rigby & Cottom 2013) and comparative studies (Thornes et al. 2005, Cottom et al. 2009, Coetzee & Ebeling 2009, Naqvi et al. 2012b, Laflamme et al. 2015) have reported functional results at least as good as those obtained with syndesmotic screw fixation. Reported problems encountered from the use of these suture-button devices have been mainly infection and pain over the knot (McMurray et al. 2008, Willmott et al. 2009, DeGroot et al. 2011). A recent systematic review by Inge et al. (2016) concluded that dynamic fixation is a viable alternative to the static fixation device, with fewer complications and lower reoperation rates. In addition, these dynamic fixation methods can accurately stabilise the ruptured syndesmosis without device breakage or loss of reduction (Inge et al. 2016).

2.7.5 Syndesmosis malreduction

Accurate reduction of the ankle syndesmosis is challenging for several reasons. The reduction is usually performed indirectly, without formal visualisation of the distal tibiofibular joint. Even the open reduction of the syndesmosis does not eliminate the possibility of syndesmosis malreduction (Miller et al. 2009, Sagi et al. 2012), which may be due to the observed marked individual variation in the anatomical landmarks of the tibiofibular syndesmosis (Mukhopadhyay et al. 2011, Dikos et al. 2012, Lepojärvi et al. 2014). Malreduction of the syndesmosis that alters tibiofibular joint kinematics may lead to degenerative changes in the upper ankle

2.8 Posttraumatic OA of the ankle joint

Osteoarthritis deformations of the ankle observed in roentgenograms are characterised by a diminution of the height of the joint space, irregularity in the articular surface, sclerosis and cysts in the subchondral bone, and spur formations arising from enchondral ossification (Cedell 1967). The aim of grading OA is to provide diagnostic information and prognostic guidance in clinical decision making by predicting the status of the joint cartilage (Moon et al. 2010). Several grading systems for ankle joint OA have been described (Kellgren & Lawrence 1957, Takakura et al. 1995, van Dijk et al. 1997, Kijowski et al. 2006, Pagenstert et al. 2007, Holzer et al. 2015). The reliability of the modified Kellgren-Lawrence, Takakura et al., and van Dijk et al. grading systems has been reported to range from 0.51 to 0.89 (Moon et al. 2010).

Compared to posttraumatic OA of the hip or the knee (< 10%), the ankle OA is more frequently (70–80%) of posttraumatic origin (Saltzman et al. 2005, Brown et al. 2006, Valderrabano et al. 2009, Lübbeke et al. 2012). About half of the patients with advanced or end-stage ankle joint OA have a history of malleolar fracture (Saltzman et al. 2005, Horisberger et al. 2009, Valderrabano et al. 2009). Posttraumatic OA of the fractured ankle has been reported to appear within two to five years after the initial trauma (Hendelberg 1943, Klossner 1962, Lindsjö 1985, Michelson 1995, Ebraheim et al. 1997), although more recent studies represent diverging opinions claiming that the development of ankle joint posttraumatic OA may even take decades (Stufkens et al. 2010, Lübbeke et al. 2012).

As early as the 1940s, Lewis & Graham suggested that posttraumatic OA of the ankle may be the result of a single severe injury to the articular surface or of repeated microtrauma induced by malreduction, which produces functional disability, and from the uneven spread of intra-articular pressures (Lewis & Graham 1940). Loss of continuity of the weight-bearing surface of the tibia, widening of the ankle joint mortise (Magnusson 1944, Leeds & Ehrlich 1984, Lindsjö 1985, Chissell & Jones 1995) and alteration of the weight-bearing planes are the main anatomical changes of the ankle joint linked to osteoarthritis changes (Lewis & Graham 1940, Palmer 1950, Klossner 1962, Michelson 1995, Thordarson et al. 1997). Furthermore, damage to the articular cartilage can predispose the joint to arthritis (Cox & Laxson 1952, Jergesen 1959, Lantz et al. 1991, Marsh et al. 2003, Stufkens et al. 2010), and these lesions are found in 79 to 90% of ankles examined arthroscopically after an ankle fracture (Hintermann et al. 2000, Thomas et al. 2005). Studies made with MRI or ankle joint arthroscopy at the acute phase have
reported that cartilage injuries, especially in the posterolateral tibia and/or talus, are common in SER-type ankle fractures and account for 58 to 73% of the cases (Hintermann et al. 2000, Loren & Ferkel 2002, Takao et al. 2004, Boraiah et al. 2009).

3 Aims of the present study

The specific aims of this thesis were:

1. To compare functional outcome and safety of three-week immobilisation with either a removable orthosis or below knee-cast versus a below knee-cast for six weeks for the treatment of isolated, stable Weber B-type ankle fractures with similar weight-bearing protocols in RCT.

2. To assess whether syndesmosis transfixation influences the ankle functional or radiological results, by comparing syndesmosis transfixation with a screw to no syndesmosis fixation in patients with SER/Weber B-type ankle fractures with accompanying syndesmosis injury in a RCT.

3. To determine whether syndesmosis injury influences the ankle functional or radiological results and pain in patients with SER/Weber B-type ankle fractures, by comparing age, sex and anatomy of the fracture matched patient pairs.

4. To compare fixation via syndesmosis screw or via a suture-button device in terms of the accuracy and the maintenance of syndesmosis reduction using bilateral CT in a RCT. The secondary purpose was to compare functional and radiological outcomes.
4 Materials and methods

4.1 RCT of non-operative treatment of stable Weber B-type ankle fractures (I)

A randomised, parallel group, multicentre, non-inferiority trial was conducted to compare three non-operative treatment methods for stable Weber B-type ankle fractures at two main trauma centres in Finland from December 2012, through June 2016. The CONSORT guidelines for non-inferiority trials were followed for both the design and reporting of this study (Piaggio et al. 2010). No changes to the study protocol were made after trial commencement.

4.1.1 Patients

All skeletally mature (16 years of age or older) patients with isolated Weber B-type fibula fractures and a reduced ankle mortise who presented at Oulu or Tampere University Hospitals between December 2012 and June 2015 were screened for trial eligibility. All patients underwent an external-rotation stress test of the fractured ankle under fluoroscopy. Other inclusion criteria were the ability to walk unaided before the accident and enrolment less than 7 days after the injury. Exclusion criteria were previous ankle fracture or deltoid ligament injury or other significant fracture in the ankle/leg area, bilateral ankle fracture, concomitant tibial fracture, pathological fracture, diabetic or other neuropathy, or inadequate cooperation. Patients residing permanently outside the catchment area of the Oulu or Tampere university hospitals were also excluded.

Fracture stability was assessed by the surgeon-on-call. The fracture was considered stable when the medial clear space (MCS) was < 5 mm, as measured between the lateral border of the medial malleolus and the medial border of the talus at the level of the talar dome. A total of 560 patients were assessed for their eligibility for this trial; 313 patients were excluded, with the most frequent exclusion criterion being an unstable ankle fracture diagnosed in the external-rotation test (n = 198). Thus, the study group comprised 247 patients, including 114 males and 133 females, with a mean age of 45.5 years (range 16–85 years).
4.1.2 Interventions and control

According to randomisation, a cast or an orthotic device was applied by a trained plaster technician using the study standards. Supporting devices were fitted individually for each participant to ensure the correct fit and comfort. Orthotic devices (Dynacast/Ortho-Glass AS, BSN Medical, Inc., Rutherford College, NC, USA) were applied according to the manufacturer’s instructions, from the middle third of the tibia to the calcaneus. The below-knee cast, made from a synthetic non-flexible cast (3M Scotchcast, St. Paul, MN, USA), was applied from the tuberosity of the tibia to the base of the toes and was lined and padded. Walking with crutches was guided by a physiotherapist, with weight bearing permitted from the time of cast or orthosis fitting for all patients. At the three-week follow-up visit, the cast or orthotic device was removed from participants in the three-week treatment group (interventions), with no additional bracing used. A new below-the-knee cast was applied for participants in the six-week cast treatment group (control). At the six-week follow-up visit, the cast was removed from the patients in the six-week cast group.

4.1.3 Follow-up

Clinical follow-up visits were scheduled at three, six and 12 weeks, and 12 months after randomisation. The participants subsequently completed questionnaires (independently) assessing ankle functional outcome, pain, and their quality of life, immediately prior to the follow-up visits at six and twelve weeks, and at 12 months. Mortise and lateral x-ray projections from the injured ankle were taken at every follow-up visit to assess ankle joint congruity.

At 12 months, 14 patients were lost to follow-up in the three-week orthosis group, and 10 and 11 in the three and six-week cast groups, respectively. One patient from the three-week cast group died, for a reason unrelated to ankle fracture. A total of 86% of the patients therefore remained in the trial at 12 months. No differences were noted in loss to follow-up between the study groups, and no differences were indicated between those remaining in the study and those lost to follow-up at 12 months (Fig. 1).
Fig. 1. Trial profile of the prospective randomised controlled trial comparing three different non-operative treatment protocols for stable Weber B-type ankle fractures.
4.1.4 Outcome measures

The primary outcome measure was the Olerud-Molander Ankle Score (OMAS; scale from 0 to 100, with lower scores indicating more severe symptoms), a validated, condition-specific, patient-reported measure of ankle fracture symptoms (Olerud & Molander 1984, Nilsson et al. 2013). The primary end point was the primary outcome measured at 12 months, as prespecified in the registered study protocol at ClinicalTrials.gov and the study protocol. Analyses of the primary outcome were also performed at six and 12 weeks, but the intention of these analyses was only to illustrate the trajectory of the treatment response.

The secondary outcome measures were (1) the Foot and Ankle Score (FAOS, 5 subscales from 0–100, with higher scores indicating better function; Roos et al. 2001), (2) a 100 mm Visual Analogue Scale for function and pain (VAS, range from 0–100, with higher scores indicating more severe pain; Chapman et al. 1985), (3) the RAND 36-Item Health Survey for health-related quality-of-life (RAND-36, 7 subscales from 0–100, with higher scores indicating better quality of life; Aalto et al. 1999), (4) range-of-motion (ROM) of the injured ankle, (5) ankle joint congruity, and (6) fracture union at one year. All secondary outcomes (The FAOS, VAS, RAND-36, ROM and ankle joint congruity) except fracture union and ankle joint congruity (at every follow-up visit) were assessed at six and 12 weeks, and at 12 months. Radiological fracture union was assessed from radiographs at 12 months and was considered complete when the fracture line disappeared; a visible fracture line designated non-union. The range-of-motion (ROM) of the injured ankle was measured using a goniometer. Possible adverse effects were recorded. The primary outcome assessor was blinded to the patients’ group assignments.

4.2 RCT mid-term results of syndesmotic transfixation versus no fixation in patients with SER IV-type ankle fractures (II)

Study II was a mid-term follow-up of a previously published RCT comparing syndesmosis transfixation to no fixation in patients with SER IV-type ankle fracture and unstable syndesmosis (Pakarinen et al. 2011c).

4.2.1 Patients

All skeletally mature patients (16 years old or older) with a unilateral SER IV-type ankle fracture treated within a week from trauma were considered eligible for the
study. Exclusion criteria were bilateral ankle fractures, pathologic fracture, concomitant tibial shaft fracture, previous significant injury or a fracture of either ankle, significant peripheral neuropathy, soft tissue infection in the region on injured ankle, or inability to complete the study protocol. In total, 166 patients were screened for eligibility for the study at Oulu University Hospital between July 2007 and June 2009. Of these, 140 patients, including 71 females and 69 males, with a mean age of 47 years (range 16–84 years), were enrolled in the study.

