Outcome of surgery for end-stage ankle arthritis

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Abstract

Background: Ankle arthrodesis (AA) and total ankle replacement (TAR) are the two most common surgical treatment options for painful end-stage ankle arthritis. Currently no general guidelines are available to determine which procedure is best for a specific patient. AA has been the gold standard for a long time, resulting in pain relief and good function, but modern TAR has become a feasible alternative. So far no high-level studies are available and not a single RCT comparing outcomes of AA with TAR.

Aims: To analyze patient-reported outcomes after primary TAR and bilateral AA, patient-reported outcomes and failure rate after revision TAR and salvage arthrodesis (SA) following TAR failure in the Swedish Ankle Registry by PROMs (EQ-5D, SF-36, SEFAS and a question on satisfaction with the surgical result).

Results: After primary TAR, all scores improved from preoperative to 24 months after surgery (p < 0.001), and 71% of the patients were satisfied with the surgical result. Postoperative SEFAS and satisfaction correlated positively with age and preoperative SEFAS, whereas we found no associations between diagnosis or prosthetic design with outcome.

Revision TAR was followed by low functional scores, and only 50% of the patients were satisfied. Estimated 5-year survival of revision TAR was 76% and 10-year survival 55%.

SA was followed by similar and low functional scores as after revision TAR but a significantly lower reoperation risk (p < 0.05).

Bilateral AA was followed by patient-reported outcome scores similar to primary TAR and 91% of the patients were satisfied. Patients with isolated tibiotalar arthrodesis in general scored higher than those with tibio-talo-calcaneal arthrodesis.

Conclusion: Primary TAR and bilateral AA seemed to have a positive impact on patient-reported outcomes in terms of foot and ankle function and general health, and most patients were satisfied with their result after these procedures. However, after TAR failure, the two salvage procedures revision TAR and SA both resulted in similar low outcome scores and low satisfaction. Revision TAR was however associated with a significantly higher reoperation rate than SA. Until studies show true benefit of revision TAR over SA, we favor SA for failed TAR. Further investigation has to be done to analyze which patients are best suited for primary TAR and for AA, preferably by means of RCT studies.
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Plantigrade feet should be a human right
— Bertil Romanus
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Summary

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Revision TAR was followed by low functional scores, and only 50% of the patients were satisfied. Estimated 5-year survival of revision TAR was 76% and 10-year survival 55%.

SA was followed by similar and low functional scores as after revision TAR but a significantly lower reoperation risk ($p < 0.05$).

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Conclusion: Primary TAR and bilateral AA seemed to have a positive impact on patient-reported outcomes in terms of foot and ankle function and general health, and most patients were satisfied with their result after these procedures. However, after TAR failure, the two salvage procedures revision TAR and SA both resulted in similar low outcome scores and low satisfaction. Revision TAR was however
associated with a significantly higher reoperation rate than SA. Until studies show true benefit of revision TAR over SA, we favor SA for failed TAR.

Further investigation has to be done to analyze which patients are best suited for primary TAR and for AA, preferably by means of RCT studies.
Original Papers

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals. The original papers are enclosed at the end of the thesis.

I. Poor prosthesis survival and function after component exchange of total ankle prostheses

Ilka Kamrad, Anders Henricsson, Magnus K Karlsson, Håkan Magnusson, Jan-Åke Nilsson, Åke Carlsson, and Björn E Rosengren


II. Outcome after Salvage Arthrodesis for Failed Total Ankle Replacement

Ilka Kamrad, Anders Henricson, Håkan Magnusson, Åke Carlsson, and Björn E Rosengren


III. Bilateral Arthrodesis of the Ankle Joint: Self-Reported Outcomes in 35 Patients from the Swedish Ankle Registry

Anders Henricson, Ilka Kamrad, Björn Rosengren, Åke Carlsson


IV. Good patient-reported outcomes and high satisfaction rate after primary total ankle replacement – 167 patients followed for 24 months in the Swedish Ankle Registry

Ilka Kamrad, Åke Carlsson, Anders Henricson, Håkan Magnusson, Magnus Karlsson, Björn E Rosengren

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Abbreviations

AA  ankle arthrodesis
EQ-5D  EuroQol 5 dimensions
f-u  follow-up
MCID  minimal clinically important difference
NSAID  non steroidal anti-inflammatory drugs
PROM  patient-reported outcome measures
ROM  range of motion
SA  salvage arthrodesis
SEFAS  self-reported foot and ankle score
SF-36  short form 36
SMO  supramalleolar osteotomy
TAR  total ankle replacement
THA  total hip arthroplasty
TKA  total knee arthroplasty
VAS  visual analogue scale
Arthritis is a condition of joint degeneration and successive cartilage breakdown and can unfortunately affect any joint in anybody. Factors such as genetics, former trauma and certain professions may increase the risk or even cause the development of arthritis, but in many cases the specific etiology is unknown. Idiopathic osteoarthritis (OA) is the most common type of arthritis, followed by post-traumatic osteoarthritis (PTA) and systemic arthritis including those originating from rheumatoid conditions (mainly rheumatoid arthritis, RA).

In the lower extremity, the three big joints are the hip, the knee and the ankle. Hip and knee degeneration is most often due to idiopathic osteoarthritis and affects elderly patients, whereas ankle arthritis in about 80% is caused by previous trauma and affects younger patients (Barg et al. 2015, Gougoulas et al. 2009, Zaidi et al. 2013). The causing trauma can be an intra-articular ankle fracture but also severe soft tissue injuries with chronic instability.

As sport-related injuries often occur at a younger age and life expectancy has increased, symptom-giving ankle arthritis is more frequent nowadays. A successive cartilage breakdown can lead to pain, stiffness, deformity and limping. Nowadays, two main surgical options for painful end-stage ankle arthritis are available: ankle arthrodesis (AA) and total ankle replacement (TAR).

AA has been regarded as gold standard for treatment of severe ankle arthritis for many decades (Gougoulas et al. 2009, van Heiningen et al. 2013, Zaidi et al. 2013) and, once solid, it most often leads to pain relief, satisfaction, adequate function and a stable ankle. The disadvantages are, however, loss of ankle motion with impaired walking pattern and a risk of degeneration in neighboring joints.

The first generation of ankle prostheses had neither satisfactory implant survival nor a good functional outcome, but since then development and improvement of implants have been undertaken. With modern prosthetic designs and refined surgical technique, TAR often leads to a well-functioning pain-free ankle. But even though short- and mid-term results are promising, implant survival is still not as high as for hip and knee prostheses (Henricson et al. 2016, Kerkhoff et al. 2016, Sadoghi et al. 2013).

So far there are no widely adopted guidelines concerning the exact indications and contraindications for TAR and AA, respectively. The literature generally infers that TAR seems to work best for the elderly, not physically demanding patient without severe hind foot deformity.
The lack of treatment guidelines for severe ankle arthritis and the fact that no high-level studies comparing the two surgical treatment options are available is the background for this thesis.

The ankle joint and arthritis

The anatomical and biomechanical complexity of the ankle joint

The foot together with the ankle joint consists of 26 bones, 33 joints and more than 100 muscles, tendons and ligaments. Together they build a complex structure that makes it possible to stand stably, to walk dynamically, to jump, to run and to bear our body during lifetime (Figure 1).

The talus, tibia and fibula build the bony structures of the normal and highly congruent ankle joint, which is stabilized by the joint capsule and ligaments. The talus is larger anteriorly than posteriorly and its cartilage is about 1.5 mm thick, which is thinner than the hip (slightly thicker) and knee joint (up to 2.5 mm) (Shepherd and Seedhom 1999). This comparatively thin cartilage layer of the ankle can restrain mechanical forces to a great extent and keep the contact pressure at a low level (Bhatia 2014). The contact area in the ankle joint is much less than in the hip and knee joint, and the impact on the joint cartilage can increase up to four times the body weight during gait and even more during high-impact sports activities (Bhatia 2014).

Figure 1. The complexity of the structures of the foot and ankle (free picture from anatomymasterclass.com)
Due to the complex anatomical and biomechanical structure the ankle joint is not only a simple hinge joint. There are three axes of movement: mainly plantar- and dorsiflexion but also inversion/eversion and external/internal rotation. The asymmetric shape of the talus causes a rotational movement in both dorsi- and plantarflexion. Additional to this, the shape of the talus leads to eversion of the foot in dorsiflexion, and to inversion in plantarflexion.

The functional range of motion (ROM) of the healthy ankle joint varies depending on the task – e.g. normal walking (around 20° ROM) and descending stairs (up to 50° ROM). The average dorsiflexion is around 15° and plantarflexion around 40°.

**Arthritis in the ankle joint**

*Etiology*

The most common etiology of ankle arthritis is previous trauma, often due to malleolar fractures or lateral ligament injury. The American Academy of
Orthopaedic Surgeons (AAOS) have in their on-line patient information a well-formulated description of the development of posttraumatic arthritis:

"An injured joint is about seven times more likely than an uninjured joint to become arthritic, even if the injury is properly treated. In fact, following an injury, your body may actually secrete hormones that stimulate the death of your cartilage cells."

This explanation will facilitate the discussion with patients who think that posttraumatic ankle arthritis is caused by improper treatment or surgical reconstruction.

