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MAJOR LOWER EXTREMITY AMPUTATIONS – OUTCOMES, COMPLICATIONS, AND PATIENT PERSPECTIVES

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Major Lower Extremity Amputations
– Outcomes, Complications, and Patient Perspectives

Thesis for Doctoral Degree (Ph.D.)

By

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To Edith, Bror, Selma, and Mikael

Popular Science Summary of the Thesis

Amputation, considered one of the oldest surgical procedures, still carries significant risks despite advances in medical care. This thesis explores the outcomes, complications and patient perspectives of lower leg amputations.

In the first study, we focused on examining the mortality rates one week following thigh amputation, specifically investigating the increased risk of death for diabetic patients after the surgery, given the inconclusive nature of current literature. Our study involved 162 individuals who underwent thigh amputation between 1996 and 2012. We found that individuals with diabetes had a higher risk of death, both one week and one year after the surgery. The mortality was high; one week after the surgery, 30% of diabetic patients had died compared to 8% of non-diabetic patients. After one year, 80% of diabetic patients had died compared to 57% of non-diabetic patients.

In the second study, we compared outcomes of two different reamputation approaches after failed lower leg amputation: thigh amputation and knee joint amputation. Reamputation requires surgeons to perform a second, higher level of amputation, when the initial lower amputation has not healed or has become infected. We included 152 patients between the years 2000 and 2020, and found that individuals who underwent thigh amputation had a lower risk of requiring additional amputations in the same leg compared to those who underwent knee joint amputation. Only 15% of thigh amputation patients required further amputations, whereas as much as 36% of knee joint amputation patients did. However, the proportion of patients receiving prosthesis after reamputation was similar between thigh and knee joint amputation groups.

The third study focused on the time it took for patients to receive a prosthesis after an amputation below the knee, comparing amputees before and after the introduction of a new guideline. The new guideline implements a specific surgical technique, replaces casts with vacuum dressing after surgery, manages swelling using a silicone sock, and a follow-up with an interdisciplinary team three weeks after the surgery. An orthopedic surgeon, a prosthetists and orthotists, a nurse, and a physiotherapist, form the team, aiming to assess the amputation stump's healing and the patient's potential for future prosthetic use. On average, after the implementation of the new guideline, patients received prosthesis 27 days

earlier compared to before introduction of the new guideline. Additionally, we found that women were less likely to receive prosthetics than men (34% compared to 58%), even after adjusting for factors such as age, prior mobility, and cognitive impairment.

In our fourth study, we conducted interviews with 15 participants who had undergone below-the-knee amputation to capture their health care experiences and involvement in treatment decisions. The concept of shared decision-making, where patients and healthcare providers work together on care decisions stood out as vital. We found that participants had a desire to be more involved in the decision-making process and highlighted the need for direct communication with engaged healthcare professionals. The participants also highlighted issues with continuity of care, particularly with the orthopedic surgeons.

To summarize, our research sheds light on the significant challenges confronting amputees. Despite high risks after amputation, our findings suggest improvements in healthcare practices particulary through new guidelines that could expedite the provision of prosthesis. Furthermore, the observed gender disparities in prosthetic fitting require additional research to ensure health care equality.

To enhance healthcare, it is crucial to bolster shared decision-making by ensuring patients play a central role in their care, aligning with their values and preferences. Establishing an interdisciplinary pre-amputation clinic, where the team consults with the patient before deciding on amputation, would promote greater patient involvement. Furthermore, assigning a dedicated contact nurse, akin to the model seen in cancer care, would significantly enhance the continuity of care. Shared decision-making is particularly important in amputations, this due to the high risks of complications. When patients actively engage in their care, are well informed and able to influence decisions on their care, the quality of healthcare outcomes is significantly enhanced.

Populärvetenskaplig Sammanfattning

Att amputera en kroppsdel anses vara ett av de äldsta kirurgiska ingreppen. Även om det gjorts framsteg inom medicinsk vård, är amputation fortfarande förknippad med stor risk för komplikationer och dödlighet efter operationen. Denna avhandling undersöker utfall, komplikationer och patienters upplevelser efter amputation av lår, knä eller underben.