4.2.2 Intervention and control

Intraoperative 7.5 Nm standardised ER stress tests were performed on both ankles of all patients after bony fixation. A positive stress examination was defined as a difference of more than 2 mm side-to-side in TTCS or TFCS on mortise radiographs: if positive, the patient was randomised to either no fixation (intervention) or syndesmosis transfixation (control) groups. Twenty-four of the 140 (17%) patients showed unstable syndesmosis and were then randomised either to syndesmosis transfixation with one three-cortical 3.5 mm cortical screw (13 patients) or no syndesmosis fixation (11 patients). Postoperative treatment was a below-the-knee cast for 4 weeks, with weight-bearing as tolerated allowed for all patients.

4.2.3 Follow-up

Clinical follow-up visits, including standard standing radiographs (mortise and lateral projections), were scheduled at two, four and 12 weeks and after a minimum of four years of follow-up. MRI (3T) scans from the injured ankle were taken at the final follow-up. One-year functional results were collected earlier via postal mail (Pakarinen et al. 2011c). All 24 randomised patients were contacted after a minimum of four years. Twenty-three patients were re-examined in 2013, after an average of 58.5 months (SD 5.5, range 48-66). One patient in the no syndesmotic fixation group was unable to attend the clinical exam visit or to have the MRI or X-ray imaging, but he returned the completed questionnaires. One patient from the syndesmotic transfixation group had a prosthesis in her inner ear and was unable to have the MRI scan. One patient in the no syndesmosis fixation group did not have plain radiographs available. Thus, functional results were obtained from all patients (24) and plain radiographs and MRI scans from 22/24 patients.
4.2.4 Outcome measures

The primary outcome measure was ankle functional outcome as assessed with OMAS. Secondary outcome measures were ankle function assessed with FAOS, VAS (function and pain), RAND 36 for health-related quality-of-life, ROM, and radiological outcome assessed with MRI and standard ankle radiographs of the injured ankle. Complications and potential reoperations were also recorded. The musculoskeletal radiologist, blinded to clinical outcome, assessed and graded the severity of OA from plain radiographs, according to the Kellgren-Lawrence (Kellgren & Lawrence 1957) classification and analysed the height of the cartilage in the talocrural (TC) joint and possible defects and osteophytes from MRI scans. The clinical observer was blinded to the patients’ treatment group assignments.

4.3 Clinical relevance of syndesmosis injury in SER IV/Weber B - type ankle fractures (III)

Study III was a case-control study from the prospectively collected patient material from study II.

4.3.1 Patients

Twenty-four patients with SER IV-type ankle fractures with unstable syndesmosis were compared with 24 patients with stable syndesmosis matched to age, sex and morphology of the fracture. Syndesmosis stability was assessed with a bilateral standardised 7.5 Nm intraoperative ER-stress test performed after fixation of the bone fractures.

4.3.2 Matching

secondarily by sex and thirdly by age. The primary criterion for the anatomy of the fracture was the medial side injury (deltoid disruption, fracture of the anterior colliculus or fracture of the medial malleolus) and the secondary criterion was the number of the fractured malleolus (uni-, bi- or trimalleolar fractures). The mean age difference between pairs was two years, ranging from 0–7 years. The mean difference in TTCS and TFCS between the injured and uninjured ankle in 7.5 Nm intraoperative external rotation test was 3.0 mm (range 1.5–7.0 mm) and 3.4 mm (range 1.5–8.0 mm) in the unstable syndesmosis group and, respectively, in the stable syndesmosis group 0.6 mm (range 0–2 mm) and 0.5 mm (range 0–2 mm).

4.3.3 Follow-up

All patients were treated and followed up with an identical postoperative protocol: a below-the-knee cast for four weeks with weight-bearing as tolerated. Clinical follow-up visits, including standard standing radiographs (mortise and lateral projections), were scheduled at two, four and 12 weeks and after a minimum of four years of follow-up. MRI (3T) scans from the injured ankle were taken at the final follow-up. All 48 patients were contacted after a minimum of four years from trauma and 47/48 patients were re-examined in 2013, after an average of 58 months (SD 5, range 48–68) of follow-up. One patient from the unstable syndesmosis group had a prosthesis in her inner ear and was unable to have the MRI scan. Another patient from the same group did not have plain radiographs available. Both patients returned the completed questionnaires.

4.3.4 Outcome measures

Primary and secondary outcome measures and assessment protocols were identical to those of study II.

4.4 RCT Suture-button versus screw for fixation of syndesmosis injury (IV)

A randomised parallel-group trial comparing fixation via a suture-button or via one 3.5-mm tricortical trans-syndesmotic screw for the treatment of syndesmosis injury in Lauge-Hansen pronation-external rotation-type ankle fractures. CONSORT-guidelines were followed to conduct this study (Schultz et al. 2010).
4.4.1 Patients

All skeletally mature patients (16 years or older) with PER IV-type ankle fracture treated at Oulu University hospital between January 2010 and December 2011 were assessed for study eligibility. Patients with associated pre- or intraoperative evidence of syndesmotic disruption based on plain radiographs or on the manual external rotation test under fluoroscopy were considered eligible for enrolment. Exclusion criteria were a previous ankle fracture, concomitant tibia fracture, diabetic or other neuropathy, a delay from trauma to surgery of more than seven days, pathological fracture or inadequate co-operation. The senior orthopaedic trauma surgeon responsible for patient care examined the patients and confirmed the diagnosis. Sixty patients with PER IV/Weber C-type ankle fracture were identified; seven of these patients had stable syndesmosis and 10 were excluded based on the exclusion criteria. Thus, the study group comprised 43 patients, with a mean age of 44.7 years (range 20–79 years). Twenty-two patients were randomised to syndesmotic screw fixation and 21 to suture-button fixation.

4.4.2 Intervention and control

Bone fractures were fixed in both groups using standard Arbeitsgemeinschaft für Osteosynthesefragen (AO) principles (Rüedi et al. 2007). The distal tibio-fibular joint was reduced without direct visualisation of the syndesmosis and held at its anatomical position by hand or with a reduction clamp without extra compression. The ankle joint was positioned at a 90° angle between the tibial shaft and the foot during syndesmosis fixation.

The suture-button device was installed as described by Cottom et al. (intervention) (Cottom et al. 2008). A 3.5-mm hole was drilled from lateral to medial through the fibula and tibia at the level of the lower syndesmosis. When plating of the fibular fracture was indicated, the hole was drilled through an empty screw hole or behind/distal to the plate. The needle attached to the leading oblong button was passed through the hole. Once the medial button was passed through the medial tibial cortex, confirmed via fluoroscopy and in some cases via a small stab wound, the assembly was tensioned by pulling the free ends of the FiberWire on the lateral side. The free ends of the FiberWire were hand-tied on the lateral side of the fibula once both buttons were seated strictly to the bone.

One 3.5-mm cortical screw purchasing three cortices was used for patients who were randomised to the traditional syndesmotic screw fixation group (control). The
postoperative treatment protocol was similar in both groups; the ankle was
immobilised in a below-the-knee cast with the ankle joint at a 90 degree angle for
six weeks, with partial weight bearing. At six weeks, the cast was removed. A
research physiotherapist instructed rehabilitation exercises. No additional bracing
was used and weight-bearing was allowed as tolerated. The syndesmotic fixation
(screw) was removed only if local irritation occurred.

4.4.3 Syndesmosis reduction assessment

To assess the syndesmosis reduction, intraoperative CT was performed of both
ankles together after syndesmosis fixation. The patient was in the supine position,
with lower limbs in the neutral position without external support. The operating
surgeon assessed syndesmosis reduction from axial sections at the level of the
epiphyseal scar, approximately 1 cm proximal from the tibial plafond; the uninjured
ankle was used as a reference. The reduction of the distal tibiofibular joint was
evaluated by measuring the width of the syndesmosis from both ankles in the
anterior (AW) and posterior (PW) borders. The mean width of the syndesmosis was
calculated as described previously (Mukhopadhyay et al. 2010): \[(AW \text{injured}
ankle- AW \text{normal side}) + (PW \text{injured ankle- PW normal ankle}) / 2\] (Fig. 2).
Malreduction was defined as an over 2 mm side-to-side difference, in accordance
with the literature. If the intraoperative CT suggested malreduction, the
syndesmosis was exposed, evaluated via direct vision and, when necessary, re-fixed
in the anatomical position and re-scanned.
Fig. 2. Intraoperative CT showing both the patient’s ankles, normal side (A), operated (B). Axial scans were reformatted parallel to the tibial plafond in the coronal and sagittal planes, and measurements were made 1 cm above proximal from joint space. A mean width of the syndesmosis: \[(AW\text{ injured ankle} - AW\text{ normal side}) + (PW\text{ injured ankle} - PW\text{ normal side})]/2, showing over 2 mm side-to-side difference indicated a malreduced syndesmosis.

4.4.4 Follow-up

Patients visited the outpatient clinic at two, six and 12 weeks and then again after a minimum of two years of follow-up. Functional and quality-of-life outcomes were also collected at 12 months. Joint congruity and fracture healing were assessed each time from plain radiographs. One patient from the syndesmosis screw group had a poor-quality intraoperative CT and was therefore excluded from the analysis. In addition, two patients from the same group were lost to follow-up. Overall, 19 patients in the syndesmosis screw group and 21 in the suture-button group were analysed (Fig. 3).
4.4.5 Outcome measures

The primary outcome measure was the accuracy and the maintenance of syndesmosis reduction as assessed by bilateral CT. The operating surgeon assessed syndesmosis reduction from intraoperative CT-scans. The musculoskeletal radiologist re-assessed the intraoperative CT scans and evaluated syndesmosis reduction from follow-up bilateral cone beam computed tomography (CBCT) scans using the same parameters as with the intra-operative CT. The OA in both ankle joints was assessed via CBCT in accordance with a standard classification (Morrey & Wiedeman 1980). Ankle functional outcome was assessed by OMAS and VAS (for function and pain) and by RAND 36 for health-related quality-of-life. Questionnaires were sent to patients by postal mail at one year and just before the
final follow-up visit. Additionally, FAOS was used to assess ankle functional outcome at the final follow-up. The minimum follow-up was two years.

4.5 Ethics

Approval of Ethical committee of Oulu University Hospital was obtained for all study protocols (I-IV). The study I protocol was also approved by the institutional ethics committee of Tampere University Hospital. Oral and written information about the study protocol was given to all patients (I-IV). All patients provided written informed consent (I-IV).

4.6 Statistical methods

All statistical analyses were performed on an intention-to-treat (ITT) basis. Summary statistics are presented as means with standard deviation (SD), unless otherwise stated. Simple between-group comparisons were performed using Student’s t-test or Mann-Whitney U-test (continuous variables) and Fisher’s exact test (categorical variables). Two-tailed p-values and 95% confidence intervals (95% CI) are reported. A p-value < 0.05 was considered significant.

When comparing repeatedly measured data between study groups (I, II, IV), the linear mixed model (LMM) was utilised. The reported p-values for LMM are: \( p_{\text{time}} \), for change over time; \( p_{\text{group}} \), for the average between-group difference; and \( p_{\text{time}\ast\text{group}} \), for the interaction between time and group.

In study II, a paired samples test was used to analyse the change from three months or one year to four years of follow-up within the groups. In study III, between group comparisons were performed with a paired samples t-test (continuous variables), and with the McNemar (or McNemar-Bowker) test (categorical variables, the latter if number of categories > 2).