Even minimal cartilage damage or incongruence can result in rapid development of joint degeneration. The time from cartilage damage to symptoms is often about 10–20 years (Englund 2014). As ankle arthritis is mostly post-traumatic and ankle injuries often occur during sports at a young age, symptoms of ankle arthritis can present already at an age of 30–40 years.

The prevalence of arthritis is difficult to examine, as not all patients with arthritis need to seek medical help. Around 10% of arthritis in general involves the ankle joint (Bhatia 2014, Crevoisier et al. 2016, Zhou and Tang 2016). In the United Kingdom the prevalence of ankle arthritis is estimated at about 48 / 100 000 inhabitants (Vaughan et al. 2015).
Kinematics
In the healthy ankle joint the talus continuously changes its rotational axis in relation to the tibia. Furthermore the talus moves in the subtalar joint in a gliding motion against the calcaneus (Zhou and Tang 2016). In the arthritic joint there is a
decrease in the triplanar joint movement leading to decreased ROM and impaired gait.

**Symptoms**

Ankle arthritis can cause swelling, decrease in ROM and deformation, but the real debilitating symptom is painful gait (Bhatia 2014).

Early symptoms of ankle arthritis are often impairment of gait and pain anteriorly getting worse in uphill walking. Later symptoms include increasing pain, decreased ROM and malalignment such as varus deformity (Figure 6) as a late consequence of lateral ligament injury or valgus deformity after previous syndesmotic injury or lateral malleolar fracture.

**Treatment**

**Non-surgical treatment** methods of ankle arthritis include exercise, lifestyle changes (e.g. weight control and good footwear) and orthotic devices. Medication includes oral NSAID or intra-articular injection of steroids or hyaluronic acid (Bhatia 2014, Crevoisier et al. 2016, Gougoulias et al. 2009).

**Minor surgical treatment** methods such as arthroscopic joint debridement, extirpation of osteophytes and synovectomy may at least temporarily reduce pain and increase ROM when arthritis is at an early- or mid-stage (Bhatia 2014, Crevoisier et al. 2016).

**Major surgical treatment** methods include supramalleolar osteotomy (SMO), ankle arthrodesis (AA) and total ankle replacement (TAR). SMO is the joint-preserving alternative and is possible in early- to mid-stage ankle arthritis with malalignment. The two joint sacrificing alternatives for painful end-stage ankle arthritis are AA and TAR. Both procedures interfere with the biomechanics and dynamics of the ankle joint, and both have advantages and disadvantages that influence the decision process as to whether AA or TAR might be the better surgical option for the individual patient.

**Ankle arthrodesis**

Ankle arthrodesis (AA) was first described in 1891 by Albert (Huntington et al. 2016). In the beginning, ankle arthrodesis was seen as a corrective, stabilizing surgical procedure for deformities of the foot. Since then, various surgical techniques with varying success rates have been described. Through time, AA gained acceptance as a treatment option for osteoarthritis.
Biomechanical aspects following AA

After fusion between tibia and talus, rotation movements and the normal continuously changing loading axis are inhibited. This may result in more loading and impact on adjacent joints with a risk of degeneration. The risk of arthritis in neighboring joints is mentioned in many of the studies on AA (Houdek et al. 2014, Huntington et al. 2016, Sheridan et al. 2006, Vaughan et al. 2015). The radiological degenerative findings, however, do not necessarily lead to clinical symptoms, and most of the patients with AA will never need additional surgery for these changes (Braito et al. 2014, Houdek et al. 2014).

AA surgery and postoperative treatment

Various techniques are presently used for AA, including open or arthroscopic technique, external or internal fixation, screw-, plate- or retrograde intramedullary nail fixation. With nailing, the talo-calcaneal joint will also be fused. Techniques depend on the patient’s circumstances but also on the personal preference of the surgeon.

After surgery patients usually get a cast (not with external fixation) for approximately three months, and weight bearing is usually not allowed for at least six weeks. This period of immobilization may be very challenging for the patient, especially for the elderly.

Figure 7. Radiograph of screw-fixed ankle arthrodesis, frontal view. The distal fibula has been removed.
Outcome of AA

The overall outcome of AA is usually reported as good or excellent, with significant increase in outcome scores and high satisfaction grades (Houdek et al. 2014, Huntington et al. 2016). Pain disappears and the ankle is stable and everlasting in its position, assuming that positioning was done properly. The ankle should be positioned in 5° hindfoot valgus, 5–10° external rotation and the talus slightly posteriorly translated on the tibia (Bloch et al. 2015).

The union rate after AA is most often reported to be 90% or more (Houdek et al. 2014), nonunion though remains a most challenging complication. Factors
associated with nonunion include certain fixation techniques, smoking, diabetes and infection (O’Connor et al. 2016).

Nonunion may be only radiological without clinical symptoms, but painful nonunion most often requires revision surgery. In most cases re-arthrodesis is performed, but the risk of nonunion after re-arthrodesis is higher (up to 20%) compared to primary AA (Huntington et al. 2016, O’Connor et al. 2016). Revision with conversion to TAR may be an option, but this procedure is uncommon, even though sparse literature shows promising first results (Hintermann et al. 2009, Huntington et al. 2016). Below-knee amputation is a radical final alternative and may be appropriate in some cases.

![Figure 9. Radiograph of nonunion after screw-fixed ankle arthrodesis, frontal view. The joint space is clearly visible.](image)

![Figure 10. Radiograph of united re-arthrodesis of the ankle joint, lateral view](image)

AA on one side has often been seen as a contraindication for AA in the contralateral ankle. For patients with bilateral painful ankle arthritis the recommendation has historically been to perform AA only in one ankle and TAR in the other in order to at least maintain mobility in one side.

Bilateral AA may however not be as bad as previously thought. The few published studies regarding outcome of bilateral AA have only small patient samples but indicate good functional outcome, similar to bilateral TAR. Residual problems with two stiff ankles however arise during stair climbing and in uneven
terrain, but overall satisfaction rate still seems above expected (Houdek et al. 2014, Vaughan et al. 2015).

Total Ankle Replacement

A brief history of ankle prostheses

The first reported total ankle replacement (TAR) was performed by Lord and Marrotte in 1970 (Lord and Marrotte 1973). They designed a prosthesis resembling an inverted hip prosthesis with the stem in the tibia, and the technique required subtotal removal of the talus. Lord and Marrotte were the TAR pioneers, but unfortunately their results were disappointing (Gougoulias et al. 2009, Kerkhoff et al. 2016). All the following so-called first-generation designs were constrained, cemented, two-component implants. Short-term results were encouraging with pain-free satisfied patients, but the enthusiasm waned when a high percentage of implants loosened after a few years. This was due to several factors such as improper prosthesis implantation, partly because of non-appropriate surgical instruments, excessive bone removal with fracture risk, implant characteristics such as small surface area associated with early loosening and insufficient distribution of axial load.

The high failure and complication rates after first-generation TAR led to recommendations to give up ankle replacement until more appropriate implants were available (Barg et al. 2015, Kerkhoff et al. 2016). In fact, the question arose whether the ankle joint could be replaced at all.

The complex anatomy and rotational axis of the ankle have been challenging for the development of implants. Since the poor results of the first-generation TAR, many prosthetic designs have been put forward with two or three components, fixed or mobile bearings, constrained or non-constrained, with different advantages and disadvantages but in general with better implant survival than the first generation. Minimal bone resection and better surgical instruments and technique, together with more appropriate implant designs, have led to promising mid- and long-term results with better implant survival, fewer complications and good function (Barg et al. 2015, Gougoulias et al. 2009, Zhou and Tang 2016).
TAR surgery and postoperative treatment

Most implants are designed for an anterior approach, but prosthetic design and scars from previous surgical procedures influence the incision planning. Postoperatively, patients are usually immobilized with a cast for 4–6 weeks, and many patients start weight bearing after two weeks. The shorter period of immobilization and non-weight bearing is thus not as arduous as after AA.
Outcome and implant survival after TAR

The functional outcome of modern TAR seems promising at both mid-term and long-term follow-up, with high satisfaction rates and good clinical and radiological results (Wood et al. 2008). Often limp and pain vanish, mobility increases, and patients often experience an increase in quality of life (Kerkhoff et al. 2016, Zaidi et al. 2013).

Even though the implant survival has clearly increased with time, the current 5-year survival rates of up to >90% are still lower than for hip and knee prostheses (Gougoulias et al. 2009, Kerkhoff et al. 2016). Periprosthetic osteolytic lesions are the main cause of loosening of the components and failure of the TAR (Gaden and Ollivere 2013). The exact pathomechanism is not quite clear, but positioning of the implant seems to have an impact on the development of such lesions (Kotnis et al. 2006, Louwerens 2015).
Revision surgery after failed TAR

A failed TAR has to be removed, and several treatment options are available. The prosthesis may be replaced, but this procedure is surgically demanding, with high risk of non-satisfactory outcome. The ankle may also be secondarily fused, but bone defects after a failed TAR lead to a challenging situation and the risk of nonunion is high. The final surgical option would be below-knee amputation in severe cases of chronic infection, severe pain or ischemic vascular disease.