I den första studien undersökte vi dödligheten en vecka efter att patienter hade genomgått en lårbensamputation. Vi fokuserade särskilt på om personer med diabetes löpte större risk att dö efter operationen, detta eftersom befintliga vetenskapliga slutsatser är motstridiga. Vi studerade 162 personer som genomgått lårbensamputation mellan åren 1996 och 2012. Det visade sig att personer med diabetes hade en högre risk att dö, både en vecka och ett år efter operationen. Dödstalen var höga; efter en vecka hade 30% av patienterna med diabetes avlidit, jämfört med 8% av de utan diabetes. Efter ett år hade 80 % av patienterna med diabetes avlidit, jämfört med 57% av de utan diabetes.

I den andra studien jämförde vi resultatet av två olika sätt att göra en reamputation. En reamputation innebär att man gör en andra amputation högre upp på benet efter att en tidigare amputation längre ner på benet inte har läkt eller blivit infekterad. Vi undersökte andelen som efter en misslyckad underbensamputation behövt genomgå ytterligare operationer efter att ha gjort en reamputation på lårbens- eller knäledsnivå. Vi inkluderade 152 patienter mellan åren 2000 och 2020. Resultaten visade att personer som genomgått en lårbensamputation hade lägre risk att behöva ytterligare amputationer i samma ben. Av de som genomgått en lårbensamputation behövde 15% göra en ny amputation, medan detta gjordes mer än dubbelt så ofta (36%) bland de som genomgått en knäledsamputation. Det var knappt en fjärdedel av alla patienter som fick en protes efter sin reamputation, men det fanns ingen skillnad mellan de som genomgått en lårbensamputation och de som genomgått en knäledsamputation.

Den tredje studien fokuserade på hur lång tid det tog för patienter att få en protes efter att ha genomgått en underbensamputation. Vi jämförde perioderna före och efter införandet av en ny riktlinje för underbensamputerade. Riktlinjen innehöll bland annat en beskrivning av en specifik operationsteknik, användningen av ett vakuumförband istället för gips efter operationen, samt

behandling av svullnad med en silikonstrumpa och ett återbesök hos ett interdisciplinärt team tre veckor efter operationen. Teamet bestod av en ortoped, en ortopedingenjör, en sjuksköterska och en fysioterapeut. Återbesökets syfte var att bedöma sårläkningen och möjligheterna för en framtida protes. Det tog i genomsnitt 27 dagar kortare tid för patienterna att få en protes efter att den nya riktlinjen hade införts. Vi upptäckte också att kvinnor fick protes i lägre utsträckning än män (34% jämfört med 58%), trots att vi i analysen tog hänsyn till faktorer som ålder, tidigare gångförmåga och kognitiv svikt, som kunde påverka andelen som får protes.

I den fjärde studien intervjuade vi 15 personer som genomgått en underbensamputation. Syftet med studien var att undersöka deras upplevelser av vården, och hur involverade de upplevde sig vara i beslutsfattandet kring sin behandling. Delat beslutsfattande, en process där patienten och vårdpersonalen samarbetar för att fatta beslut om vård och behandling, framkom som en viktig aspekt. Deltagarna önskade vara mer delaktiga i beslutsprocessen, och betonade vikten av god och helst muntlig kommunikation mellan patient och engagerad vårdpersonal. De tyckte även att kontinuiteten i vården, särskilt med ortopedläkarna var bristfällig.

Sammanfattningsvis visar vår forskning på att det finns utmaningar och problem för patienter som har genomgått en amputation. Riskerna efter operationen är fortsatt höga, vilket understryker behovet av att noggrant överväga risker och nytta med ingreppet för varje enskild patient. Våra resultat tyder på att vården kan förbättras och att införandet av nya riktlinjer kan förkorta tiden till protes för underbensamputerade. Könsskillnader i protesförsörjning, där kvinnor i lägre utsträckning än män får protes, behöver ytterligare utredas vidare i fler vetenskapliga studier.

För att förbättra vården behöver vi bli bättre på ett delat beslutsfattande där patienten får större möjlighet att vara aktivt involverad i sin vård, och får sina värderingar och personliga preferenser tillgodosedda. Ett sätt att öka patientens delaktighet i vården är att införa en interdisciplinär mottagning före amputationen där hela teamet träffar patienten. Ett annat är att införa en kontaktsjuksköterska, som man ofta har inom cancervården, för att öka kontinuiteten i kontakten med vården för patienterna. Delat beslutsfattande är särskilt viktigt vid amputationer, där komplikationerna är vanliga. När patienter

kan delta aktivt i sin vård, är välinformerade och har möjlighet att påverka besluten, blir utfallet och patientupplevelsen av vården bättre.