4.6.1 Sample size calculations

In study I, sample size calculations were performed assuming a two-arm study (six-week cast vs. three-week cast or six-week cast vs. three-week orthotic device). The primary outcome measure was the OMAS and the primary end point at 12 months; this outcome measure was used for sample size calculations. Based on our previous study of stable ankle fractures treated non-operatively, a mean OMAS of 88, with a SD of 20, was anticipated at 12 months of follow-up (Pakarinen et al. 2011a). The
The non-inferiority margin was set at 10% (= 8.8 points). The non-inferiority margin was set only for the primary outcome and primary end point (OMAS at 12 months). The 8.8-point margin was lower than the minimum clinically important difference (12 points) reported in a recent evaluation of the OMAS (Nilsson et al. 2013) An \( \alpha = 0.05 \), power 80% (1-\( \beta \) = 0.8), a non-inferiority margin of 10% (= 8.8 points) and a dropout rate of 20% resulted in 82 patients per group (total \( n = 246 \)).

For study IV, based on previous studies, we hypothesised that 50% of screw-fixed and no more than 5% of suture-button fixed syndesmosis would be in malposition. Thus, the required sample size was determined as 19 patients per group (\( \alpha = 0.05 \), \( \beta = 0.1 \), dropout rate = 20%).

4.6.2 Randomisation and masking

In studies I, II and IV, patients were randomly allocated to study groups according to a computer generated list, compiled by a biostatistician who was not involved in the clinical care of the trial patients. Randomisation was performed in blocks, where the block size varied randomly between six, nine, and twelve (study I), four and six (study II), and four, six and eight (study IV). A separate randomisation list was created for both centres (study I). A research assistant (not involved in patient care) sealed the randomisation lists into numbered, opaque envelopes, to ensure secrecy.

In study I, besides the patients, only the recruiting surgeons and two research assistants (both uninvolved in any further patient treatment) were aware of the group assignments. The primary outcome assessor was blinded to the group assignments. In study II, the primary outcome assessor, the radiologist and orthopaedic resident carrying out the follow-up visits were blinded to the group assignments. In study IV, the orthopaedic surgeon who conducted the follow-up visits and the primary outcome assessor were blinded to the interventions and to the earlier functional results, and the radiologist assessing intraoperative and follow-up CT was blinded to the functional results.
5 Results

5.1 RCT of non-operative treatment of stable Weber B-type ankle fractures (I)

Baseline characteristics of the trial participants are presented in Table 1.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>3-week orthosis (n = 80)</th>
<th>3-week cast (n = 83)</th>
<th>6-week cast (n = 84)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at fracture, mean (SD) [range], y</td>
<td>46 (19) [16–82]</td>
<td>46 (17) [16–82]</td>
<td>45 (18) [17–85]</td>
</tr>
<tr>
<td>Number of patients aged over 50 years (%)</td>
<td>36 (45)</td>
<td>37 (45)</td>
<td>33 (41)</td>
</tr>
<tr>
<td>Sex, number (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>36 (45)</td>
<td>40 (48)</td>
<td>38 (46)</td>
</tr>
<tr>
<td>Women</td>
<td>44 (55)</td>
<td>43 (52)</td>
<td>46 (55)</td>
</tr>
<tr>
<td>Level of education, number (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic education (ISCED 2)</td>
<td>11 (13.8)</td>
<td>11 (13.3)</td>
<td>12 (14.3)</td>
</tr>
<tr>
<td>Upper secondary education (ISCED 3-4)</td>
<td>31 (38.8)</td>
<td>27 (32.5)</td>
<td>26 (31.0)</td>
</tr>
<tr>
<td>Short-cycle tertiary education (ISCED 5)</td>
<td>10 (12.5)</td>
<td>16 (19.3)</td>
<td>8 (9.5)</td>
</tr>
<tr>
<td>Bachelor, Master or Doctoral (ISCED 6-8)</td>
<td>22 (27.5)</td>
<td>26 (31.3)</td>
<td>29 (34.5)</td>
</tr>
<tr>
<td>Did not wish to answer or missing</td>
<td>6 (7.5)</td>
<td>3 (3.6)</td>
<td>9 (10.7)</td>
</tr>
<tr>
<td>Type of trauma, number (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Free time</td>
<td>66 (82.5)</td>
<td>66 (79.5)</td>
<td>61 (72.6)</td>
</tr>
<tr>
<td>Work</td>
<td>5 (6.3)</td>
<td>7 (8.4)</td>
<td>10 (11.9)</td>
</tr>
<tr>
<td>Sport</td>
<td>5 (6.3)</td>
<td>4 (4.8)</td>
<td>8 (9.5)</td>
</tr>
<tr>
<td>Home</td>
<td>3 (3.8)</td>
<td>5 (6.0)</td>
<td>2 (2.4)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (1.3)</td>
<td>1 (1.2)</td>
<td>3 (3.6)</td>
</tr>
<tr>
<td>Pain (NRS) in ER-stress test, mean</td>
<td>5</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Initial ankle medial side clinical findings, number (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain at palpation of medial malleolus, haematoma or swelling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No medial side findings</td>
<td>44 (55.0)</td>
<td>52 (62.7)</td>
<td>53 (63.1)</td>
</tr>
<tr>
<td>One</td>
<td>11 (13.8)</td>
<td>17 (20.5)</td>
<td>13 (15.5)</td>
</tr>
<tr>
<td>Two</td>
<td>15 (18.8)</td>
<td>10 (12.0)</td>
<td>10 (11.9)</td>
</tr>
<tr>
<td>Three</td>
<td>9 (11.3)</td>
<td>4 (4.8)</td>
<td>8 (9.5)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (1.3)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Medial clear space in ER-stress test mm, mean</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>
5.1.1 The Olerud-Molander Ankle Score (OMAS)

At one year, the mean OMAS was 89.8 (SD 18.4) points in the three-week orthosis group, and 91.7 points (SD 12.9) and 87.6 (SD 18.3) points for three- and six-week cast groups, respectively. Values for the difference between means were 1.7 points (95% CI from -4.0 to 7.3, \( p = 0.56 \)) when comparing the three-week orthosis and six-week cast groups, and 3.6 points (95% CI from -1.9 to 9.1, \( p = 0.20 \)) for three-week and six-week cast groups. In both cases, the confidence intervals did not include the specified inferiority margin of -8.8 points. Although statistically significant between-group differences were detected for the time/group interaction (time*group) in the OMAS, these differences were not clinically relevant (Table 2, Fig. 4).

Table 2. Primary outcome measure for the Orthosis 3 week, Cast 3 week and Cast 6 week groups at 6 and 12 weeks, and 12 months. The LMM p-values are those for \( p_{\text{time}} \) (change between measurement points), \( p_{\text{group}} \) (average between-group difference), and \( p_{\text{time}\times\text{group}} \) (for the interaction between time and group).

<table>
<thead>
<tr>
<th>Group</th>
<th>Olerud-Molander Ankle Score (scale 0-100)</th>
<th>( p_{\text{time}} )</th>
<th>( p_{\text{group}} )</th>
<th>( p_{\text{time}\times\text{group}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthosis 3 week</td>
<td>Mean (SD) 55 (20) 73 70 (21) 66 90 (18)</td>
<td>0.73</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>Cast 3 week</td>
<td>Mean (SD) 54 (18) 73 73 (19) 73 92 (13)</td>
<td>&lt; .0001</td>
<td>0.73</td>
<td>0.005</td>
</tr>
<tr>
<td>Cast 6 week</td>
<td>Mean (SD) 60 (21) 73 69 (23) 73 88 (18)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^{1}\)Primary time point
5.1.2 Secondary Outcomes (FAOS, VAS, RAND 36, ROM and fracture union)

During the follow-up, all other secondary outcome measures, except for the RAND-36 general health score, improved in all groups (Table 3 and 4). Ankle plantarflexion and ankle function, as assessed with VAS, were the only outcome variables that differed significantly between the groups ($p_{\text{group}} = 0.03$ and $p_{\text{group}} < 0.01$). In the ankle plantarflexion, the six-week cast group had the lowest range of motion at every follow-up, and in VAS (function), the six-week cast group had the lowest scores at six weeks and one year, whereas the three-week cast group had the highest scores at every follow-up (Table 3). Significant between-group differences were observed for the interaction between time and group for all variables measuring pain (VAS pain, FAOS pain, and RAND-36 bodily pain) (Table 3 and 4). Patients in the six-week cast group had lower levels of pain at six weeks, which subsequently increased as assessed at twelve weeks, whereas the pain levels continuously declined in patients in the three-week orthosis or cast groups. All ankle joints remained congruent at the follow-up and no surgery due to
widening of the ankle mortise was needed in any of the study patients. However, two cases of non-union were found among the trial participants, both from the 3-week cast group. One patient required surgery 11 months after their initial trauma. No additional treatment was warranted for the other non-union patient, who scored 95/100 points on the Olerud-Molander Ankle Score at one year, with no symptoms at his ankle. Overall, the rate of fracture union was high (99.2%) and no significant between-group difference were found in this outcome (p = 0.33) (Table 3).

Table 3. Secondary outcomes (FAOS, VAS, ROM) at 6 and 12 weeks, and 12 months, and fracture union at the 12-month follow-up (ITT-analysis). The LMM p-values are those for $p_{\text{time}}$ (change between measurement points), $p_{\text{group}}$ (average between-group difference), and $p_{\text{time}\times\text{group}}$ (for the interaction between time and group).