Figure 14. Radiograph of TAR failure, lateral view  Figure 15. Radiograph of revision TAR, lateral view

Comparison of TAR with hip and knee prostheses

The first hip prosthesis was implanted in Germany in 1891 by Professor Glück, using carved ivory for replacement of destroyed femoral heads after tuberculosis (Knight et al. 2011). Continuous improvement of implants and surgical techniques has led to gradually improving results. For many decades, hip and knee replacement have been standard procedures in orthopedic units, and almost everybody nowadays knows somebody with a hip or knee prosthesis.

The history of TAR is thus much younger, and there is not the same diversity of prosthetic designs on the market compared to hip and knee prostheses. Discouraging results after first-generation TARs have certainly led to a decrease in interest from the industry and affected the velocity of implant development. But also the fact that there is a surgical alternative, AA, decreases the need for
industrial solutions compared to other joint replacements. Unlike the hip and knee, where fusion is not an attractive treatment option, AA seems associated with satisfactory results concerning pain and function, comparable to TAR.

Patients scheduled for surgery due to ankle arthritis in general differ from their counterparts with hip and knee arthritis. Since about 80% of ankle arthritis is post-traumatic (in hip and knee patients the vast majority have primary osteoarthritis), and since trauma in the ankle most often occurs at younger ages, patients with ankle arthritis are about 10 years younger than their counterparts scheduled for hip and knee replacement (Barg et al. 2015, Crevoisier et al. 2016). Having a patient between 50 and 60 years old and knowing that even the most modern ankle prostheses have limited survival and knowing that secondary surgery is not quite easy, makes the primary decision difficult whether or not an ankle prosthesis might be convenient.

Younger et al. compared the total costs of surgery of TAR, AA, total hip arthroplasty (THA) and total knee arthroplasty (TKA). In their analysis the equipment costs were higher for TAR than for THA and TKA, but due to shorter hospital stay after TAR the total costs were similar. AA on the other hand was significantly less expensive, at approximately half of the cost (Younger et al. 2015a).

Concerning the cause for revision surgery, there are clear differences between ankle, hip and knee prostheses. Aseptic loosening is the main reason for revision in all artificial joints. However, 15% of TAR is revised due to discomfort or loosening associated with technical error and 10% of TKA is revised because of pain, whereas 12% of THA is revised due to luxation (Sadoghi et al. 2013). Experience of TAR is many decades shorter than THA and TKA and there may still be potential to counteract some reasons for failure with future development of implants and surgical technique.

**TAR in Sweden**

In Sweden less than 100 ankle replacements are performed each year, which is a lower frequency than in other countries. According to national registry data in the UK (www.njrcentre.org.uk) their rate is about double that of Sweden. In Norway (www.nrlweb.ihelse.net) almost three times as many ankle prostheses are implanted compared to Sweden, and in New Zealand (www.nzoa.org.nz) and Australia (www.aoanjrr.sahmri.com) the rate is approximately four times as high.

In 2015 seven units performed TAR in Sweden, but four centers took care of 88% of the cases. Five prosthetic designs were used, with Rebalance (Biomet) and Trabecular Metal™ ankle implanted in almost 90% of cases (www.swedankle.se).
SwedAnkle

SwedAnkle is one of more than 100 official national certified quality registries in Sweden, founded in 1997. TAR procedures were then retroactively registered back to 1993, when third-generation implants were introduced in Sweden, and the registry has had virtually full coverage for TAR since then. The administration of the registry was first located in Falun but was moved in 2007 to the orthopedic department of Skåne University Hospital, Malmö. Since 2008, patient-reported outcome measures (PROM) and AA registration have been included. The coverage for AA has gradually increased and was 96% in 2015 (www.swedankle.se). Even SMO registration is possible since 2008, but this procedure is most uncommon in Sweden and coverage uncertain.

The surgery report form contains information about the patients’ medical background and specific surgical data. In addition to that, PROM registration is recommended preoperatively and 6, 12 and 24 months postoperatively and for TAR also 60 months postoperatively. The follow-up registrations are patient-reported only without clinical follow-up data or radiographic documentation in the registry.

Under the terms of the Swedish National Quality Registries’ regulations, patients are informed about the registry written and/or verbally, and participation is voluntary. At any time, participation can be withdrawn.

Figure 16. The Mobility™ prosthesis
What is the purpose of this thesis?

We have currently no well-grounded advice to give the middle-aged patient with painful end-stage ankle arthritis for which surgical treatment suits him or her best. There is no general algorithm and in literature no high-level studies are found that could support and facilitate the decision. There are however absolute and relative contraindications for both TAR and AA, but the final decision is most often influenced by the subjective considerations and experience of the surgeon. By analyses of the Swedish Ankle Registry data I want to try to deepen our knowledge about primary TAR and AA and revision surgery after failed TAR in Sweden. The results of the studies in this thesis can hopefully support surgeons in their clinical decision-making and in informing patients about the outcomes and risks of the different surgical treatments.
Aims of the studies

The overall aim of this thesis was to describe outcomes after TAR and AA and thereby hopefully add important information to gaps, mainly regarding better patient selection and patient information.

The specific aims were:

I. To analyze the patient-reported outcome after primary TAR.
   (paper IV)

II. To analyze the survival and patient-reported outcome after revision TAR.
    (paper I)

III. To analyze the patient-reported outcome after salvage arthrodesis after failed primary TAR.
    (paper II)

IV. To analyze the patient-reported outcome after bilateral AA.
    (paper III)
Research questions

I. Does TAR lead to functional improvement for patients with painful end-stage ankle arthritis?

II. When primary TAR fails, are revision TAR and SA reliable surgical treatments?

III. Does bilateral AA lead to satisfactory functional outcome?
Subjects and methods

The patients in the Swedish Ankle Registry (SwedAnkle)

Until January 2016, which was the time limit for inclusion in the analyses in papers I–IV in this thesis, there were 1176 primary TARs and 1743 primary AAs registered in SwedAnkle. So far no patient has declined participation, but not all patients send back the follow-up questionnaires, and there is even a lack of preoperative PROMs from many patients.

Depending on the surgical procedure, the registration forms differ slightly. All surgical forms include date of birth, height and weight, smoking habits, hospital and surgeon, side and date of surgery.

For primary TAR and AA the registration of primary diagnosis, symptoms from the other ankle, other musculoskeletal disease or conditions influencing gait, associated surgery, former surgery on the foot or ankle of interest, and perioperative complications are added. Implant-specific details are included in the primary TAR form. AA registration, on the other hand, includes preoperative malalignment, perioperative bone transplantation, surgical technique and fixation method.

Concerning revision registrations of TAR, the order of the current revision surgery is registered, the reason for revision, and the type of revision (revision TAR, salvage arthrodesis, amputation).

Outcome evaluation

SwedAnkle uses two generic scores, EQ-5D (European Quality of Life – 5 dimensions) and SF-36 (Short Form 36 health survey), to estimate overall patient health. The EQ-5D has questions about 5 categories: mobility, self-care, usual activity, pain and anxiety/depression. Each category is ranked from 1 to 3 depending on level of disability. The calculated score ranks from 0 (equal to death) to 1 (full health). It is theoretically possible to get a negative score, but any score below 0 is designated as 0. In addition to the 5 questions there is a visual
analogue scale (EQ-VAS) for self-scaling of general health (0 worst thinkable, 100 best thinkable).

The SF-36 contains 36 questions related to 8 subscales (physical functioning, physical role limitations, bodily pain, general health, vitality, social functioning, emotional role limitations, mental health). Each scale results in a separate index, and the 8 subscales can further be summarized in 2 final indices (physical and mental score). All scores (subscales and summarized) rank from 0 to best possible 100.

There are many region-specific foot and ankle scores available but SwedAnkle uses the relatively new and validated SEFAS (self-reported foot and ankle score) to estimate the impact of a surgical treatment on the function of the ankle (Coster et al. 2012). The questionnaire contains 12 questions with 5 possible answers for each question. Each answer gives 0 to 4 points, and the overall count can reach from worst possible 0 to best possible 48.

Finally, there is a question on how satisfied the patient is with the result after surgery, graded on a Likert scale (very satisfied, satisfied, neither satisfied nor dissatisfied, dissatisfied, very dissatisfied) (Likert 1932).
Subjects for each study

For every study, the patient cohort of interest was collected in the registry. To analyze survival and background data of revision TAR in paper I, all 69 cases could be included. PROM evaluation on the other hand could only be done for 29 patients (Figure 18).

![Figure 18. Patients with revision TAR for paper I](image-url)
All 114 patients with 118 SA for paper II could be included for analysis of background data and failure. Here too, there were missing data for PROM evaluation (Figure 19).

![Figure 19. Patients with SA for paper II](image)
Paper III analyses 51 patients with bilateral AA, and PROM evaluation could be done for 35 patients (Figure 20).

![Figure 20. Patients with bilateral AA for paper III](image)

In paper IV we included only patients with both preoperative and at least one postoperative PROM evaluation. Of the 506 primary TARs during the time of interest, no preoperative PROMs were available in over 50% of the patients. Only patients who filled in the preoperative PROM were asked to fill in postoperative PROMs as well, and over 90% of those patients sent the questionnaires back. Figure 21 shows the follow-up time of the evaluable 241 patients.