Abstract

An amputation is considered to be one of the oldest surgical procedures; yet, despite advancements in medical care, it continues to be associated with high rates of complications and postoperative mortality. This thesis aims to shed light on the complications, outcomes, and patient perspectives surrounding major lower extremity amputations (LEA).

Study I investigated mortality rates following the first-ever transfemoral amputation (TFA) at 1 week and 1 year, focusing on the potential influence of diabetes. A total of 162 individuals who underwent their first-ever TFA between 1996 and 2012 were included. Diabetes was present in 30 patients (19%). Mortality rates were notably higher for patients with diabetes compared to those without at both 1 week (30% versus 8%, p = 0.001) and 1 year (80% versus 57%, p = 0.02). This difference remained significant after conducting a multivariable analysis.

Study II examined and compared outcomes after two different reamputation levels following a failed transtibial amputation (TTA) – TFA and knee disarticulation (KD). The primary outcomes were further reoperation and reamputation. A total of 152 patients were included, with 66 cases of KD and 86 cases of TFA. Following KD, the reamputation rate was 36% compared to 15% after TFA (p = 0.004). In the multivariable analysis, TFA was associated with a decreased risk of reamputation, with an odds ratio of 0.31 (95% CI 0.14 – 0.69). The reoperation rate was 22% after TFA, compared to 38% after KD (p = 0.03). Prosthetic fitting was achieved in 30% of KD cases and 19% of TFA cases (p = 0.1), however, this was not statistically significant. Mortality did not significantly differ between the two reamputation levels.

Study III analyzed the impact on days to prosthesis after the implementation of a new guideline for transtibial amputations. We included 263 TTA patients after the new guideline was implemented and compared them against 169 patients undergoing TTA before the new guideline. Following the implementation of the new guideline, there was a significant reduction of time to prosthesis compared to before (76 versus 103 days, p < 0.001). The rates of prosthetic fitting were similar in the two cohorts, but female gender was significantly associated with lower prosthetic fitting rates also after adjusting for potential confounders. Mortality rates did not differ between the two cohorts.

Using a qualitative method, Study IV explored patients' experiences of their care trajectory, the given information, and involvement in care following the implementation of a new guideline. In total, 15 participants were selected and interviewed, all with experience of a TTA within the care under the new guideline. The interviews were analyzed using content analysis, and three themes emerged: (1) The mixed experience of becoming an amputee; (2) The need to be seen during the amputation process; and (3) The importance of being involved in the care. The main discovery is the participants' desire for increased involvement in the decision-making process, with our interdisciplinary team follow-up serving as an exceptional demonstration of shared decision-making. While participants appreciated the printed information, oral communication was deemed most significant presenting the gravity of the subject. Participants also noted a lack of continuity throughout their care trajectory.

In conclusion, the prevalence of postoperative complications following major LEA underscores the need for improved optimization and careful consideration of surgical approaches and treatment for each patient. Nevertheless, there are ways to enhance care for transtibial amputees, as demonstrated by the implementation of a new guideline, which has the potential to reduce the transition time from surgery to prosthetic fitting in a clinical setting. Gender disparities in prosthetic fitting persist as a significant concern, warranting further investigations. Another important enhancement in clinical practice would involve bolstering shared decision-making processes, facilitating greater involvement and information exchange with patients and their families. In this regard, introducing an interdisciplinary pre-amputation meeting and assigning a contact nurse for improved continuity could represent meaningful improvements. Shared decision-making holds particular significance in surgical interventions like amputations, given the elevated risk of complications.