<table>
<thead>
<tr>
<th>Measure</th>
<th>Group</th>
<th>6 Week</th>
<th>12 Week</th>
<th>12 Month</th>
<th>$p_{\text{time}}$</th>
<th>$p_{\text{group}}$</th>
<th>$p_{\text{time}\times\text{group}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No.</td>
<td>Mean (SD)</td>
<td>No.</td>
<td>Mean (SD)</td>
<td>No.</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>VAS Pain</td>
<td>Orthosis 3 weeks</td>
<td>75</td>
<td>30 (22)</td>
<td>72</td>
<td>24 (23)</td>
<td>66</td>
<td>9 (17)</td>
</tr>
<tr>
<td></td>
<td>Cast 3 weeks</td>
<td>77</td>
<td>28 (22)</td>
<td>72</td>
<td>18 (21)</td>
<td>72</td>
<td>7 (12)</td>
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<td></td>
<td>Cast 6 weeks</td>
<td>70</td>
<td>19 (19)</td>
<td>70</td>
<td>21 (21)</td>
<td>72</td>
<td>10 (18)</td>
</tr>
<tr>
<td>VAS Function</td>
<td>Orthosis 3 weeks</td>
<td>74</td>
<td>40 (23)</td>
<td>72</td>
<td>28 (24)</td>
<td>65</td>
<td>9 (17)</td>
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<td></td>
<td>Cast 3 weeks</td>
<td>77</td>
<td>38 (24)</td>
<td>72</td>
<td>20 (23)</td>
<td>72</td>
<td>7 (10)</td>
</tr>
<tr>
<td></td>
<td>Cast 6 weeks</td>
<td>70</td>
<td>49 (28)</td>
<td>70</td>
<td>26 (24)</td>
<td>72</td>
<td>11 (20)</td>
</tr>
<tr>
<td>FAOS Pain</td>
<td>Orthosis 3 weeks</td>
<td>75</td>
<td>71 (15)</td>
<td>72</td>
<td>79 (15)</td>
<td>65</td>
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<td>74</td>
<td>84 (13)</td>
<td>73</td>
<td>95 (8)</td>
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<tr>
<td></td>
<td>Cast 6 weeks</td>
<td>65</td>
<td>82 (15)</td>
<td>71</td>
<td>79 (16)</td>
<td>72</td>
<td>92 (12)</td>
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<tr>
<td>FAOS Symptoms</td>
<td>Orthosis 3 weeks</td>
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<td>61 (22)</td>
<td>72</td>
<td>70 (21)</td>
<td>65</td>
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<td>71</td>
<td>68 (21)</td>
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<td>84 (17)</td>
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<td>FAOS ADL</td>
<td>Orthosis 3 weeks</td>
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<td>79 (18)</td>
<td>72</td>
<td>88 (21)</td>
<td>65</td>
<td>94 (15)</td>
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<td></td>
<td>Cast 3 weeks</td>
<td>78</td>
<td>81 (12)</td>
<td>74</td>
<td>92 (12)</td>
<td>73</td>
<td>97 (7)</td>
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<td>80 (17)</td>
<td>71</td>
<td>89 (16)</td>
<td>72</td>
<td>95 (12)</td>
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<tr>
<td>FAOS Sport&amp;Rec</td>
<td>Orthosis 3 weeks</td>
<td>75</td>
<td>43 (27)</td>
<td>72</td>
<td>65 (28)</td>
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<td>65</td>
<td>42 (28)</td>
<td>71</td>
<td>61 (27)</td>
<td>72</td>
<td>84 (25)</td>
</tr>
<tr>
<td>FAOS QoL</td>
<td>Orthosis 3 weeks</td>
<td>75</td>
<td>46 (20)</td>
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<td>85 (20)</td>
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<td>Measure</td>
<td>6 Week</td>
<td>12 Week</td>
<td>12 Month</td>
<td>p&lt;sub&gt;time&lt;/sub&gt;</td>
<td>p&lt;sub&gt;group&lt;/sub&gt;</td>
<td>p&lt;sub&gt;time*group&lt;/sub&gt;</td>
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<td></td>
</tr>
<tr>
<td>Group</td>
<td>No. Mean (SD)</td>
<td>No. Mean (SD)</td>
<td>No. Mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cast 6 weeks</td>
<td>65 47 (24)</td>
<td>71 60 (27)</td>
<td>72 85 (22)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Ankle Dorsiflexion (degree)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthosis 3 weeks</td>
<td>78 18 (8)</td>
<td>73 21 (10)</td>
<td>66 25 (10)</td>
<td>&lt;.0001</td>
<td>0.18</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>Cast 3 weeks</td>
<td>82 17 (8)</td>
<td>75 21 (9)</td>
<td>73 25 (9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cast 6 weeks</td>
<td>81 13 (8)</td>
<td>73 19 (10)</td>
<td>73 24 (9)</td>
<td></td>
<td></td>
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<tr>
<td>Ankle Plantarflexion (degree)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthosis 3 weeks</td>
<td>78 41 (10)</td>
<td>73 48 (8)</td>
<td>66 53 (8)</td>
<td>&lt;.0001</td>
<td>0.001</td>
<td>0.012</td>
<td></td>
</tr>
<tr>
<td>Cast 3 weeks</td>
<td>82 41 (10)</td>
<td>75 48 (9)</td>
<td>73 53 (8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cast 6 weeks</td>
<td>81 35 (10)</td>
<td>73 46 (8)</td>
<td>73 51 (8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fracture Union at 12 months (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Orthosis 3 weeks</td>
<td>77 66 (100)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.33&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Cast 3 weeks</td>
<td>70 97</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cast 6 weeks</td>
<td>71 100</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup> Fisher's exact test

**Table 4. Health-related quality of life scores as assessed using the RAND-36 Health Item Survey.**

<table>
<thead>
<tr>
<th>Measure</th>
<th>6 Week</th>
<th>12 Week</th>
<th>12 Month</th>
<th>p&lt;sub&gt;time&lt;/sub&gt;</th>
<th>p&lt;sub&gt;group&lt;/sub&gt;</th>
<th>p&lt;sub&gt;time*group&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>No. Mean (SD)</td>
<td>No. Mean (SD)</td>
<td>No. Mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Function</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthosis 3 weeks</td>
<td>77 58 (28)</td>
<td>72 72 (24)</td>
<td>66 86 (22)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cast 3 weeks</td>
<td>79 61 (21)</td>
<td>74 77 (22)</td>
<td>73 89 (17)</td>
<td>&lt;.0001</td>
<td>0.17</td>
<td>0.06</td>
</tr>
<tr>
<td>Cast 6 weeks</td>
<td>76 49 (29)</td>
<td>70 74 (25)</td>
<td>71 87 (20)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General Health</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthosis 3 weeks</td>
<td>77 73 (20)</td>
<td>72 70 (21)</td>
<td>66 71 (21)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cast 3 weeks</td>
<td>79 74 (20)</td>
<td>74 74 (21)</td>
<td>73 74 (21)</td>
<td>0.23</td>
<td>0.60</td>
<td>0.47</td>
</tr>
<tr>
<td>Cast 6 weeks</td>
<td>76 72 (18)</td>
<td>70 72 (19)</td>
<td>71 74 (22)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental Health</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthosis 3 weeks</td>
<td>76 74 (21)</td>
<td>71 80 (17)</td>
<td>66 85 (13)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cast 3 weeks</td>
<td>79 74 (18)</td>
<td>74 81 (17)</td>
<td>73 82 (15)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cast 6 weeks</td>
<td>76 74 (17)</td>
<td>70 79 (14)</td>
<td>71 82 (15)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Role Function (physical)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthosis 3 weeks</td>
<td>77 24 (35)</td>
<td>71 59 (42)</td>
<td>66 85 (33)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cast 3 weeks</td>
<td>79 23 (35)</td>
<td>74 66 (42)</td>
<td>73 86 (29)</td>
<td>&lt;.0001</td>
<td>0.51</td>
<td>0.46</td>
</tr>
<tr>
<td>Cast 6 weeks</td>
<td>76 20 (31)</td>
<td>70 54 (44)</td>
<td>71 86 (30)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### 5.1.3 Adverse effects

Adverse effects (Harms) were rare and no significant between-group differences were detected. Eight patients were diagnosed with symptomatic DVT. Five of these were in the six-week cast group and three in the three-week cast group ($p = 0.10$). One case of superficial peroneal nerve compression was detected in the six-week cast group and one patient in the three-week cast group developed a complex regional pain syndrome ($p > 0.9$).

### 5.1.4 Protocol violations

Protocol violations occurred uniquely in the six-week cast group, with six patients declining to continue cast treatment after the three-week control visit. Three patients used a removable orthotic device for the next three weeks, while the remaining three patients used no additional support. In the intention-to-treat analysis, all these six patients were included in the 6-week cast group. No changes in the initial, randomly assigned, treatment strategies were made following clinical or radiographic findings at the study follow-up visits.
5.2 Syndesmosis screw fixation versus no syndesmosis fixation (II)

Baseline characteristics of the patients are shown in Table 5.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Syndesmotic transfixation</th>
<th>No Syndesmotic fixation</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Age (years)</td>
<td>42.5 (SD 11.6)</td>
<td>44.9 (SD 14.2)</td>
</tr>
<tr>
<td>Male/Female</td>
<td>8/5</td>
<td>7/4</td>
</tr>
<tr>
<td>Lauge-Hansen SE-4, n/N</td>
<td>13/13</td>
<td>11/11</td>
</tr>
<tr>
<td>Anatomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibula</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Fibula + medial malleolus</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Fibula + posterior malleolus</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Trimalleolar</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Open fracture</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Comorbidity(^1), n</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>

\(^1\) diabetes, Arteriosclerosis obliterans (ASO) and alcoholism

5.2.1 Functional results

After a minimum of four years of follow-up (mean 58 months), the mean OMAS improved from 80 to 81 points in the syndesmotic screw fixation group and respectively from 84 to 93 points in the no syndesmotic fixation group (\(p_{\text{time}} = 0.08\), \(p_{\text{group}} = 0.12\), \(p_{\text{time}\times\text{group}} = 0.21\)). Improvements were noted in all secondary outcome measures; VAS (Pain and Function) and RAND 36 (Physical and Pain) showed no significant differences in LMM-analysis between the groups during the follow-up (Table 6). Within the syndesmotic transfixation group, no significant improvements were observed in any functional parameters and pain measurements; whereas the no syndesmotic fixation group showed significant improvements in OMAS and VAS pain (Table 7). The ROM of the injured ankle improved in both groups during the follow-up period, with no significant between group differences (Table 6).
Table 6. Function parameters at follow-up. P-values reported with LMM are $p_{time}$ for change between measurement points, $p_{group}$ for average between group difference, and $p_{time\times group}$ for interaction between time and group.

<table>
<thead>
<tr>
<th>Variable</th>
<th>1 year</th>
<th>≥4 years</th>
<th>$p_{time}$</th>
<th>$p_{group}$</th>
<th>$p_{time\times group}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OMAS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syndesmotic transfixation</td>
<td>80 (13)</td>
<td>81 (16)</td>
<td>0.083</td>
<td>0.116</td>
<td>0.209</td>
</tr>
<tr>
<td>No syndesmotic fixation</td>
<td>84 (15)</td>
<td>93 (9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS Function (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syndesmotic transfixation</td>
<td>23 (25)</td>
<td>12 (15)</td>
<td>0.027</td>
<td>0.193</td>
<td>0.834</td>
</tr>
<tr>
<td>No syndesmotic fixation</td>
<td>15 (15)</td>
<td>6 (8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS Pain (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syndesmotic transfixation</td>
<td>25 (25)</td>
<td>11 (15)</td>
<td>0.014</td>
<td>0.056</td>
<td>0.350</td>
</tr>
<tr>
<td>No syndesmotic fixation</td>
<td>11 (13)</td>
<td>4 (8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAND-36 Physical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syndesmotic transfixation</td>
<td>78 (23)</td>
<td>86 (19)</td>
<td>0.119</td>
<td>0.186</td>
<td>0.341</td>
</tr>
<tr>
<td>No syndesmotic fixation</td>
<td>88 (19)</td>
<td>92 (15)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAND-36 Pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syndesmotic transfixation</td>
<td>63 (33)</td>
<td>78 (22)</td>
<td>0.174</td>
<td>0.059</td>
<td>0.331</td>
</tr>
<tr>
<td>No syndesmotic fixation</td>
<td>84 (14)</td>
<td>89 (12)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROM ($^\circ$) (degree), Mean</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td>0.562</td>
<td>0.302</td>
</tr>
<tr>
<td>Syndesmotic transfixation</td>
<td>62</td>
<td>75</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No syndesmotic fixation</td>
<td>58</td>
<td>75</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 12 weeks and a minimum of 4 years of follow-up

Table 7. Within-group changes in functional parameters from one year to a minimum of four years of follow-up.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Syndesmotic fixation</th>
<th>No syndesmotic fixation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean difference</td>
<td>95% CI</td>
</tr>
<tr>
<td>OMAS</td>
<td>2</td>
<td>5 to -10</td>
</tr>
<tr>
<td>VAS Pain (mm)</td>
<td>-15</td>
<td>-32 to 2</td>
</tr>
<tr>
<td>VAS Function (mm)</td>
<td>-11</td>
<td>-27 to 5</td>
</tr>
<tr>
<td>RAND-36 Physical</td>
<td>10</td>
<td>-5 to 25</td>
</tr>
<tr>
<td>RAND-36 Pain</td>
<td>-16</td>
<td>-31 to 0.1</td>
</tr>
</tbody>
</table>

5.2.2 Radiological results

The plain radiographs showed that the ankle mortise remained congruent in all patients, and the measurements showed no differences between groups (Table 8).
Osteoarthritis was graded as K-L class I in one patient, and K-L class II in 12 patients in the syndesmotic transfixation group, and as class II in 7 and class III in two patient in the no syndesmotic transfixation group ($p = 0.101$, Mann-Whitney U test). Syndesmotic calcification was detected in 8 (62%) patients in the syndesmotic transfixation group vs. 1 (11%) patient in the no syndesmotic fixation group ($p = 0.031$, Fischer’s Exact Test). One patient’s syndesmotic screw was broken and left in place. All syndesmotic screws that were intact and in place showed clear radiological evidence of screw loosening.