![Figure 21. Patients with primary TAR for paper IV](image)
Statistics

All statistical analyses were done with SPSS (statistical package for the social sciences®) version 21 and 22. Results are presented as numbers, proportions (%), medians and means with 95% confidence intervals (95% CI), ranges or standard deviation (SD).

The CI of mean scores was estimated assuming normal distribution. In paper I, Fisher’s exact test was used for CI of absolute counts due to small numbers in subgroups. Changes in scores (papers II and IV) were analyzed with paired Student’s t-tests.

Group differences in paper II were estimated with independent t-tests of means and with chi-square tests for categorical variables. Due to small numbers in each group, changes within groups were tested by Wilcoxon rank-sum test (also in paper III).

Kaplan-Meier survival analyses were used to estimate the survival (no registration of further revision surgery on the ankle) of patients with revision TAR (paper I) and after SA (paper II).

In paper IV, Pearson and Spearman’s correlation analyses were used to find associations between different factors and outcome scores. Outcomes between groups were compared with ANOVA. Where significant group differences were found, Tukey post-hoc tests were performed. Partial correlation analyses adjusted for age were done to examine the influence of preoperative SEFAS on postoperative outcome.

Ethics

All studies in this thesis were approved by the Regional Ethical Review Board in Lund (Dnr 2009/698) and were performed in accordance with the Declaration of Helsinki.

In agreement with the Patient Data Act (patientdatalagen) and Personal Data Act (personuppgiftslagen) all patients are informed before registration in SwedAnkle, this is done in writing or orally preoperatively. All patients are free to withdraw from future or all participation at any time.

All registry data used in this thesis are presented in aggregated form only.
Summary of papers

Paper I

Poor prosthesis survival and function after component exchange of total ankle prostheses – An analysis of 69 patients in the Swedish Ankle Registry

Background

Total ankle replacement (TAR) is an alternative to fusion for some patients with end-stage ankle arthritis, but failure rate after TAR is higher than after hip and knee prostheses. In cases with TAR failure, secondary fusion is often the treatment of choice. Revision TAR with exchange of the implant components is another option for which some high-volume units have reported promising results. We analyzed implant survival, self-reported function and patient satisfaction in patients having undergone revision TAR.

Patients and methods

We identified 69 patients in the Swedish Ankle Registry who, after failed primary unilateral TAR, underwent 73 revision procedures (3 patients were revised more than once) with exchange of the talar and/or the tibial component. The mean age at primary surgery was 53 years and at the time of revision 55 years. Survival of revision TAR was estimated by Kaplan-Meier analysis. We evaluated patient-reported outcome measures (PROM) SEFAS, SF-36 and EQ-5D and patient satisfaction at least 12 months after revision surgery.

Results

Time from primary to revision surgery was a median of 22 months (range 0–101). Of the 69 revision TARs, 24 failed again after a median of 26 months (range 1–110). The 5-year revision TAR survival rate was 76% and the 10-year survival 55%. PROM evaluations at a mean 8 years after revision showed the following mean scores: SEFAS 22, SF-36 physical 37 and mental 49, EQ-5D index 0.6 and EQ-VAS 64. Fifteen out of 29 patients were very satisfied or satisfied and 9 were
dissatisfied or very dissatisfied. Neither primary diagnosis nor cause of failure seemed to influence the outcome.

Figure 22. Flowchart failures revision TAR

Conclusion
The prosthesis survival rate after revision TAR in our study was much lower than previously published results after primary TAR at both 5 and 10 years. Only half of the patients were satisfied and outcome scores were low. Future studies should focus on identifying patients who may benefit from revision TAR, and whether these demanding procedures are better done only in highly specialized units.
Outcome after salvage arthrodesis for failed total ankle replacement

Background
For patients with a failed primary total ankle replacement (TAR), a decision must be made about whether revision prosthesis can be performed or if salvage arthrodesis (SA) is the better choice. We aimed to analyze failure rate and patient-related outcomes after SA.

Patients and methods
Of 1110 primary TARs found in the Swedish Ankle Registry, 188 had failed. Of these, 118 were revised with SA and 70 with revision TAR. The patients with SA were a mean 55 years old at the time of primary surgery and 61 at the time of revision. Failure of SA was defined as repeat arthrodesis or amputation. A SA was considered solid when no further surgical procedure on the ankle was found in the registry. Both generic and region-specific PROMs of 68 patients with a solid unilateral SA performed at least one year before were included in the analyses.

Results
Ninety percent of SA cases were considered solid after the first attempt. Of the 12 nonunion SA, 2 patients underwent below-knee amputation and 10 were revised again with arthrodesis, of which 3 nonunited once more. Of these 3 patients, one was amputated, resulting in a total of 3 patients with below-knee amputation. Twenty-five of 53 patients with solid first-attempt SA were satisfied or very satisfied, and 13 dissatisfied or very dissatisfied. The mean PROM scores were low: SEFAS 22, SF-physical 34, SF-mental 50, EQ-5D index 0.6 and EQ-VAS 59. Scores and satisfaction were similar to revision TAR but total reoperation rates were significantly lower in SA. Ninety-one percent of patients were revision-free after 5 years and 83% after 10 years.
Conclusion

In our study, 90% of the patients with SA after failed TAR did not need further revisions on their ankle. Significantly lower reoperation and revision rates were found after SA compared to after revision TAR. Similar to revision TAR, only 50% of the patients were satisfied and functional scores were low.

Similar outcome scores but significantly lower reoperation rate in SA compared to revision TAR lead to our recommendation to favor SA for failed TAR until further studies can show true benefit of revision TAR over SA.
Bilateral arthrodesis of the ankle joint: self-reported outcomes in 35 patients from the Swedish Ankle Registry

Background

Ankle arthrodesis (AA) on one side has historically been said to be a relative contraindication for AA on the contralateral side due to subsequent gait impairment and high risk of arthritis in adjacent joints. Patients not eligible for prosthesis in the contralateral ankle may be considered for bilateral AA but bilateral AA is uncommon. Very little is found about outcome after bilateral AA in literature, but the few reports infer satisfactory results. We analyzed patient-reported function and satisfaction of patients with bilateral AA.

Patients and methods

We identified 51 patients with bilateral AA in the Swedish Ankle Registry. For only 35 of these (mean age 63 years) a minimum of 12 months follow-up data (after the latest AA) were available. 36 ankles were fused in the talo-crural joint (TC), and 34 in the tibio-talo-calcaneal (TTC) joint complex.

Results

The mean follow-up time for the 35 included patients was 47 months. During this period no subtalar fusions due to secondary subtalar arthritis were registered in the TC group. The mean PROM scores were as following: SEFAS 33, SF-36 physical 39, SF-36 mental 54, EQ-5D index 0.67 and EQ-VAS 70. Scores were similar irrespective of diagnosis, but patients with TTC arthrodesis had lower scores after surgery than TC arthrodesis patients. Ten of the 35 patients were very satisfied with the surgery of both their ankles, and of the total 70 ankles, 64 were reported as very satisfactory of satisfactory for the patients.

Conclusion

The relatively high degree of satisfaction after bilateral AA is in line with the few studies found in literature. Other studies showed that even bilateral TAR and TAR on one side and AA on the other side lead to high satisfaction rates in both ankles. Our study shows that bilateral AA, in a mid-term perspective, may be a realistic treatment option for patients not suitable for TAR, as patient-estimated functional outcome and satisfaction seem relatively high.
Good patient-reported outcomes and high satisfaction rate after primary total ankle replacement – 167 patients followed for 24 months in the Swedish Ankle Registry

Background
Total ankle replacement (TAR) has gained popularity for severe ankle arthritis, but it is still not used as frequently as ankle arthrodesis (AA). The functional outcome after TAR seems comparable to AA and patient satisfaction is high. There are however few studies on TAR with more than 100 patients. We ascertained patients having undergone TAR in the Swedish Ankle Registry and analyzed self-estimated functional outcome and satisfaction.

Patients and methods
A total of 241 patients at a mean age of 62 years with both preoperative and at least one postoperative PROM evaluation were included, of whom 167 had their latest follow-up at 24 months. Both generic and region-specific PROMs were evaluated as well as a question on satisfaction with the surgical result. Thirty-seven percent of the patients underwent TAR due to posttraumatic arthritis (PTA), 28% due to rheumatoid arthritis (RA), 25% due to idiopathic osteoarthritis (OA) and 10% for other reasons. We analyzed the influence of age, diagnosis, prosthetic design and preoperative functional score on the postoperative outcome.

Results
All scores increased significantly from before to 24 months postoperatively. Significant increase of SEFAS was also found between 6 and 24 months postoperatively, but not between 12 and 24 months. Some 71% of the patients were very satisfied or satisfied and 12% dissatisfied or very dissatisfied. Postoperative SEFAS and satisfaction correlated positively with age and preoperative score. Neither diagnosis nor prosthetic design seemed to influence the outcome.

Conclusion
TAR led to a significant improvement in patient-reported function and to a high satisfaction rate in a 24-month perspective. Diagnosis and prosthetic design did not seem to influence the outcome whereas age did. Long-term studies are needed to determine whether short-term outcome may predict implant failure.
General discussion

Registry research

Using solely registry data is a clear limitation of all four longitudinal observational studies in my thesis. All included variables are predefined, which gives registry studies in general a rigid structure. Another problem is the uncertainty of completeness of reporting but also the question whether the reporting individuals (both clinicians and patients) can cause a selection bias. On the other hand there is always a selection bias in single-center studies, and by using registry data this potential problem can be, if not eliminated, at least reduced.