List of Scientific Papers

I. INCREASED MORTALITY AMONG PATIENTS WITH DIABETES FOLLOWING FIRST-EVER TRANSFEMORAL AMPUTATION
Sjödin L, Enocson A, Rotzius P, Lapidus LJ
Diabetes Res Clin Pract. 2018 Sep;143:225-231

II. KNEE DISARTICULATION VS. TRANSFEMORAL AMPUTATION AFTER FAILED TRANSTIBIAL AMPUTATION: SURGICAL OUTCOME AND PROSTHETIC FITTING IN PATIENTS WITH PERIPHERAL VASCULAR DISEASE
Sjödin L, Ottoson C, Lapidus LJ
Prosthtet Orthot Int. 2024 Jan 1;48(1):25-29

III. SHORTER TIME TO PROSTHESIS AFTER IMPLEMENTATION OF A NEW GUIDELINE FOR TRANSTIBIAL AMPUTEES
Sjödin L, Enocson A, Lapidus LJ
Submitted

IV. TRANSTIBIAL AMPUTEES' PERSPECTIVES ON INFORMATION AND SHARED DECISION-MAKING
Sjödin L, Lapidus LJ, Torbjörnsson E
Submitted

Contents

List of Abbreviations

ASA	American Society of Anesthesiologists Physical Status Classification System
CI	Confidence Interval
CLI	Critical Limb Ischemia
CLTI	Chronic Limb-Threatening Ischemia
ERAS	The Enhanced Recovery After Surgery
HCPs	Healthcare Professionals
ISO	The International Organization for Standardization
KD	Knee Disarticulation
LEA	Lower Extremity Amputation
OR	Odds Ratio
PAD	Peripheral Artery Disease
PIN	Personal Identity Number
PROMs	Patient Reported Outcome Measures
PVD	Peripheral Vascular Disease
RRD	Removable Rigid Dressing
SwedeAmp	Swedish Amputation and Prosthetic Registry for the Lower Extremity
TFA	Transfemoral Amputation
TTA	Transtibial Amputation
WIfi	the Wound, Ischemia, and foot Infection score

1 Introduction

An amputation, defined as the surgical removal of a limb or part of a limb, is believed to be one of the oldest surgical procedures, first described in the sixth century BC.[1] Nevertheless, many of the surgical principles recommended by Hippocrates are still valid today.[2] Early milestones in the history of amputations included the use of ligation of vessels, the tourniquet, and the invention of prostheses.[1, 3] Unfortunately, the lack of anesthesia and aseptic technique led to great suffering and numerous complications. Thus, the procedure gained more acceptance when anesthesia and aseptic techniques were introduced.[4]

Figure 1. A painting from the year 1510 showing two saints attempting to heal a patient suffering from a diseased leg. Credit: Württemberg State Museum, Stuttgart/Germany, Hendrik Zwietasch

Even though the indications for amputation and surgical techniques have evolved over time, the rationale for amputation remains to save life, regain function, and alleviate pain by the removal of a limb. Despite advances in the medical field, amputation is still a high-risk procedure associated with mortality as well as morbidity. Today, more due to advanced age and the multiple comorbidities among many patients undergoing the procedure.[5, 6]