Table 8. Congruity of the ankle mortise assessed from plain radiographs.

<table>
<thead>
<tr>
<th>Variable</th>
<th>12 weeks</th>
<th>&gt; 4 years</th>
<th>$p_{\text{time}}$</th>
<th>$p_{\text{group}}$</th>
<th>$p_{\text{time*group}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>TTCS (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syndesmotic transfixation</td>
<td>3.5 (0.8)</td>
<td>2.8 (0.8)</td>
<td>0.006</td>
<td>0.62</td>
<td>0.17</td>
</tr>
<tr>
<td>No Syndesmotic fixation</td>
<td>3.2 (0.6)</td>
<td>2.9 (0.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TFCS (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syndesmotic transfixation</td>
<td>5.4 (2.0)</td>
<td>5.5 (1.3)</td>
<td>0.60</td>
<td>0.83</td>
<td>0.86</td>
</tr>
<tr>
<td>No syndesmotic fixation</td>
<td>5.5 (1.2)</td>
<td>5.9 (0.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Twelve patients had joint cartilage defects visible in the ankle MRI; 8 (67%) in the syndesmotic fixation group vs. 4 (40%) in the no syndesmosis fixation group. No between-group differences were observed with regard to joint cartilage findings, talocrural (TC) joint cartilage height (anterior and posterior border) or height of the posterior facet in the MRI results (Table 9).

Table 9. Magnetic resonance imaging (MRI) parameters at follow-up.

<table>
<thead>
<tr>
<th>MRI findings</th>
<th>Syndesmotic transfixation</th>
<th>No Syndesmotic fixation</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height of the TC-joint cartilage anteriorly (mm), Mean (SD)</td>
<td>1.8 (0.5)</td>
<td>1.6 (0.4)</td>
<td>0.16</td>
</tr>
<tr>
<td>Height of the TC-joint cartilage posteriorly (mm), Mean (SD)</td>
<td>2.1 (0.4)</td>
<td>2.0 (0.3)</td>
<td>0.46</td>
</tr>
<tr>
<td>Height of the posterior facet cartilage (mm), Mean (SD)</td>
<td>2.4 (0.4)</td>
<td>2.2 (0.3)</td>
<td>0.18</td>
</tr>
<tr>
<td>Joint cartilage defects, Number of patients (%)</td>
<td>8 (67%)</td>
<td>4 (40%)</td>
<td>0.39</td>
</tr>
<tr>
<td>Medial Talus, Number of patients (%)</td>
<td>3 (25%)</td>
<td>1 (10%)</td>
<td>0.23</td>
</tr>
<tr>
<td>Lateral Talus, Number of patients (%)</td>
<td>0 (0%)</td>
<td>1 (10%)</td>
<td>0.46</td>
</tr>
<tr>
<td>Medial Tibia, Number of patients (%)</td>
<td>6 (50%)</td>
<td>3 (30%)</td>
<td>0.42</td>
</tr>
<tr>
<td>Lateral Tibia, Number of patients (%)</td>
<td>2 (17%)</td>
<td>3 (30%)</td>
<td>0.62</td>
</tr>
</tbody>
</table>
5.2.3 Reoperations

The syndesmotic screw was removed from two patients (both two months after fracture fixation) because of local irritation. Both the screws and plate were removed from one patient because of local irritation (15 months after fracture fixation). No re-operations due to infection or widening of the ankle mortise were needed.

5.3 Clinical relevance of syndesmosis injury in SER IV/Weber B - type ankle fractures (III)

Baseline characteristics of the patients are shown in Table 10.

Table 10. Baseline characteristic of the study participants.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unstable Syndesmosis (n = 24)</th>
<th>Stable Syndesmosis (n = 24)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (SD)</td>
<td>43.7 (12.6)</td>
<td>44.3 (12.2)</td>
<td></td>
</tr>
<tr>
<td>Males/Females</td>
<td>15/9</td>
<td>15/9</td>
<td></td>
</tr>
<tr>
<td>Lauge-Hansen SE 4 n/N</td>
<td>24/24</td>
<td>24/24</td>
<td></td>
</tr>
<tr>
<td>Anatomy, n</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1Mean TTCS difference</td>
<td>3.0 [1.5–7.0]</td>
<td>0.6 [0–2]</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>1Mean TFCS difference</td>
<td>3.4 [1.5–8.0]</td>
<td>0.5 [0–2]</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Fibula</td>
<td>15</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Fibula &amp; medial malleolus</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Fibula &amp; posterior malleolus</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Trimalleolar</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Open fracture</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Comorbidity*, n</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

1 At the intraoperative standardised 7.5 Nm external rotation test, 2 diabetes, Arteriosclerosis obliterans (ASO) and alcoholism

5.3.1 Functional results

The mean OMAS was 86 points in patients with unstable syndesmosis and 90 points in patients with stable syndesmosis (p = 0.28). All secondary outcome measures – FAOS, VAS (pain and function) and RAND 36 – showed no significant
difference between the groups, and the ROM of the injured ankle was similar in both groups (Table 11).

### Table 11. Functional, Pain, Health-related Quality of Life and ROM scores at follow-up.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Unstable Syndesmosis Mean, (SD)</th>
<th>Stable Syndesmosis Mean, (SD)</th>
<th>95% CI of difference</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OMAS</td>
<td>86 (15)</td>
<td>90 (16)</td>
<td>-3 to 10</td>
<td>0.28</td>
</tr>
<tr>
<td>VAS Pain [mm]</td>
<td>8 (12)</td>
<td>7 (13)</td>
<td>-6 to 4</td>
<td>0.73</td>
</tr>
<tr>
<td>VAS Function [mm]</td>
<td>9 (13)</td>
<td>7 (11)</td>
<td>-6 to 3</td>
<td>0.51</td>
</tr>
<tr>
<td>RAND 36-Item Health Survey, Pain</td>
<td>83 (19)</td>
<td>77 (23)</td>
<td>-19 to 6</td>
<td>0.28</td>
</tr>
<tr>
<td>RAND 36-Item Health Survey, Physical</td>
<td>89 (17)</td>
<td>88 (18)</td>
<td>-8 to 7</td>
<td>0.91</td>
</tr>
<tr>
<td>FAOS, Symptoms</td>
<td>85 (13)</td>
<td>88 (13)</td>
<td>-3 to 10</td>
<td>0.31</td>
</tr>
<tr>
<td>FAOS, Pain</td>
<td>92 (11)</td>
<td>92 (13)</td>
<td>-4 to 5</td>
<td>0.81</td>
</tr>
<tr>
<td>FAOS, Function &amp; daily living</td>
<td>97 (7)</td>
<td>94 (11)</td>
<td>-6 to 2</td>
<td>0.31</td>
</tr>
<tr>
<td>FAOS, Function, sports and recreational activities</td>
<td>91 (16)</td>
<td>86 (23)</td>
<td>-14 to 5</td>
<td>0.32</td>
</tr>
<tr>
<td>FAOS, Quality of Life</td>
<td>82 (16)</td>
<td>84 (22)</td>
<td>-7 to 11</td>
<td>0.63</td>
</tr>
<tr>
<td>ROM</td>
<td>75 (10)</td>
<td>73 (10)</td>
<td>-7 to 5</td>
<td>0.64</td>
</tr>
</tbody>
</table>

#### 5.3.2 Radiological results

The incidence of the ankle joint OA assessed from plain radiographs showed no significant difference between the groups, and the ankle joint retained its anatomical congruity in all patients (Table 12).

### Table 12. Parameters from plain radiographs.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Unstable Syndesmosis Mean (SD)</th>
<th>Stable Syndesmosis Mean (SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TTCS [mm], Mean (SD)</td>
<td>2.9 (0.8)</td>
<td>3.0 (0.6)</td>
<td>0.40</td>
</tr>
<tr>
<td>TFCS [mm], Mean (SD)</td>
<td>5.7 (1.1)</td>
<td>5.2 (1.5)</td>
<td>0.32</td>
</tr>
<tr>
<td>Kellgren-Lawrence classification, No. (%)</td>
<td></td>
<td></td>
<td>0.34</td>
</tr>
<tr>
<td>K-L class I</td>
<td>1 (5)</td>
<td>5 (21)</td>
<td></td>
</tr>
<tr>
<td>K-L class II</td>
<td>19 (86)</td>
<td>18 (75)</td>
<td></td>
</tr>
<tr>
<td>K-L class III</td>
<td>2 (9)</td>
<td>1 (4)</td>
<td></td>
</tr>
<tr>
<td>K-L class IV</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

1 Ankle radiographs were missing from two patients in the unstable syndesmosis group

MRI scans showed TC-joint cartilage defects in 54% of the patients; 12 (56%) in the unstable syndesmosis group vs. 13 (54%) in the stable syndesmosis group (p > 0.9) (Table 13). No chondral defects were found in 10 (45%) patients, one
defect was found in 3 (14%) and two or more defects in 9 (41%) patients from the unstable syndesmosis group, while no chondral defects were found in 11 (46%), one defect in 5 (21%) and two or more defects in 8 (33%) patients from the stable syndesmosis group \((p = 0.87)\). The location distribution of the cartilage defects showed no significant differences between the groups (Table 13). The anterior and posterior height of the TC-joint cartilage and the height of the posterior facet in the MRI showed insignificant differences between the groups (Table 13).