TAR registration in SwedAnkle has been complete or almost complete, which is a clear strength of our studies. On the other hand, the surgeon who decides that a patient is suitable for TAR, can cause patient selection. The only way to avoid this problem would be RCTs.

SwedAnkle uses registration forms with relatively few questions that only take a few minutes to fill out. By this we hope to get a high response rate, but there are still a fair amount of missing data in our studies.

SwedAnkle has no automatic registration of complications and includes no radiological or clinical findings at follow-up. The post-operative outcome evaluation is done only by PROMs, but further registration of secondary surgery is a way to identify failed cases.

Difficulties in measuring patient outcomes

In the end it is the subjective judgment of the patient whether or not a treatment has been successful. In many studies generic health scores combined with region-specific scores are used to evaluate the effect of a treatment out of the patients view.

A dilemma is that the answers to a PROM questionnaire may be subjective with the risk that daily mood, experience of the treatment, patient-doctor relation and other factors influence the answers. To minimize such influences as much as
possible, PROM scores should have high reliability and responsiveness and should be validated.

SwedAnkle uses two generic scores that are frequently used in other studies, which makes a certain comparison with other study results possible. The validated region-specific SEFAS, on the other hand, is not yet widespread, which makes it difficult to set our results in perspective, as there are so far no normative data available.

In all our studies (papers I–IV) we had missing data concerning PROM responses. In paper IV, only patients who returned PROMs preoperatively and at least once postoperatively were included. To find out whether there was a selection bias we compared those patients’ basic data – such as diagnosis, mean age, hospital – with all registered patients with primary TAR and did not find any statistically significant differences.

The patients in SwedAnkle are also asked whether they are satisfied with the surgical result. Also satisfaction may be subjective. We think (or hope) that by this question patients evaluate pain and function. Pain is difficult to assess. Pain coming solely from intra-articular degeneration will probably wane after surgery. But in many cases pain is a more complex factor and can originate from the surroundings as well, or as a consequence of a systemic disease. It is crucial to evaluate whether there is a realistic chance of obtaining sufficient pain relief by only addressing the joint surgically. Other non-physical factors such as depression and social aspects can also influence the intensity of experienced pain.

Besides pain and function we have to consider that satisfaction can also depend on other aspects such as scars, swelling or not being able to wear certain shoes, even if the result of the procedure from the surgeon’s point of view is good.

The clinical dilemma

Nowadays many patients are aware of their diagnosis and different treatment options. It is unfortunately not always possible to avoid the possibility that only incomplete information reaches the individual searching for it. In an era where joint replacement in general has become a routine procedure, it is understandable that many patients think that prosthesis is the best solution also for ankle arthritis, especially as ankle fusion, considered as the gold standard by the medical profession for almost 100 years (Crevoisier et al. 2016), at first glance does not seem like an attractive alternative to many patients. This may be due to a misconception of what it means to have a fused ankle but also to the fact that there are no general guidelines available with exact indications for AA or TAR (Goldberg et al. 2016). Without this and without data on outcomes for comparable
groups of patients we still have to make clinical decisions for the best possible outcome for the individual patient and to inform them about the options.

Our study of primary TAR (paper IV) justifies this procedure as a treatment option for painful ankle arthritis, but the results of the revision procedures (papers I and II) imply that the risk of failure should be kept in mind from the beginning, and TAR should only be chosen when the risk of failure can be minimized as much as possible.

First of all, a patient wanting and being considered suitable for TAR has to develop a realistic preoperative expectation. Expectation reflects the patient’s goal with surgery and influences the outcome after TAR (Younger et al. 2015b). Then the diagnosis has to be made thoroughly. The grade of arthritic changes seems to influence the outcome after TAR with clearly better scores when receiving surgery for severe (grade 4) arthritis compared to low- or mid-grade (Chambers et al. 2016). A thorough analysis of the patient’s symptoms must be done to get an idea of whether joint sacrificing surgery really leads to adequate pain relief.

There are no randomized controlled trials comparing the outcomes of TAR with AA, and published results are usually from observational studies (Goldberg et al. 2016, Henricson et al. 2016, SooHoo et al. 2007, van Heiningen et al. 2013). To date, patients selected for TAR and for AA may differ in several aspects. There are several exclusion criteria for TAR but very few for AA. Most of the factors that were or are regarded as contraindications for TAR however also are risk factors for AA failure (O'Connor et al. 2016). The preoperative conditions are most often dissimilar between patients selected for TAR and AA. The two surgical options also differ with regard to postoperative immobilization and rehabilitation, as immobilization of the ankle after TAR is about half the time compared to after AA, and the time of non-weight bearing is about three times longer after AA. It therefore seems unlikely that a patient who is suitable for both TAR and AA would agree to a randomization, and RCTs are thereby very difficult to perform.

However, in the UK a protocol for a RCT TAR versus AA has been published and it will be very interesting to see if the study can include patients and be performed as planned (Goldberg et al. 2016). The results of this study will hopefully add important information to those currently available, which all are observational studies, either case series or registry studies.

An approach to success

The most recent ankle prostheses seem to have a success rate up to 90% after 10 years (Barg et al. 2015). “Success” should be divided into several aspects. Implant survival, for example, varies widely depending on the study type. Registry studies report a 10-year implant survival of a mean 73% whereas non-registry studies
report a mean 89%, as Zaidi et al. found in their meta-analysis (Zaidi et al. 2013). The implant survival is increasing steadily compared to first- and second-generation designs, but is still lower than for hip and knee prostheses (Labek et al. 2011b, Sadoghi et al. 2013, Younger et al. 2015a). Previous TAR survival analysis from SwedAnkle showed a 5-year survival of 81% and a 10-year survival of 69% (Henricson et al. 2011). Other studies from highly specialized units report higher survival rates both for primary and secondary TAR (Hintermann et al. 2013, Labek et al. 2011a, Prissel and Roukis 2013).

Another important factor defining “success” is the patient-reported outcome of the procedure. Our study on primary TAR (paper IV) shows that ankle prosthesis can lead to high satisfaction and good functional outcome as well as improved general health status. The study, however, only reports results up to 24 months, and neither survival of the implants nor long-term outcome is known for this patient cohort. Only newest third-generation prosthetic designs were used in these patients, and it can be hypothesized that the survival of those implants may be higher than the previously reported survival of TAR in Sweden.

The low annual number of implanted TARs in Sweden (less than 100 cases annually) indicates that TAR is not a routine operation in our country, and probably that the patients are thoroughly selected. Even in the best-case scenario, the risk of loosening after TAR must be considered, especially for the many relatively young patients. The mean age in our study of primary TAR (paper IV) was 62 years, and around 20% of the patients were younger than 55 years while only 20% were over 70, and younger patients in our study had lower functional outcome scores. Age is an important factor to think of when considering TAR.

When TAR has failed, the decision must be made as to whether it is possible to exchange the prosthetic components or not. Decreased bone stock of the talus and infection have historically been contraindications for revision TAR, but even these problems can nowadays often be solved with a revision prosthesis as a two-stage-surgery in cases with infection or by massive bone transplantation in cases with severe bone loss (Espinosa and Wirth 2013, Kotnis et al. 2006, Wunschel et al. 2013). Modern primary implants that require minimal bone resection have better prerequisites for further component exchange than the older implants. There are not many published studies on revision TAR, but here too, highly specialized units report better results than others. Hintermann et al. did a study on 117 patients with revision TAR and report a 9-year implant survival of 83%. Our study on 69 revision TAR patients (paper I) does not support these encouraging results. In our study, the estimated 10-year survival of revision TAR was only 55%. Furthermore, only half of the patients were satisfied, and the PROM scores were low at a follow-up of an average 8 years. These differences might be partly due to patient selection but also due to the fact that different hospitals, surgeons, prosthetic designs with various prerequisites are included in our registry study, reflecting more a real-world situation compared to highly specialized units.
The outcome of the alternative limb-saving revision procedure for failed TAR, salvage arthrodesis (SA), was in our study (paper II) similar to the outcome of revision TAR. We analyzed self-reported outcome as well as the risk of new failure for patients with SA and found similar low outcome scores to those we found after revision TAR. In this group too, only half of the patients were satisfied. However, compared to revision TAR there was a significantly lower risk of secondary surgery and for new failure. Ten percent of the patients were registered with re-revisions, comparable to the rates found in literature (Deleu et al. 2014, Gross et al. 2015, Henricson and Rydholm 2010, Hopgood et al. 2006).

The mean time from primary TAR to revision surgery in our studies for all patients with failed TAR (papers I and II) was four years. Considering this and the relatively poor outcome scores in Sweden after revision surgery, and being aware of the fact that primary TAR is often performed before or around the age of 60 might influence the decision procedure concerning the convenient primary procedure.