2 Thesis Overview

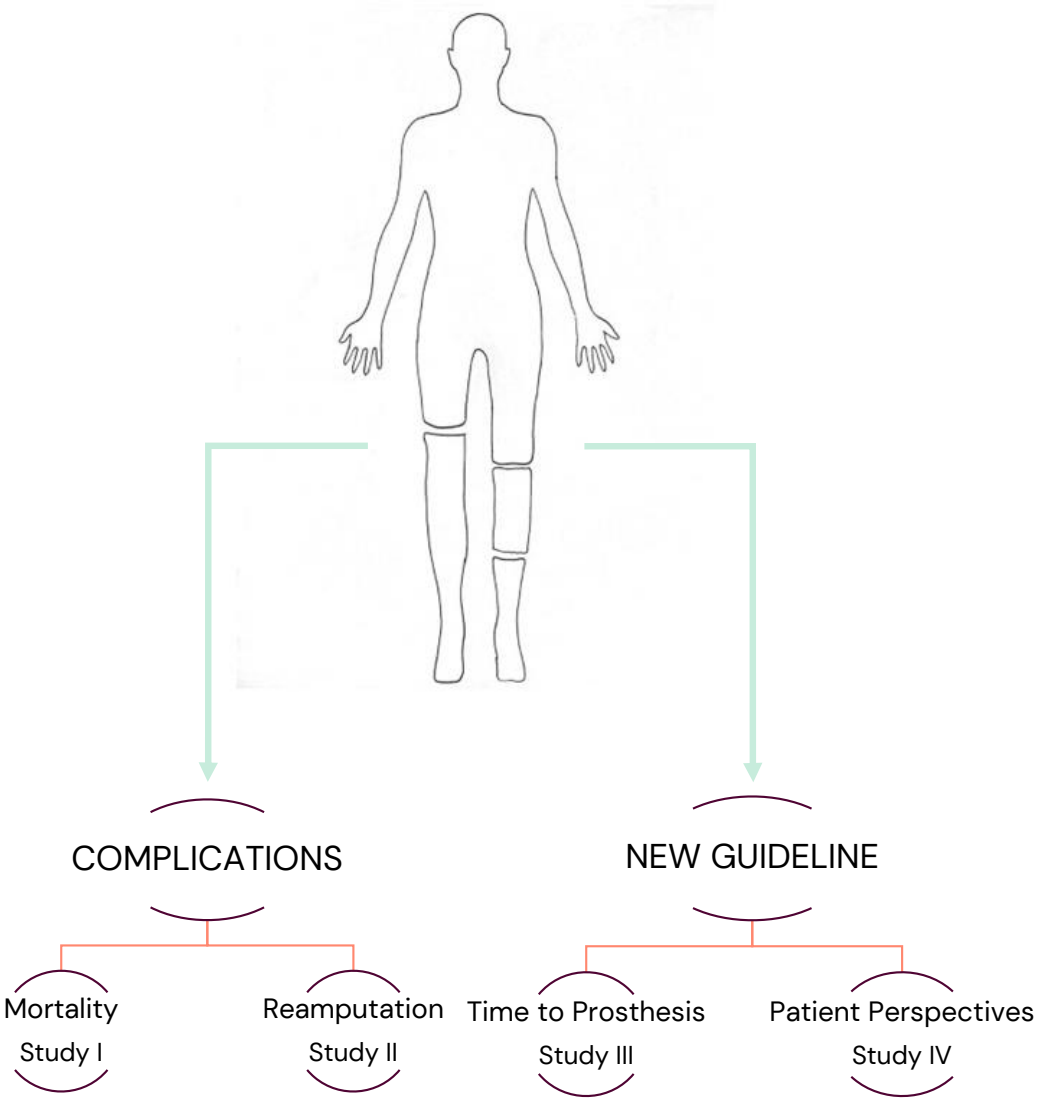

Figure 2. Thesis overview, Studies I-IV.

3 Literature Review

3.1 Definitions

Major lower extremity amputation (LEA) is defined as an amputation at or proximal to the ankle joint[7] and is then divided into different amputation levels (Figure 3). A minor amputation is defined as an amputation distal to the ankle joint, including toe amputation and partial foot amputations.

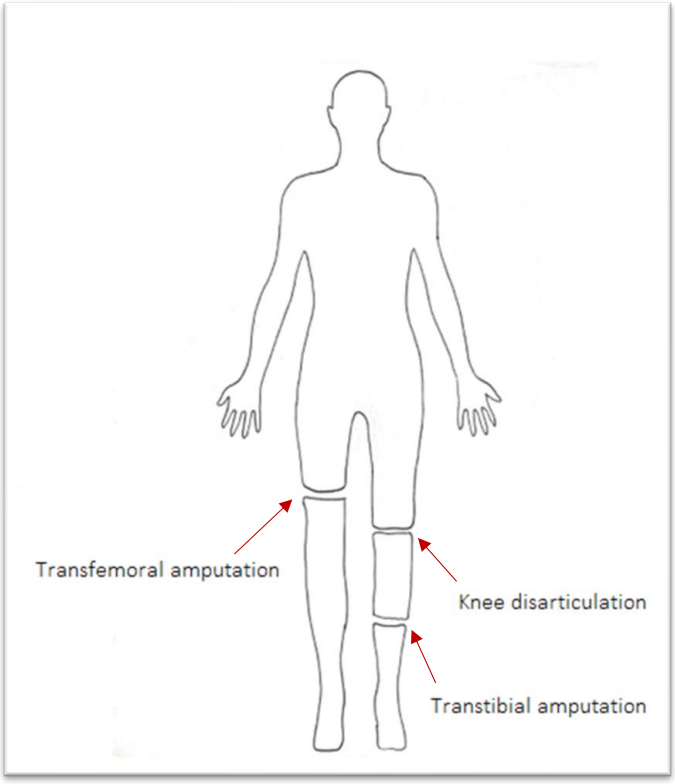

Figure 3. Classification of the major lower extremity amputation levels in this thesis, according to the International Organization for Standardization (ISO) 8549-4:2020.