<table>
<thead>
<tr>
<th>MRI findings</th>
<th>Unstable Syndesmosis</th>
<th>Stable Syndesmosis</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height of the TC-joint cartilage anteriorly [mm], Mean (SD)</td>
<td>1.8 (0.5)</td>
<td>2.0 (0.6)</td>
<td>0.19</td>
</tr>
<tr>
<td>Height of the TC-joint cartilage posteriorly [mm], Mean (SD)</td>
<td>2.1 (0.4)</td>
<td>2.2 (0.5)</td>
<td>0.10</td>
</tr>
<tr>
<td>Height of the posterior facet cartilage [mm], Mean (SD)</td>
<td>2.3 (0.4)</td>
<td>2.4 (0.5)</td>
<td>0.33</td>
</tr>
<tr>
<td>Cartilage defects, Number of patients (%)</td>
<td>12 (56%)</td>
<td>13 (54%)</td>
<td>&gt; 0.9</td>
</tr>
<tr>
<td>Medial Talus, Number of patients (%)</td>
<td>4 (18%)</td>
<td>4 (17%)</td>
<td>&gt; 0.9</td>
</tr>
<tr>
<td>Lateral Talus, Number of patients (%)</td>
<td>1 (5%)</td>
<td>3 (13%)</td>
<td>0.63</td>
</tr>
<tr>
<td>Medial Tibia, Number of patients (%)</td>
<td>9 (41%)</td>
<td>9 (38%)</td>
<td>0.73</td>
</tr>
<tr>
<td>Lateral Tibia, Number of patients (%)</td>
<td>5 (23%)</td>
<td>8 (33%)</td>
<td>0.27</td>
</tr>
</tbody>
</table>

5.4 Suture-button fixation versus screw fixation (IV)

Baseline characteristics of the patients are shown in Table 14.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Suture-button ((n = 21))</th>
<th>Screw ((n = 21))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at the fracture, mean (SD) [range], y</td>
<td>46.0 (14.8) [20–79]</td>
<td>43.5 (15.7) [20–73]</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>13/8</td>
<td>14/8</td>
</tr>
<tr>
<td>Lauge-Hansen PER, n/N</td>
<td>21/21</td>
<td>21/21</td>
</tr>
<tr>
<td>Anatomy of fibula fracture</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maisonneuve fracture(^1)</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Weber type C</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Fracture anatomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibula</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Fibula and medial malleolus</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Fibula and posterior malleolus(^2)</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Trimalleolar fracture</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>
Variable Suture-button (n = 21) Screw (n = 21)
---
Open Fracture 0 0
Co-morbidity\(^3\), n 3 4

\(^1\) A spiral fracture of the proximal third of the fibula associated with a tear of the distal tibiofibular syndesmosis and the interosseous membrane (Maisonneuve 1840). \(^2\) Avulsion fracture of the posterior malleolus (< 1/3 of distal tibia joint surface), not fixed. \(^3\) Arteriosclerosis obliterans (ASO), diabetes mellitus, alcoholism or mental illness

### 5.4.1 Syndesmosis reduction

According to the surgeons’ evaluation based on the intraoperative CT, one patient had incongruent syndesmosis after screw fixation and required open exploration with re-fixation. In seven cases, syndesmoses were considered malreduced after suture-button fixation (Fig. 5a). Open exploration was carried out, but in all cases the syndesmoses were found well reduced if the ankle was at 90° of dorsiflexion, and no re-fixation was needed. Of these patients, postoperative CT of the ankle at 90° of dorsiflexion in a below-knee cast showed no malreduction of the distal tibiofibular joint (Fig. 5b).

Fig. 5. An example of a false positive finding of intraoperative CT in suture-button group. (A) Intraoperative CT shows a slight external rotation and posterior slide of the fibula, probably due to flexible nature of the fixation of the suture-button. (B) Postoperative CT of the same patient with the ankle supported at 90° angle by a cast. The fibula rotates internally and the syndesmosis reduces, which was also verified intraoperatively by open exploration.
After retrospective re-evaluation of the intraoperative and postoperative CT scans by the musculoskeletal radiologist, one case of malreduction was found to have gone unnoticed in each group; thus, the malreduction rate was 1/21 (5%) in both groups (Table 15). Follow-up standing CBCT showed that syndesmosis was malreduced in three patients (3/19, 16%) in the screw fixation group and in one patient (1/21, 5%) in the suture-button group (p = 0.33) (Table 15). All syndesmotic screws with malreduced syndesmosis showed signs of loosening at the follow-up radiographs.

Table 15. Malreduction of the syndesmosis in the screw and suture-button groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Screw</th>
<th>Suture-button</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malreduction on intra-operative CT³</td>
<td>1/21 (5%)</td>
<td>1/21 (5%)</td>
<td>&gt;0.9²</td>
</tr>
<tr>
<td>Malreduction after 2 years on CBCT⁴</td>
<td>3/19 (16%)</td>
<td>1/21 (5%)</td>
<td>0.33²</td>
</tr>
</tbody>
</table>

¹ Malreduction was defined as > 2 mm side-to-side difference in the mean width of the syndesmosis, ² Fisher’s exact test, ³ Bilateral intraoperative CT O-arm, patient in supine position, ⁴ Bilateral CBCT, patient in standing position

5.4.2 Functional results

According to LMM-analysis, the OMAS and VAS (function) significantly improved from one year to the latest follow-up, but no significant between-group differences were detected at the last follow-up (Table 16). All functional scores improved from one year to the last follow-up within the suture-button group (OMAS from 75 to 82, p = 0.008; VAS pain from 15 to 11, p = 0.02; VAS function from 22 to 16, p = 0.02; paired-sample t-tests), whereas, in the syndesmotic screw group, only VAS function significantly improved (from 19 to 11 p = 0.002; paired-sample t-test). Only one of the eight sections (mental health) of the 36 RAND significantly differed between the groups (Table 16).
Table 16. Function parameters after one year and at the final follow-up. P-values reported with LMM are: $P_{\text{time}}$ for change between measurement points, $P_{\text{group}}$ for average between-group difference, and $P_{\text{time*group}}$ for the interaction between time and group.

<table>
<thead>
<tr>
<th>Measure</th>
<th>1 year</th>
<th>2 years</th>
<th>$P_{\text{time}}$</th>
<th>$P_{\text{group}}$</th>
<th>$P_{\text{time*group}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>OMAS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suture-button</td>
<td>75</td>
<td>82</td>
<td>0.002</td>
<td>0.56</td>
<td>0.76</td>
</tr>
<tr>
<td>Screw</td>
<td>80</td>
<td>84</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS function</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suture-button</td>
<td>22</td>
<td>15</td>
<td>&lt; 0.001</td>
<td>0.50</td>
<td>0.63</td>
</tr>
<tr>
<td>Screw</td>
<td>19</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suture-button</td>
<td>16</td>
<td>12</td>
<td>0.21</td>
<td>0.80</td>
<td>0.57</td>
</tr>
<tr>
<td>Screw</td>
<td>13</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAND-36 bodily pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suture-button</td>
<td>75</td>
<td>78</td>
<td>0.33</td>
<td>0.78</td>
<td>0.94</td>
</tr>
<tr>
<td>Screw</td>
<td>72</td>
<td>76</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAND-36 physical function</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suture-button</td>
<td>78</td>
<td>87</td>
<td>0.02</td>
<td>0.83</td>
<td>0.97</td>
</tr>
<tr>
<td>Screw</td>
<td>76</td>
<td>84</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAND-36 general health</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suture-button</td>
<td>70</td>
<td>72</td>
<td>0.17</td>
<td>0.36</td>
<td>0.57</td>
</tr>
<tr>
<td>Screw</td>
<td>63</td>
<td>69</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAND-36 mental health</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suture-button</td>
<td>82</td>
<td>87</td>
<td>0.08</td>
<td>0.02</td>
<td>0.59</td>
</tr>
<tr>
<td>Screw</td>
<td>69</td>
<td>77</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAND-36 role function (physical)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suture-button</td>
<td>77</td>
<td>85</td>
<td>0.17</td>
<td>0.47</td>
<td>0.70</td>
</tr>
<tr>
<td>Screw</td>
<td>68</td>
<td>80</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAND-36 vitality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suture-button</td>
<td>70</td>
<td>73</td>
<td>0.23</td>
<td>0.31</td>
<td>0.78</td>
</tr>
<tr>
<td>Screw</td>
<td>62</td>
<td>69</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAND-36 social function</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suture-button</td>
<td>88</td>
<td>89</td>
<td>0.25</td>
<td>0.27</td>
<td>0.36</td>
</tr>
<tr>
<td>Screw</td>
<td>76</td>
<td>86</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAND-36 role function (emotional)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suture-button</td>
<td>93</td>
<td>89</td>
<td>0.52</td>
<td>0.09</td>
<td>0.18</td>
</tr>
<tr>
<td>Screw</td>
<td>70</td>
<td>83</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

At the final follow-up, the FAOS subscales and the range of motion of the injured ankle showed only minor, statistically insignificant differences between the groups (Table 17). All functional scores showed statistically insignificant difference.
between patients with malreduced syndesmosis and those with reduced syndesmosis on the final follow-up CBCT (Table 18).

Table 17. FAOS at the final follow-up.

<table>
<thead>
<tr>
<th>FAOS</th>
<th>Suture-button</th>
<th>Screw</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms</td>
<td>81 (18)</td>
<td>78 (24)</td>
<td>0.64</td>
</tr>
<tr>
<td>Pain</td>
<td>92 (15)</td>
<td>89 (15)</td>
<td>0.59</td>
</tr>
<tr>
<td>Daily living</td>
<td>93 (14)</td>
<td>94 (12)</td>
<td>0.84</td>
</tr>
<tr>
<td>Sports and free time</td>
<td>85 (28)</td>
<td>82 (27)</td>
<td>0.75</td>
</tr>
<tr>
<td>Quality of life</td>
<td>78 (27)</td>
<td>78 (24)</td>
<td>0.95</td>
</tr>
<tr>
<td>ROM(^1), degree</td>
<td>83 (10)</td>
<td>82 (9)</td>
<td>0.81</td>
</tr>
</tbody>
</table>

\(^1\) range of motion of the injured ankle

Table 18. Effect of syndesmosis malreduction on ankle functional outcome at the final follow-up.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Reduced, n = 36</th>
<th>Malreduced, n = 4</th>
<th>p-value(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OMAS</td>
<td>85 (18)</td>
<td>69 (39)</td>
<td>0.46</td>
</tr>
<tr>
<td>VAS, pain</td>
<td>9 (14)</td>
<td>38 (47)</td>
<td>0.31</td>
</tr>
<tr>
<td>VAS, function</td>
<td>10 (14)</td>
<td>32 (35)</td>
<td>0.31</td>
</tr>
<tr>
<td>FAOS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms</td>
<td>83 (17)</td>
<td>65 (32)</td>
<td>0.36</td>
</tr>
<tr>
<td>Pain</td>
<td>92 (12)</td>
<td>77 (31)</td>
<td>0.41</td>
</tr>
<tr>
<td>Daily living</td>
<td>96 (10)</td>
<td>81 (26)</td>
<td>0.35</td>
</tr>
<tr>
<td>Sports and free time</td>
<td>87 (25)</td>
<td>61 (43)</td>
<td>0.33</td>
</tr>
<tr>
<td>Quality of life</td>
<td>81 (20)</td>
<td>53 (51)</td>
<td>0.36</td>
</tr>
</tbody>
</table>

\(^1\) Student’s t-test

5.4.3 Posttraumatic OA according to CBCT-scans

Posttraumatic OA was more common in the injured ankle than in the uninjured ankle in both groups, but no significant difference was detected between the screw and the suture-button fixation groups (Table 19).
Table 19. OA grade assessed on standing CBCT and graded according to the classification of Morrey & Wiedeman (1980) at the final follow-up.