Figure 24 shows the Kaplan-Meier analyses for the estimated revision-free cases after primary TAR (Henricson et al. 2011), revision TAR (paper I) and SA (paper II) in Sweden. The survival curve for primary TAR from Henricson et al. was re-calculated and adapted to our definition of failure. Henricson et al. included in their definition of failures removal of at least one of the three prosthetic components including the meniscus, except incidental exchange of the meniscus. In papers I and II we defined failure as the situation when one or both of the metallic components must be removed, but we included not solely replacement of the meniscus. Our justification for this definition was that the situation for the patient is much severe when the metallic components must be removed compared to only replacement of the meniscus. The survival curves show that patients after once solid SA need virtually no further ankle surgery, but also that re-revisions after SA were done up to several years after first SA.

The failure rates and outcomes after revision TAR and SA from papers I and II, combined with the results from other studies, can be summarized thus: both revision procedures were less satisfactory than the primary procedures (primary TAR and primary AA) but the reoperation risk was considerably lower after SA compared to revision TAR.
With this information about still relatively low implant survival after primary TAR and poor results after revision procedures, the merit of the primary TAR procedure must be questioned.

Historically, bilateral AA has been avoided due to expected postoperative severe gait impairment and the high risk of arthritis in adjacent joints. However, the few studies available on bilateral AA show that the outcome seems satisfactory and comparable to bilateral TAR (Houdek et al. 2014, Vaughan et al. 2015). Our study on 35 patients with bilateral AA (paper III) likewise strengthens this view, and we found no indication of severe impairment of quality of life postoperatively. As a consequence of this, the indication for bilateral AA can possibly be widened when it is doubtful that TAR can be performed successful in the other ankle. Our results indicate that outcome is comparable to after primary TAR, and more studies analyzing bilateral AA are needed.
Treatment choice: TAR or AA?

Ankle arthritis is associated with gait dysfunction and decreased walking speed (Queen et al. 2014). Historically, one of the most convincing advantages of TAR over AA has been preservation of mobility and an opportunity for near normal gait (Braito et al. 2014, Gougoulias et al. 2009, Huntington et al. 2016, Kim et al. 2017, van Heiningen et al. 2013). Studies with gait analyses after TAR and AA, however show that none of the procedures led to a symmetric walking pattern even though function clearly improves after both procedures (Vaughan et al. 2015). Braito et al. describe better postoperative ROM in TAR than AA patients but also found that the postoperative ROM was dependent on preoperative ROM (Braito et al. 2014). Gait analysis between patients having undergone TAR or AA and healthy individuals have found that TAR patients have a more normal gait than AA patients but that walking pattern, ankle movement and power as well as plantar flexion are all significantly lower after both treatments compared to healthy individuals (Singer et al. 2013). Other studies have also confirmed that ROM is not normal after TAR and that gait asymmetry is found between the TAR ankle and the healthy side (Braito et al. 2014, Queen et al. 2014, Zhou and Tang 2016). Patients should be informed that a significant improvement of ROM is not one of the benefits of TAR (Gougoulias et al. 2009).

Gait analyses are usually done barefoot. Frigg et al. questioned whether the more natural joint movements after TAR really are clinically relevant when wearing shoes. They investigated the walking patterns after TAR, AA and in healthy individuals (Frigg and Frigg 2016) and found that walking speed increased with shoes compared to barefoot in all groups with equal improvement for AA and TAR patients, but both still performed inferiorly compared to healthy individuals. They also found that patients with TTC arthrodesis performed worse than those with TC arthrodesis and TAR both barefoot and with shoes.

We did not investigate gait in our studies. However, interpreting others’ results of gait analyses and considering that outcome scores in our studies were comparable between TAR and AA, leads to speculation as to whether this often distinguished advantage of TAR over AA, better motion and less limp, actually might be overestimated from a clinical perspective.

To be able to answer the question whether TAR or AA is better for the individual patient, the surgeon has to be well aware of the contraindications and potential risk factors for failure for the respective procedure. Literature provides many potential risk factors for TAR failure. The implant itself might play a role. A few studies comparing outcome and survival depending on different modern types of prosthesis could find hardly any differences in functional outcome and survival (Coetzee et al. 2016, Henricson et al. 2011), except that the Agility™ prosthesis had high complication rates (Kim et al. 2017, Roukis and Prissel 2013). Nor could
we find associations between different prosthetic designs and outcome (paper IV), but more studies are necessary comparing different prosthetic designs.

Infection or severe hindfoot deformity have traditionally been relative contraindications for TAR (Barg et al. 2015, Bloch et al. 2015, Gougoulias et al. 2009, Louwerens 2015). Nowadays, however, neither infection nor deformity is an absolute contraindication for TAR. Infection must be securely treated and alignment established properly through osteotomies and ligament stabilization before TAR implantation, and then both implant survival and outcome can reach good results (Hobson et al. 2009, Louwerens 2015).

Patient selection is a key to success (Bloch et al. 2015). Concerning the underlying diagnosis there is controversy in the literature regarding primary OA (Barg et al. 2015), RA (Zaidi et al. 2016) and PTA (Criswell et al. 2012) as a risk factor for TAR failure. We did not investigate failure after primary TAR in paper IV, but comparison of the patients in our studies showed that 34% of all patients with failure of primary TAR (papers I and II) had RA compared to 28% of the patients analyzed for primary TAR (paper IV). Younger age is often put forward as a risk factor. Even though we did not do survival analyses for primary TAR in paper IV and did not investigate the influence of age on TAR survival, our failed cases from paper I and II can support other studies concluding that younger age is associated with a higher risk of failure and with lower outcome scores (Brunner et al. 2013, Criswell et al. 2012, Spirt et al. 2004).

In paper I, many of the failures of primary TAR were reported to be due to technical or unspecified reasons. The exact reasons in the individual cases are unfortunately not specified any further in many registries including SwedAnkle. The comparatively high amount of technical failure leaves a margin for further development of the surgical techniques and implants (Sadoghi et al. 2013). For every failed case with revision for technical reasons, detailed information should be mandatory regarding whether failure was implant-related or due to surgical instruments, technique or inexperience. Only if the sources of technical failure are precisely defined, potential shortcomings of the current approach are possible to identify and address in order to reduce failure rates in the future. Pain as a reason for revision certainly gives TAR a disadvantage compared to AA. It can be assumed that there are patients with remaining pain after AA as well, but when the arthrodesis is radiological fused, there is no indication for re-arthrodesis. This is important to consider when interpreting failure and revision rates after TAR.

Also concerning AA there are considerations to take. Knee mobility has to be included in the preoperative evaluation of ankle arthritis. With a fused ankle, knee flexion around 110° is desirable to be able to rise comfortably from sitting to standing position.

One of the disadvantages of AA, as claimed in many studies, is the risk of development of symptoms giving arthritis in adjacent joints (Braito et al. 2014, Gougoulias et al. 2009, Huntington et al. 2016, van Heiningen et al. 2013, van Heiningen et al. 2013,
Vaughan et al. 2015). Sheridan et al., however, question whether ipsilateral arthritis really is a long-term effect after AA. In their investigation they found already preoperatively radiographic arthritic changes in any of adjacent joints (mostly subtalar) in 96% of their cases (Sheridan et al. 2006). Houdek et al. found that adjacent arthritis is present in >60% of patients after AA but radiographic findings did not correlate with pain and 85% of the patients managed without any further fusion. Other authors likewise question the relevance of such arthritic changes (Bloch et al. 2015, Houdek et al. 2014). Another interesting aspect comes from Braito et al. who describe clinical asymptomatic adjacent joint arthritis in most patients after AA but also development of adjacent joint degeneration as a long-term complication after TAR. Literature does not provide any further information on this, and nor could we investigate the subject because additional joint fusion cannot be considered as a revision procedure after primary TAR or AA and would therefore not be registered in SwedAnkle. The question though obviously arises whether or not this often claimed advantage of TAR over AA is really true, and future studies will be necessary analyzing this.

One of the probably most convincing advantages of AA over TAR is that, once solid, the patient most likely does not have to worry about future surgical procedures on the ankle.