Transtibial amputation (TTA) stands as the most common level of major LEA[8, 9] and is believed to be the highest level of amputation that can restore a relatively normal function. When compared to transfemoral amputation (TFA), the second most common level, there is a higher probability of prosthetic fitting but also of reamputation.[8, 10]

Knee disarticulation (KD) involves the removal of the lower leg through the knee joint. There are some differences across health care settings, but overall, it is a rarely used amputation level.[11, 12] However, KD could be an amputation level of choice for both ambulatory and non-ambulatory patients. Since thigh muscles are preserved, it offers functional advantages over TFA as an end-bearing stump, with greater seated balance and better usage of a prosthesis.[13, 14] Prosthetic fitting is possible, even though the rates are lower than for TTA.[15, 16] KD seems to have comparable surgical outcomes and complications to TTA even in the presence of peripheral artery disease (PAD).[17]

Transfemoral amputation is associated with lower reamputation rates than more distal levels.[18, 19] However, transfemoral amputees use their prosthesis less and have an impaired function compared to more distal amputation levels.[13, 20]

Hip disarticulation and ankle disarticulation (Syme's amputation) are levels rarely used.

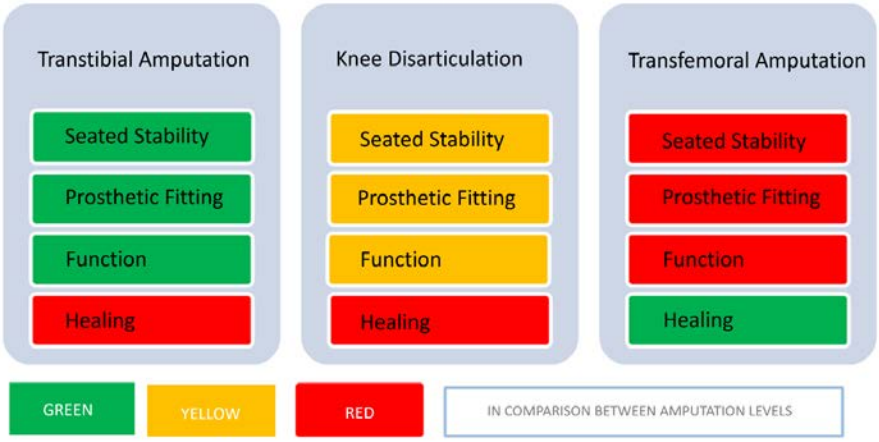

Figure 4. Comparison of amputation levels with their respective advantages and disadvantages. Green indicates a positive correlation; red indicates a negative correlation and yellow represents a neutral or mixed correlation.
Source: Stockholm regional guideline for lower extremity amputation, 2019.

Decision-making requires consideration of both the optimal level of amputation, the medical and surgical aspects, as well as the patients' preferences, and is often complex. (Figure 4).

3.2 Vocabulary

There are several challenges in the research field of amputations. One issue is vocabulary inconsistency. For the same amputation level, several different names exist in the literature, such as above-knee amputation or transfemoral amputation; below-knee amputation or transtibial amputation; and knee disarticulation or transgenicular amputation. In the existing literature, controversy remains regarding the definition of major and minor LEA, particularly when it comes to amputation levels close to the ankle joint.

However, in 2014, the International Organization for Standardization (ISO), proposed a classification system, currently updated in 2020 (Figure 3, page 4).[21]

The heterogeneity of the patient group is another issue. It is not uncommon to include both minor and major LEA, as well as different levels of major LEA, in the same study. Additionally, amputations and reamputations, or patients with traumatic as well as non-traumatic amputations could be grouped together. Another difficulty is that reamputations sometimes includes ipsilateral as well as contralateral amputation or both reamputation with shortening of bone and/or wound revision.[22, 23] Hence, drawing general conclusions can be difficult and makes meta-analysis challenging.