<table>
<thead>
<tr>
<th>Grade of OA</th>
<th>Syndesmotic screw (n = 19)</th>
<th>Suture-button (n = 21)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Injured ankle Uninjured ankle</td>
<td>Injured ankle Uninjured ankle</td>
<td></td>
</tr>
<tr>
<td>Grade 0</td>
<td>4 11</td>
<td>0 7</td>
<td></td>
</tr>
<tr>
<td>Grade I</td>
<td>8 7</td>
<td>7 10</td>
<td></td>
</tr>
<tr>
<td>Grade II</td>
<td>6 1</td>
<td>11 3</td>
<td></td>
</tr>
<tr>
<td>Grade III</td>
<td>1 0</td>
<td>3 1</td>
<td></td>
</tr>
</tbody>
</table>

Number of patients with OA one or more grades more serious in the injured ankle than in the uninjured ankle: 11/19 13/21 > 0.9
6 Discussion

6.1 General considerations

This thesis has several strengths. Three of the four studies were randomised controlled trials, and the fourth study was conducted from prospectively collected material from patients who underwent intraoperative syndesmosis stability testing with standardised methods on all patients. Good to excellent (86% to 98%) follow-up rates, as well as the reasonably long follow-up (from one year to six years) in all our studies, confirm the findings. Study I is clearly the largest RCT on ankle fractures in terms of sample size. In addition, it is the first study to examine the non-operative treatment of ankle fractures with adequate stability assessment of the ankle mortise. The three non-operative treatment methods compared in study I comprehensively cover the spectrum of non-operative treatment modalities currently available, and study IV compares dynamic and static implants for the treatment of unstable syndesmosis.

In study I, the 8.8 point difference in the OMAS set for the non-inferiority margin is clearly lower than the previously reported minimal clinical important difference (MCID) of this scoring system (12 points) (Nilsson et al. 2013). Furthermore, the 95% CI was sufficiently narrow to provide a conclusive confirmation that the study interventions (three-week cast or orthosis) were not inferior to the control treatment (six-week cast). We also consider our follow-up rates acceptable: >95% at 3 and 6 weeks and >85% at 12 weeks and 12 months. The use of validated and condition-specific functional outcome measures (OMAS, FAOS and VAS) in all our studies enabled a reliable comparison of the treatment methods. The mid-term radiological and functional results of Studies II and III expand the findings of the previously published study by Pakarinen et al., which presented functional scores and was the first clinical study to evaluate the indication for syndesmosis transfixation in SER/Weber B-type ankle fracture (Pakarinen et al. 2011c). The use of advanced imaging technology (3T MRI, intra- and postoperative CT and CBCT) in conjunction with traditional plain radiographs enabled a more comprehensive comparison of different treatment strategies. The formation of pairs using known prognostic factors in Study III enabled a more accurate assessment of the clinical relevance of syndesmosis injury in this fracture pattern.

Our studies have also some limitations. It can be argued that due to the non-inferiority design of our study I, protocol violations at the 6-week cast treatment
group (n=6) potentially skew our ITT-analyses. However, the findings of the ITT analyses were confirmed in the per-protocol analyses. In study I, one could also question the appropriateness of the timing of the first questionnaire at six weeks after injury, as patients at the longer (6-week) cast group were just off the cast at that time point. It is true that this could explain the observed lower range-of-motion of the ankle and also the higher pain scores at the 12 week follow-up (vs. the 6-week follow up) in the 6-week cast group. However, the six-week follow-up appointment point was merely chosen to enable comparison of the relative superiority of the 3-week cast and orthosis groups at an early stage. The relatively small number of patients in Study II leaves us with the possibility of type II error in some functional scores and in the incidence of ankle joint OA. However, in Study III, we were able to gain enough statistical power by combining all patients with a syndesmosis injury into a single group, since the MCID in OMAS is 12 points (Nilsson et al. 2013), and our 95% CI of the difference in mean was −3 to 10; thus, we were able to rule out type II error. We are also aware that syndesmosis fixation may have affected the results, although, the direction of this effect is unclear. Study IV was sufficiently powerful to show a difference in syndesmosis malreduction rates, but it was probably underpowered to demonstrate possible differences in functional outcome and in OA grade.

6.2 Non-operative treatment of stable Weber B-type fibula fracture

Our results showed that, in terms of ankle function, a three-week immobilisation treatment with a removable orthosis or a cast resulted in non-inferior outcomes when compared to a conventional six-week cast immobilisation, in ER-stress stable Weber B-type isolated fibular fractures. Although small clinically insignificant differences were detected, all groups improved similarly in terms of all ankle functional outcomes, at every follow-up point. All treatment methods maintained ankle joint congruency despite being fully weight bearing, with no significant differences in fracture union. Patient compliance with the orthosis and the shorter cast immobilisation was excellent. All serious adverse effects (i.e. DVT and cases of non-union) were associated with cast treatment, although differences between functional and cast treatment were statistically insignificant.

We are not aware of any published comparative studies about the non-operative treatment of stable Weber B ankle fracture with a reasonably long follow-up and adequate statistical power. Previous RCTs with relatively small patient numbers have only reported early results [i.e. after three months (Stuart et al. 1989) or six
months (Port et al. 1996)]. The fundamental methodological difference between our trial and most previous studies was the means to determine whether the fracture (ankle mortise) was stable immediately after the injury. Most previous studies have used fracture stability assessment based on plain radiographs (fracture gap < 2 mm), sometimes combined with the absence of “red flag” clinical findings (tenderness, swelling, haematoma) on the medial side of the ankle. (Magnusson 1944, Yde & Kristensen 1980a, Bauer 1985, Bauer et al. 1985, Kristensen & Hansen 1985, Stuart et al. 1989, Zeegers et al. 1989, Ryd & Bengtson 1992, Brink et al. 1996, Port et al. 1996). The stability of the ankle mortise is widely regarded as the most crucial factor when treating ankle fractures, and assessments based solely on static radiographic and clinical signs are presently considered inadequate in terms of differentiating between stable and unstable injuries (Michelson 1995, Michelson et al. 2001, McConnell et al. 2004, Tile 1987, Gill et al. 2007, Gougoulias et al. 2010, Nortunen et al. 2015). Therefore, the results of these previous studies are not directly comparable to our data since they may have also included unstable injuries, leading to a less favourable result in the non-operative treatment.

Stable ankle fractures, unlike unstable fractures, cannot be displaced by physiologic forces (Tile 2005, Gougoulias et al. 2010). Our results confirmed that, when the stability assessment at the beginning of the treatment is conducted adequately, treating stable Weber B-type fibula fractures simply with orthosis immobilisation for three weeks and with early full weight bearing is safe and maintains ankle joint congruity. No operative treatment was needed due to widening of the ankle mortise for any of the study patients. It is very likely that those studies reporting widening of the ankle mortise during follow-up, and transition from non-operative to operative treatments, used inadequate methods in their primary stability assessment (Magnusson 1944, Kristensen & Hansen 1985, Ryd & Bengtson 1992). Our finding of no loss of congruity suggests that repetitive routine follow-up radiographs are not required, provided that the initial assessment of ankle stability is adequately carried out using ER-testing. It has been proposed that, stable Weber B-type ankle fractures may be “an unnecessary fracture clinic burden” because of needless repetitive visits and radiographs (Michelson et al. 1995b, Martin 2004, Jain et al. 2008, Pakarinen et al. 2011a).

Our study results showed that the patient’s compliance with a shorter cast time or orthosis treatment was excellent, with no crossovers, whereas six patients assigned to the six-week cast group declined to continue cast treatment after their three-week visit. The removable design of the orthotic device enables normal
washing and treatment of the skin of the injured limb and also allows the patients
to wear their own shoes, thereby possibly improving patient comfort. The patient
can also easily adjust the fit of the removable orthotic device at home, negating any
need for visits to outpatient clinics (e.g. to change a cast). Consequently, the costs
treatment with orthoses are probably lower than those associated with casts. Our
study results clearly show that a shorter immobilisation of stable Weber B ankle
fractures is safe, efficacious and probably also cost effective.

6.3 Indications for syndesmosis fixation in SER -type ankle fractures

Our study showed that leaving an unstable syndesmosis unfixed in a SER-type
ankle fracture patient led to similar functional and radiological results at mid-term
follow-up when compared with syndesmosis transfixation. No widening of the
ankle mortise was detected, regardless of syndesmosis transfixation or no fixation
in SER IV/Weber B -type ankle fractures. The 3T MRI scans showed several
cartilage lesions in both groups, with no significant differences between the groups.
Posttraumatic OA was mild in weight-bearing radiographs or MRI, and an unfixed
syndesmosis did not lead to any increased incidence of osteoarthritis.

In contrast to recommendations from the previous studies, we found that
intraoperatively defined syndesmosis disruption left without fixation did not lead
to worse functional outcomes, misalignment of the ankle mortise, or increased
radiographic findings of OA when compared with syndesmotic screw fixation
(Lindsjö 1985, Boytim et al. 1991, Ogilvie-Harris & Reed 1994, Xenos et al. 1995,
Stark et al. 2007, Bauer et al. 2009, Elgafy et al. 2010). Authors who recommend
syndesmosis transfixation when intraoperative syndesmosis stress-tests show
unstable syndesmosis after fixation of the bone fractures base their opinion on the
assumption that cast immobilization alone after ankle fracture fixation is
insufficient and late instability of the syndesmosis would lead to worse functional
outcome and early osteoarthritis. These assumptions are generated mainly from
biomechanical studies, which have shown that even a slight displacement of the
talus, as little as one mm, can increase joint contact loads by as much as 42%,
probably leading to the development of early ankle joint OA (Ramsey & Hamilton
1976, Clarke et al. 1991, Harris & Fallat 2004). However, the assumption that the
late instability of the syndesmosis, if the talus remains anatomically under the tibial
plafond, leads to development of early osteoarthritis and to poor functional
outcome is not strongly affirmed in the clinical settings. Actually, only one clinical study by Leeds & Erglich has shown a correlation between the late syndesmosis instability, found in an external rotation stress test, and the level of arthritis and functional outcome (Leeds & Erglich 1984). That retrospective study of 34 patients with bi- or trimalleolar ankle fractures (6 PER, 4 SA II and 24 SER IV) used plain radiographs to estimate the postoperative quality of reduction of the bone fractures and the syndesmosis. In addition, plain radiographs were used to assess syndesmosis stability in the external rotation test and to grade posttraumatic OA after an average of four years of follow-up. Syndesmosis transfixation was used only in two cases of PER IV-type ankle fracture both in which no additional lateral fixation was used. The authors concluded that torn syndesmosis ligaments in SER-type ankle fractures can heal with appropriate lengths resulting stable syndesmosis if the anatomy of the bones is restored to normal and protected with immobilisation in a cast (Leeds & Erglich 1984).

In addition, one conflicting issue is the finding that MRI scans of the fractured ankles have revealed a high incidence of unsuspected syndesmosis disruption in SER-type ankle fractures (Nielson et al. 2004). The clinical relevance of these findings is unknown, but they are used to argue against the recommendations for syndesmosis transfixation presented in a landmark biomechanical study (Boden et al. 1989) and to recommend the indication for syndesmosis transfixation based on intraoperative syndesmosis stress tests instead (Nielson et al. 2004, Jenkinson et al. 2005, Weening & Bhandari 2005, Egol et al. 2006, Stark et al. 2007, Tornetta et al. 2012). However, the original RCT study by Pakarinen et al. and the present mid-term follow-up study from the same patient material are the only clinical studies that have evaluated the clinical relevance of syndesmosis transfixation with a screw in patients with instability appearing in the intraoperative syndesmosis stress test performed after malleolar fixation (Pakarinen et al. 2011c).