Patient-reported outcome

The studies in this thesis (papers I–IV) include analyses of the PROMs SEFAS, EQ-5D, SF-36 and subjective satisfaction after surgery. The results of primary TAR, revision TAR, revision to SA and bilateral AA have been analyzed in detail. The missing aspect for the overall view is the outcome after primary AA. The work on analyzing these results in detail is in progress. Nevertheless, I want to present preliminary and not statistically analyzed basic results that can complete the overall picture (tables 1 and 2). Comparison between the different patient cohorts must be done with care, as patients are selected for each procedure based on many different criteria.
Table 1. Basic data of patients from all papers including preliminary data primary AA
(f-u: follow-up time; TAR: total ankle replacement; SA: salvage arthrodesis; AA: ankle arthrodesis; OA: osteoarthritis; RA: reumatoid arthritis; PTA: post-traumatic arthritis; prim: primary surgery; rev: revision surgery)

<table>
<thead>
<tr>
<th></th>
<th>primary TAR</th>
<th>revision TAR</th>
<th>SA</th>
<th>bilateral AA</th>
<th>primary AA</th>
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<tbody>
<tr>
<td>n (% women)</td>
<td>241 (57)</td>
<td>69 (64)</td>
<td>118 (62)</td>
<td>35 (43)</td>
<td>256 (41)</td>
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<tr>
<td>f-u time</td>
<td>≤ 2 yrs</td>
<td>mean 8 yrs</td>
<td>mean 2 yrs</td>
<td>mean 4 yrs</td>
<td>≤ 2 yrs</td>
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<tr>
<td>mean age in years</td>
<td>62</td>
<td>prim 53</td>
<td>prim 55</td>
<td>63</td>
<td>62</td>
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<tr>
<td>primary diagnosis</td>
<td></td>
<td>rev 55</td>
<td>rev 61</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OA</td>
<td>25%</td>
<td>20%</td>
<td>22%</td>
<td>29%</td>
<td>28%</td>
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<tr>
<td>RA</td>
<td>28%</td>
<td>23%</td>
<td>40%</td>
<td>40%</td>
<td>13%</td>
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<tr>
<td>PTA</td>
<td>37%</td>
<td>55%</td>
<td>34%</td>
<td>14%</td>
<td>39%</td>
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<tr>
<td>other</td>
<td>10%</td>
<td>2%</td>
<td>4%</td>
<td>17%</td>
<td>20%</td>
</tr>
</tbody>
</table>

Table 2. PROM scores, SD (standard deviation) within brackets, and satisfaction of patients from all papers including preliminary data primary AA.
(s: very satisfied or satisfied; n: neither satisfied nor dissatisfied; d: dissatisfied or very dissatisfied)

<table>
<thead>
<tr>
<th></th>
<th>primary TAR</th>
<th>revision TAR</th>
<th>SA</th>
<th>bilateral AA</th>
<th>primary AA</th>
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<td>postop</td>
<td>preop</td>
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<td>24 mths</td>
<td>24 mths</td>
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<td>SEFAS</td>
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<td>31 (9)</td>
<td>22 (8)</td>
<td>22 (10)</td>
<td>33 (9)</td>
</tr>
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<td></td>
<td>15 (7)</td>
<td>31 (11)</td>
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<tr>
<td>EQ-5D</td>
<td>0.4 (0.3)</td>
<td>0.7 (0.3)</td>
<td>0.6 (0.3)</td>
<td>0.7 (0.3)</td>
<td>0.4 (0.3)</td>
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<td></td>
<td>0.7 (0.3)</td>
<td>0.7 (0.3)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>EQ-VAS</td>
<td>54 (22)</td>
<td>73 (18)</td>
<td>64 (20)</td>
<td>59 (23)</td>
<td>70 (19)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>58 (21)</td>
<td>73 (19)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF-36 phys</td>
<td>29 (9)</td>
<td>40 (11)</td>
<td>37 (9)</td>
<td>39 (11)</td>
<td>29 (8)</td>
</tr>
<tr>
<td></td>
<td>40 (12)</td>
<td></td>
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</tr>
<tr>
<td>SF-36 ment</td>
<td>49 (16)</td>
<td>53 (13)</td>
<td>49 (16)</td>
<td>50 (15)</td>
<td>49 (15)</td>
</tr>
<tr>
<td></td>
<td>54 (13)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Satisfaction s</td>
<td>71%</td>
<td>52%</td>
<td>47%</td>
<td>91.5%</td>
<td>75.5%</td>
</tr>
<tr>
<td></td>
<td>17%</td>
<td>17%</td>
<td>28%</td>
<td>7%</td>
<td>8.5%</td>
</tr>
<tr>
<td></td>
<td>12%</td>
<td>31%</td>
<td>25%</td>
<td>1.5%</td>
<td>16%</td>
</tr>
</tbody>
</table>

Patients who need revision surgery after failed primary TAR were younger in our studies at the time of primary surgery than the average patient undergoing primary TAR or primary AA. The PROM scores of all patient cohorts show that patients after primary TAR, primary AA and also bilateral AA (which is two primary operations) have similar generic and region-specific outcome scores and similar satisfaction rates. Primary TAR and primary AA led to equivalent mean improvement from preoperative to 24-months postoperatively. We unfortunately did not have preoperative scores for all patients with revision TAR and SA (papers
I and II), which would have been very valuable for the overall picture. Table 3 shows the very few patients in each cohort with both pre- and postoperative scores.

<table>
<thead>
<tr>
<th>Table 3. PROM scores pre- and postoperative for patients with revision TAR and SA</th>
</tr>
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<tbody>
<tr>
<td>revision TAR (n = 7)</td>
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<tr>
<td>preop</td>
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<tr>
<td>SEFAS</td>
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<tr>
<td>EQ-5D</td>
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<tr>
<td>EQ-VAS</td>
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<td>SF-36 phys</td>
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<td>SF-36 ment</td>
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</table>

The two generic scores (EQ-5D and SF-36) we used in our studies are frequently used in other reports. But the region-specific SEFAS, though validated, is so far not found in many other studies. It might be reasonable to include e.g. the AOFAS, which is more common, in SwedAnkle as well as postoperative radiographic documentation so that results can be compared more easily with the outcome of other studies. The disadvantage with the AOFAS score is that it is only partially validated and includes a clinical examination, and it is not available in Swedish.

To put our PROM results into perspective, a comparison with normative data or minimal clinical important difference (MCID) can be made. In Sweden, normative EQ-5D index for patients 60–69 years old is about 0.8 and EQ-VAS is 80 (Eriksson and Nordlund, Szende and William 2004). For the SEFAS there are so far no normative data available, but Cöster et al. have found the MCID in SEFAS for hindfoot disorders to be 5 points (Coster et al. 2017). Our improvements after primary TAR (15 points) and AA (16 points) show that both surgical procedures give patients an increased foot function way over the MCID.

Patients undergoing AA probably have more risk factors for adverse events during and after surgery in general and even for failure than those scheduled for TAR. Still, postoperative outcome and satisfaction seem similar in our (paper III) as well as in other studies (Braito et al. 2014, Haddad et al. 2007, Saltzman et al. 2009, van Heiningen et al. 2013). This counts not only for the primary procedures but also when comparing SA (paper II) with revision TAR (paper I). This could lead to speculation as to whether arthrodesis might be the better procedure, or if patients who are suitable for TAR but get an AA might be less satisfied with a fused ankle. However only randomized studies will be able to answer to this, and as reasoned before it is difficult to perform RCTs on this subject.

It is important that any future RCT include data on many aspects of both the patient and the procedure. From the above reasoning at least the following aspects should be included: preoperative radiographs including diagnosis of arthritis in
adjacent joints, ROM, generic and region-specific PROMs, patient expectation; at follow-up (short-, mid- and long-term) radiographs including diagnosis of arthritis in adjacent joints, ROM, generic and region-specific PROMs and satisfaction, gait analysis, complications and secondary surgical procedures. Moreover, patients suitable for both AA and TAR have to be thoroughly informed about both procedures, with the aim of eliminating as much patient selection as possible.

Clinical implications

Due to the non-randomized design of our studies and other studies in literature there is still no clear answer as to which primary procedure to choose. However, the results of the studies in this thesis add important information.

Ankle arthrodesis, even bilateral, is a surgical treatment that leads to pain relief and good functional outcome. Once solid, the risk of further surgery on the ankle is low. Total ankle replacement, on the other hand, can lead to good functional outcome as well, and survival of the implants can nowadays reach high rates. Anyhow, the risk of TAR failure must be considered, and our results show that the two available limb-saving revision procedures after failed TAR do not give satisfactory results. The association between younger age and lower postoperative outcome scores in our study (paper IV) might help in the decision process.

But many questions remain and only RCTs will lead to reliable clinical guidelines for end-stage ankle arthritis.
Limitations and strengths

This thesis and its studies have limitations. No RCT is included, which reduces the level of the studies. As with all registry studies, there is only limited data available for each patient, and further potentially interesting patient-specific background and clinical data cannot easily be included. Likewise, concerning the results and especially when comparing with other studies, the predetermined data give a non-flexible structure for the research questions. Furthermore there is always the concern of completeness of reporting. Even if the coverage for primary procedures is very high, revisions and reoperations can only be captured via reports to the registry. True revisions are assumed to have high coverage but other reoperations might partially be lacking and the rate of reoperations might be underestimated. And even if the surgical procedure is registered, not all reports include answers to all questions such as fixation technique for AA or prosthetic design for TAR.

A further weakness is the high amount of missing PROM registrations, which may introduce selection bias.

Normative SEFAS scores would without doubt have increased the value of all our results. So far, only comparison with other studies using SEFAS as outcome score is possible, and the knowledge of MCID.

Radiographic and gait analyses might have given additional aspects on the outcomes of all studies. It might be worth considering inclusion of radiographs and certain clinical evaluation into the registry to increase the value of future studies.

Our studies also have strengths. SwedAnkle has to date 100% coverage for primary TAR compared to national health authority data. For AA the coverage is somewhat lower and in 2015 was reported to be 96% (www.swedankle.se). The data collection is nationwide and includes different hospitals, surgeons, patients and implants, so that the results reflect a real-world scenario.

Even though the number of patients in each study is not large, each study (papers I–IV) has one of the largest patient cohorts found in the literature regarding the respective subject.
The research questions can be answered as follows:

I. Primary TAR surgery resulted in significant improvements in patient-reported outcome from preoperative to 24 months after surgery. 71% of the patients were very satisfied or satisfied.