3.3 Background

Peripheral artery disease (PAD) often refers to atherosclerotic arterial disease, commonly affecting the lower extremities. It mainly consists of atherosclerosis, causing obstruction and impaired circulation to the lower extremities.[24] There is a spectrum of PAD, ranging from asymptomatic stages to end-stage advanced chronic limb-threatening ischemia (CLTI). CLTI manifests with ischemic rest pain, gangrene in foot or lower limb, diabetic foot ulcer or lower limb ulceration that has lasted for more than two weeks.[25] An ankle-brachial index is the reference measurement for PAD diagnosis, with surgical and endovascular interventions commonly conducted within the vascular surgeon's department.

Regardless of the type, diabetes is associated with a higher risk of peripheral atherosclerotic disease, often presented with a more distal involvement of the disease.[26]

In 2014 the Society for Vascular Surgeons proposed a classification system for limbs threatened by amputation, the Wound, Ischemia, and foot Infection (WIfI) score,[27] merging classifications for both ischemia and diabetic ulcers. The score has been taken into clinical practice and appears to be an interesting tool for assessing the risk of amputation at 1 year and the need for revascularization.

PAD and/or diabetes are the most common underlying diseases causing the need for amputation in the western world.[8, 28] Among other causes are trauma, infection, and deformities. The management of amputation patients frequently involves multiple health care specialists, including vascular surgeons, endocrinologists, orthopedic surgeons, infectious disease specialists and/or geriatric or rehabilitation specialists.

The incidence of major LEA has continuously dropped over the last decades.[6, 29, 30] In Sweden it has in the last years stabilized around 22 per 100 000.[5, 29, 31] However, there is a large variance in the global incidence for the total population, between 3.6 to 68.4 per 100 000.[30] This probably reflects different economical, geographical, and social factors linked to healthcare provision, as well as opportunities for limb salvage and diabetes treatment, throughout the globe.

3.4 Complications

3.4.1 Mortality

The high postoperative mortality is one of the biggest clinical challenges in the care of amputee patients. The population is elderly, has multiple comorbidities and the majority of the amputations are done due to PAD and/or diabetes, indications associated with a high rate of postoperative mortality.[32, 33] The high mortality rates are seen both in the short and long term.[33-35]

Short-term mortality after major LEA is described in a systematic review of in-hospital mortality and 30-days mortality, to be 5 to 51%.[35, 36] The spread indicates that the populations studied are heterogeneous and differ both in age and inclusion criteria.

One-year mortality is correspondingly high, with several papers describing about a third of the patients deceased.[37-39] Even higher rates (44 to 52%) were seen for predominantly elderly patients.[40-42] Despite the fact that these patients are predominately elderly with multiple comorbidities, patients with critical limb

ischemia (CLI) treated without amputation had a lower 1-year mortality than those going through amputation and one can speculate if the amputation procedure itself render a higher mortality or if it can be explained by selection bias.[40]

Long-term mortality, often described as 5-year mortality, is remarkably high. Some studies indicate that 5-year mortality rates range from 52 to 90%,[33] while others show lower mortality rates of around 18%.[36]

3.4.2 Risk Factors for Mortality

Postoperative mortality increases with older age, transfemoral amputation (TFA), and comorbidities.[32, 33, 37, 43] However, the relationship is complex since TFA can be the natural choice for elderly and non-ambulatory patients, and a higher level of amputation can also be a sign of a more advanced disease leading more often to fatal outcome. Renal failure and chronic heart failure are associated with high mortality in several studies,[37, 44, 45] but also the number of comorbidities seems to contribute to higher mortality rates.[41, 46] The American Society of Anesthesiologists (ASA) physical status classification system is a common measure of comorbidities, and ASA-class ≥ 4 has been linked to increased mortality.[32, 47] Frailty, often defined as a syndrome of ageing-related psychological decline with marked vulnerability for adverse health outcomes, also seems to be associated with higher risks of complications and death.[48, 49]

While many studies suggest that multiple comorbidities appear associated with postoperative mortality the effect of diabetes is less clear cut. Some studies show lower mortality,[50, 51] some higher,[32, 52-57] and some no difference in mortality.[11, 37, 39, 58-60]

Apart from patient factors, there are other factors that also seem to influence mortality. Delaying the surgery increases the risk of death with 2% for each day,[61] and surgery outside office hours seems to affect the mortality.[47] However, a confounding factor could be that patients undergoing out-of-office surgery are in a worse medical condition and therefore need surgery more urgently. There is also a possibility that doctors working out-of-office hours are less experienced and have less backup present at the hospital.