Similar to our results, Kennedy et al., in their RCT study, found no difference in functional or radiological results between patients with low Weber C/SER-type ankle fractures (< 5 cm proximal from the TC joint) and associated syndesmosis injury, following treatment with or without syndesmotic screw fixation (Kennedy et al. 2000). They used only preoperative plain radiographs to detect syndesmosis injury, and no intraoperative syndesmosis stability testing was performed. Our suggestion that a syndesmotic screw fixation is not indicated for SER-type ankle fractures when bone fractures are fixed with restoration of a normal medial joint space is supported by many authors (Mast & Teipner 1980, Leeds & Erglich 1984,

6.4 Clinical relevance of the syndesmosis injury in SER-type ankle fractures

Our results showed similar functional outcome and pain scores after a minimum of four years from initial trauma in patients with or without associated syndesmosis injury in SER IV fractures. The rates of posttraumatic OA and cartilage lesions, as well as ankle joint congruence, did not differ in patients with SER IV ankle fractures, regardless of the stability or instability of the syndesmosis determined in the intraoperative ER-stress test.

Litrenta et al. found different recovery curves in patients with SER/Weber B-type ankle fractures based on syndesmotic injury. The detected difference was at the limit of clinical significance, and contrasted with our results, and the authors concluded that syndesmotic injury slightly worsens the outcome of operatively treated SER/Weber B fractures (Litrenta et al. 2015). However, the slight difference in the recovery curves found between the groups may also be due to the use of markedly different postoperative treatment protocols: non–weight bearing for 10–12 weeks if syndesmotic fixation was used and 4–6 weeks if it was not (Litrenta et al. 2015). Instead, a similar postoperative treatment protocol was used in our study, regardless of syndesmosis injury; a below-the-knee cast for four weeks and weight-bearing allowed as tolerated. Thus, we were able to eliminate possible effects of postoperative treatment methods on the patient outcome.

Previous studies have reported several adverse effects associated with prolonged cast immobilisation of the lower limb, including decreased range of motion, muscle atrophy, diminished strength, and an increased risk for DVT (Brodie & Denham 1974, Stuart et al. 1989, Chesworth & Vandervoort 1995, Vandenborne et al. 1998, Shaffer et al. 2000, Jørgensen et al. 2002, Stevens et al. 2004, Patil et al. 2007, Lin et al. 2012, Drakos & Murphy 2014), which may explain the minor deteriorating effects of the syndesmosis injury reported by Litrenta et al. (Litrenta et al. 2015).

Veen and Zuurmond also published a retrospective study that compared 23 Weber B/C-type ankle fracture patients with unstable syndesmosis treated with transsyndesmotic screw fixation and 33 Weber B/C-type ankle fracture patients with stable syndesmosis (Veen & Zuurmond 2015). These authors concluded that their patient groups had comparable radiological and functional results at six years
after the trauma. However, the groups were compared without making any adjustment for possible confounding factors (i.e. fracture type, patient sex or age.)

Our results contrast with those of previous studies which have reported inferior outcomes in ankle fracture patients requiring syndesmosis transfixation (Colvin et al. 2009, Still & Atwood 2009, Egol et al. 2010). However, the heterogeneity in the fracture morphologies between the groups, the lack of a standard treatment algorithm and the variation in postoperative treatment protocols used in those studies complicate comparison of these investigations to ours. Furthermore, none of these studies precisely addressed the clinical relevance of syndesmosis injury in conjunction with SER/Weber B-type ankle fracture. In addition, a widely cited retrospective study by Pettrone et al. on the prognostic factors of the results after fracture of the ankle found that syndesmosis injury, identified from preoperative radiographs, did not predict a worse clinical outcome (Pettrone et al. 1983). Instead, syndesmosis widening or malreduction, evaluated from postoperative radiographs, was an indicator of a worse clinical outcome. Our study results show that an associated syndesmosis injury in a SER IV ankle fracture has no influence on the functional or radiological outcome at four to six years after the trauma and is therefore probably not clinically important.

6.5 Dynamic or static syndesmosis fixation?

Our RCT of patients with PER/Weber C-type ankle fractures and associated syndesmosis injury showed that either syndesmotic screw or suture-button fixation resulted in a low malreduction rate (5%) and both methods maintained the reduction well (syndesmotic screw 84% and suture-button 95%). Previous studies using advanced intraoperative imaging technology – CT or 3D fluoroscopy – reported malreduction rates ranging from 6% to 38% with syndesmotic screw fixation (Franke et al. 2012, Davidovitch et al. 2013). However, in those studies, the syndesmosis reduction was not evaluated by a side-to-side comparison since only the injured side was scanned intraoperatively (Franke et al. 2012, Davidovitch et al. 2013). The marked individual variation in measurements of syndesmosis width (Mukhopadhyay et al. 2011, Dikos et al. 2012, Naqvi et al. 2012, Sagi et al. 2012, Lepojärvi et al. 2014) and the central position of the fibula in tibiofibular groove in only 30% of uninjured ankles (Lepojärvi et al. 2014) have led to the recommendation of bilateral imaging for reliable assessment of syndesmosis reduction (Mukhopadhyay et al. 2011, Dikos et al. 2012, Naqvi et al. 2012, Sagi
et al. 2012, Lepojärvi et al. 2014). Consequently, comparison of our syndesmosis reduction results to those published previously is difficult.

We also found that, due to the dynamic nature of the fixation, intraoperative CT scanning of the ankles with suture-button fixation can be misleading unless the scanning technique is meticulous and the ankle is supported at a 90 degree angle. The less rigid nature of fixation of the suture button device may explain the high rate of false positive findings noted from intraoperative CT. The flexible feature of the suture button device means that the fibula can slightly rotate and slide posteriorly when the lower limb is in a free position (i.e. somewhat externally rotated in plantar flexion) because the weight of the foot imposes a slight gravity stress on the ankle (Fig. 5a). When the ankle is set at 90 degrees, the fibula rotates internally and the distal tibio-fibular joint reduces, as verified by open exploration and postoperative CT (Fig. 5b).

In our study, follow-up bilateral CBCT-scans after two years suggested that the rate of syndesmosis malreduction may slightly increase when a syndesmotic screw fixation is used, whereas the reduction was well maintained following suture-button fixation. Previous studies of syndesmotic screw fixation using bilateral CT to assess syndesmosis reduction reported malreduction rates of 15–44% over 1.5–8.4 years of follow-up (Wikeroy et al. 2010, Naqvi et al. 2012, Sagi et al. 2012). However, none of these studies used intra- or early postoperative CT, and they could not assess whether the malreduction was due to a technical error intraoperatively or developed during the follow-up. Additionally, they used slightly different measuring techniques for syndesmosis reduction, which may have affected the results (Wikeroy et al. 2010, Naqvi et al. 2012, Sagi et al. 2012). Furthermore, syndesmotic screws were routinely removed in all these other studies, which may have resulted in late diastasis in some cases, as described previously (Hsu et al. 2011, Schepers et al. 2011). We did not routinely remove the syndesmosis screws, so the different rate of late syndesmosis diastasis might be attributable to the different biomechanics of the fixation devices.

Our 5% syndesmosis malreduction rate for suture-button fixation is comparable to the published rates. Most previous studies that evaluated suture-button fixation for unstable syndesmosis have reported 0% malreduction rates, but only plain radiographs were used to assess syndesmosis reduction (Thornes et al. 2005, Cottom et al. 2008 & 2009, DeGroot et al. 2011, Naqvi et al. 2012a&b, Rigby et al. 2013). Only the study by Treon et al. reported an 11% syndesmosis malreduction rate when the suture-button was used (Treon et al. 2011). Naqvi et al. compared syndesmotic screw and suture-button fixation using CT of both ankles to
assess syndesmosis reduction and found no malreduction with suture-button fixation in 23 patients after a minimum of 18 months of follow-up (Naqvi et al. 2012b).

In our study, both the syndesmosis screw and suture-button fixations yielded similar functional outcomes. A RCT by Coetzee & Ebeling, which included only preliminary results with a small number of patients, also reported no significant difference in the ankle functional outcome between syndesmotic screw and suture-button fixation (Coetzee & Ebeling 2009). In addition, Naqvi et al., in their cohort study, reported trends toward better clinical outcome in patients treated with suture-button fixation, but when they adjusted groups for potential confounders, they found no significant difference between the syndesmotic screw and suture-button fixation cohorts (Naqvi et al. 2012b). By contrast, Laflamme et al., in their RCT study, reported statistically but not clinically better ankle functional scores when using suture-button fixation compared to syndesmotic screw fixation (LaFlamme et al. 2015).

The present study showed that mild OA was more common in the injured ankle than in the uninjured ankle after both fixation methods, without significant between-group differences. To our knowledge, only Wikeroy et al. previously assessed the incidence of ankle joint OA in this fracture type using CT-scans after syndesmosis screw fixation and reported episodes of OA in 67% of the patients (Wikeroy et al. 2010). Our study, which used side-to-side comparison, determined that OA was one or more grades more serious in the injured ankle than in the uninjured ankle in 58% of patients in the syndesmotic screw fixation group. To our knowledge, no published studies have reported the incidence of OA assessed via CT for suture-button fixed ankles. The results presented here suggest that the method of syndesmosis fixation has no influence on the incidence of OA.

### 6.6 Clinical implications and future studies

The results of this thesis indicate that immobilisation of stable lateral malleolar fractures can be safely and effectively shortened to three weeks, and routinely repeated ankle radiographs are unnecessary when the stability assessment is adequate. Additionally, intraoperative assessment of syndesmosis stability and syndesmosis fixation in SER-type ankle fractures with congruent ankle mortise after fixation of bone fractures seems to be unnecessary. When syndesmosis fixation is indicated in PER-type ankle fractures, either a transfixation screw or suture-button device can be used for syndesmosis fixation with comparable
outcomes. The deployment of the findings of this thesis in clinical practice could reduce the burden and costs to healthcare systems, as well as patients’ exposure to radiation from intraoperative and follow-up ankle radiographs.

Recent studies have suggested that the stability of the ankle mortise is a continuum from stable to unstable (Nortunen et al. 2014). Therefore, a positive ER-stress test might overestimate the need for surgical treatment in SER/Weber B-type ankle fractures (Weber et al. 2010, Hoshino et al. 2012, Sanders et al. 2012, Hastie et al. 2015 Holmes et al. 2016). Future studies about the non-operative treatment of ankle fractures should include patients with ankle fractures that are unstable in the ER-stress test but show normal ankle joint congruity in weight-bearing radiographs.

In addition, due to lack of high quality evidence about the amount of clinically relevant syndesmosis malreduction detected from bilateral CT scans (Warner et al. 2015), future studies should focus on assessing the limits of the clinically relevant magnitude of syndesmosis malreduction. Syndesmosis reduction assessment should be based on bilateral CT-scanning, conducted at the beginning of treatment and after a sufficient follow-up period.
7 Conclusions

1. ER-stress stable Weber B-type fibula fractures can be treated effectively and safely, with early weight bearing and with a three-week cast or orthotic immobilisation, instead of the traditional six-week cast immobilisation.

2. After fixation of bone fractures, leaving an unstable syndesmosis unfixed in a SER/Weber B-ankle fracture yields similar ankle functional and radiological results when compared to syndesmosis transfixation with a screw after a minimum of four years of follow-up.

3. Syndesmosis injury in SER IV/Weber B-type ankle fractures has no effect on functional or radiological outcome and pain after a minimum of four years of follow-up.

4. Syndesmotic screw and suture-button fixation have similar postoperative malreduction rates in patients with PER/Weber C-type ankle fractures and associated syndesmosis injury. After at least two years of follow-up, the rate of syndesmosis malreduction may slightly increase when syndesmotic screw fixation is used, but the suture-button maintains the reduction well. The syndesmotic fixation method has no influence on the functional outcome or the incidence of ankle joint OA.
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