II. Both revision TAR and SA after failed TAR resulted in low outcome scores, and only half of the patients were satisfied. The risk of further reoperations was significantly lower after SA compared to revision TAR.

III. Bilateral AA gave high satisfaction rates and good functional outcome, comparable to primary TAR.
Perspective

As J. Louwerens reasons, there is definitely a place for TAR for the right patient and when surgery can be performed in the right institution (Louwerens 2015). Implant survival after primary TAR has reached satisfactory rates, and the functional outcome at least in a mid-term perspective seems to be good. But even in the best-case scenario the risk of future revision surgery after TAR must not be disregarded. It is crucial to give the patient detailed information about the potential complications and reoperation risk before a decision for or against TAR is made. Surgeons who have been involved in the development of an implant design present so far better results and higher implant survival compared to registry studies. There might be several reasons for this, and patient selection might be one of them. But it cannot be ruled out that surgeon designers are extremely familiar with the implant and are very experienced with the surgical technique. This fact would support the strategy to reserve TAR surgery only for centers of excellence.

AA has been gold standard for end-stage ankle arthritis for many years and it still is a reliable procedure that leads to good functional outcome and satisfaction with low risk of failure. The leading arguments of disadvantages of AA compared to TAR – impairment of gait and risk of adjacent joint arthritis – may be overestimated according to the literature, but this must be further examined.

Only RCTs can eliminate patient selection and give the appropriate information to develop clinical guidelines on the choice of TAR or AA for patients with severe ankle arthritis. Until such guidelines are available, careful patient selection, very detailed information, realistic expectations (of both the patient and the surgeon) and surgery performed by the right surgeon is crucial if primary and revision TAR surgery is to be successful.
Populärvetenskaplig sammanfattning på svenska

Artros är en ledsjukdom som kan drabba alla leder i kroppen. Den är vanligast hos äldre, och särskilt artros i höft- och knäled ger hos många äldre stora besvär. Artros kan även drabba fotleden, men till skillnad från i höft- och knäled, där artros oftast uppstår utan uppenbar orsak, så är den vanligaste orsaken till artros i fotleden en tidigare skada i fotleden såsom benbrott eller ledbandsskada. Patienterna med fotledsartros besväras vanligen av hälta, nedsatt rörlighet i fotleden samt tilltagande smärta.

Hos de med måttliga besvär kan livsstilsförändringar som viktnedgång, motion, rätt skor och ortopedtekniska hjälpmedel vara tillräckligt. Även inflammationsdämpande tableetter kan hjälpa och i vissa fall kan kortisoninjektion i fotleden dämpa besvären åtminstone temporärt. För de som får värre besvär eller där de ovan nämnda åtgärderna inte är tillräckliga kan operation bli aktuellt. Titthålsoperation och borttagning av benpålagringar kan förbättra rörligheten och reducera besvären i alla fall på kort sikt. Vid felställningar i fotleden kan även operation med omvinkling av underbenet förbättra belastningsaxeln i fotleden och därmed hjälpa. Vid uttalade besvär och kraftig nedslitning av fotleden finns dock enbart stora operationer att tillgå: antingen genomförs en steloperation av fotleden eller ersätts leden av en fotledsprotes.

Steloperation i fotleden är en välbeprövad metod som ofta ger smärtfrihet och god funktion. Fotleden blir stabil, risken för behov av fler operationer i fotleden är låg och de flesta patienter blir nöjda trots att fotleden är helt stel. Steloperation rekommenderas ofta till yngre patienter med höga krav på belastning samt till sjuka patienter eller till de med svagt skelett, diabetes, dålig blodcirkulation eller de som röker.

Operation med moderna fotledsprteser leder också till smärtfrihet och god funktion med nöjda patienter i de flesta fall. Efter operationen kan patienten fortfarande röra i fotleden. Dock är risken för framtidiga ytterligare operationer (följeoperationer) större då en protes inte håller för alltid. Protes rekommenderas ofta till äldre patienter med låga krav på fysisk belastning av fotleden och för de utan uttalade felställningar i bakfoten.
För de ganska få patienter som har artros i båda fotlederna rekommenderar man oftast att steloperera enbart en sida och istället sätta in en fotledsprotes på andra sidan för att bibehålla en viss rörlighet i åtminstone den ena fotleden. I vissa fall är detta dock inte möjligt och man behöver då trots allt göra en steloperation av båda fotlederna men detta är ovanligt och man vet inte hur bra dessa patienter blir.


För att se hur bra patienter som genomgått fotledsprotes blir använde vi 241 patienter som genomgått operation med fotledsprotes och som hade fyllt i frågeformulär både före och efter operationen. Vi fann att både den generella hälsan och fotledsfunktionen förbättrades avsevärt efter operationen och att 71% av patienterna var nöjda eller mycket nöjda med operationsresultatet. När vi analyserade resultaten närmare fann vi också att lägre ålder vid operation var associerad med sämre utfall efter operationen, däremot verkade varken bakomliggande orsak till operationen eller vilken protesmodell man fått ha något samband med hur bra de blev.

Vi analyserade även 183 patienter som först fått en fotledsprotes som sedan hade havererat, 69 av dessa fick en ny protes och 114 blev stelopererade. I båda grupperna visade sig resultaten otilfredsställande i den mån att självupplevd funktion och det allmänna hälsotillståndet angavs som låga, och enbart ungefär hälften av patienterna i vardera grupp var nöjda med operationsresultatet. Vi fann också att 24 (35%) av de 69 utbytesproteserna havererade på nytt och krävde ytterligare operationer. I gruppen som istället fick en steloperation efter havererad protes var andelen med behov av ny operation bara 10%.

Vår analys av 51 patienter som genomgått steloperation i båda fotlederna visade att mer än 90% av patienterna var nöjda eller mycket nöjda med resultatet efter ingreppen, och att både den självuppskattade funktionen och hälsotillståndet angavs som goda.

Patienter med framskriden och smärtsam fotledsartros som genomgår operation med fotledsprotes hade god och förbättrad självupplevd funktion och hälsa, och de flesta patienterna var nöjda eller mycket nöjda med operationsresultatet. För protesoperation var dock lägre ålder vid ingreppet associerad med sämre självupplevd funktion och nöjdhet. När en fotledsprotes havererar så leder båda
möjliga operationsmetoder (utbytesprotes eller steloperation) till dålig funktion och låg andel nöjda patienter. Patienter som genomgår steloperation i båda fotlederna blir nöjda och anger god funktion.

Acknowledgements

“Never again.” That’s what I promised myself when I was finally done with my German doctoral thesis. I also never intended to work at a University Hospital. Both worked out quite well, as you see…

When it became clear that my German thesis would not be automatically accepted as a PhD thesis, I had a discussion with Leif Dahlberg about whether I should try to get it accepted anyway, or if I should rather leave it and start the PhD program instead. After thinking for a short time I gave in, and I never regretted it. So thank you, Leif, for encouraging me to re-consider my former promises and jump on the real research train!

These almost four years of research were definitely exciting, with many ups and downs. I developed an honest interest for research, what I thought never could be possible. Even though I was the main actor in this, many people were involved in the whole process to make all things work, and I am very thankful to every single one.

There are, however, a few persons to whom I would like to express my special gratitude.

I assume and hope that the following counts for every PhD student, but I certainly had by far the best supervisors! Somehow they managed from the beginning to keep me under a continuous light pressure to deliver; otherwise I might have lost my motivation again. Thank you, Björn Rosengren, for having been my main supervisor! I am really impressed how you could always give feedback in a way that I never felt stupid or “small” but in a way that left very often a good feeling and motivated me to continue and become even better. Well, sometimes the time aspect was a bit frustrating. The minimal possible time from my question to your answer seems to count for you under almost all circumstances. Feeling first a bit stressed about that, I soon managed successfully to eliminate the bad conscience about the fact that some people actually are able to use all 24 hours of a day.

This elimination thing was even easier with Magnus Karlsson, my co-supervisor, because your speed of sending back corrections is just out of every earthly dimension. Anyway, speed was definitely never negatively correlated with the quality of the comments and suggestions. Thank you, Magnus, for always having
found (many…) more aspects in all papers and presentations to improve, and for always having ready a motivating comment.

A bit more earthly and always calm and definitely non-stressing would describe my other co-supervisor Åke Carlsson. Thank you Åke, that you often came with a slightly different point of view a micro-unit slower from question to response compared to the other two, which gave me some breathing space from time to time. As the heart of SwedAnkle you could always help me to get control over all data, and especially in the beginning, when everything was a confusing hurly-burly, this felt very comforting.

Håkan Magnusson, co-author in all the papers, has been my clinical mentor in many ways, and your expertise in ankle prosthesis surgery influenced definitely my own criticism of the procedure.

Anders Henricson, co-author in all the papers and as deeply familiar with SwedAnkle as Åke, thank you for all the input with all the manuscripts and for your help with registry dilemmas.

Jan-Åke Nilsson, co-author and statistical support, thank you for making statistics understandable and for never giving up on me when I came back with the same problems again and again.

Without all my team colleagues, who took care of my patients while I was busy doing research, all this would not have worked out.

All colleagues acting opponent at the “predisputation”, thank you for your valuable questions and comments.

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