Treating patients in a unit with a multidisciplinary team with expertise in frail patients seems beneficial and could lower mortality.[38] For elderly patients, yet another study showed that discharge to inpatient rehab instead of skilled

nursing home could increase 1-year survival.[62] However, patients with less comorbidities could be more likely to be referred to rehabilitation, therefore selection bias cannot be excluded. Similarly, receiving a prescription for a prosthesis or a referral to prosthetic fitting also seems to be associated with lower mortality, even after adjusted for potential confounders.[54, 63, 64]

3.4.3 Predicting Mortality

Several attempts to predict mortality after an amputation have been made, but the role of prediction models in a clinical context is unclear.[65, 66] Though, it is a clinically appealing strategy to target patients at-risk for the possibility of optimization preoperatively. In a Danish study there was a significantly higher percentage of postoperative pneumonia, acute myocardial infarction, and sepsis among those who died within 30 days, but many of them had active lifesaving care curtailed.[52] The dilemma of offering the right patient surgery with high-quality postoperative care or offering non-surgical palliative care to those with the highest risk of fatal outcome is discussed in several papers. This is one of the greater ethical challenges as a surgeon; to know when to lay down arms and refrain from surgery.

As mentioned earlier, the comparison of mortality between different studies is often difficult since study populations differ markedly.

3.4.4 Reamputation and Reoperation

A known and frequent problem after a major LEA is the risk of reamputation, revision amputation, or wound revision surgery. In general, reamputation is a subsequent amputation to a higher level than the first; a revision amputation is a subsequent amputation at the same level and wound revision surgery is a revision of soft tissue but not bone. However, the definition and inclusion differ between different studies, making comparisons challenging.

The risk of reamputation depends on the level of amputation. Numerous studies have shown that TFA has a lower risk than transtibial amputation (TTA), and knee disarticulation (KD) of further revision or reamputations.[10, 23, 67] This emphasizes the importance of conducting meticulous individual preoperative planning, considering healing capacity, circulation, underlying diseases, and the possibility for future prosthetic fitting before deciding on the level of reamputation. Determining the level of reamputation often relies on clinical assessment. Although various attempts have been made with more objective measurement

options, to find the level where an amputation stump will heal, none have truly gained widespread clinical adaptation. However, consideration of the patient's vascular status and location of occlusions or stenosis, in consultation with a vascular surgeon, is preferable. A revascularization could be an option for maintaining the reamputation level as low as possible for some patients. There is also a significant benefit in involving the patient and employing shared decision-making in this process.

Reamputation rates show a large variety across literature. The rates after TTA are described as 16 to 30%, after KD as 0 to 34%, and after TFA as 2 to 10%.[16, 18, 23, 45, 68] KD is not as common as the other levels but seems to have similar reamputation rates as TTA.

The majority of reamputations for patients with diabetes occur within 6 to 7 months after the index amputation.[69-71] For patients with both PAD and/or diabetes, a Swedish study noted 90% of all reamputations occurred within two months of the index amputation,[11] and in a Danish study 58% within one month.[23] A conclusion to be drawn is that few reamputations occur if the wound heals.

3.4.5 Risk Factors for Reoperation

Risks of reamputation include dyslipidemia, smoking, PAD, ischemic pain, prior vascular surgery, socioeconomical disadvantages, multiple comorbidities, and renal insufficiency.[19, 23, 57, 72] Non-patient factors such as daytime scheduled surgery may reduce the risk of reamputation and revision surgery,[73] but the evidence of the impact of the surgeons' experience is contradictory.[74, 75]

There is limited literature addressing mortality rates after reamputation; however, Curran et al[76] demonstrated a twofold increase in mortality for those who were readmitted within 30 days after a major LEA.

Ambulation after reamputation is not addressed in many studies. Nijmeijer et al[16] found that patients with reamputation to TFA after a KD were significantly less ambulant than those without a reamputation. A problem is that the rate of reamputation is often not the primary outcome, and in some studies reamputation includes both ipsilateral and contralateral amputation which can hinder comparison between studies.[77, 78]

There is a lack of knowledge about the fate of the reamputations - both regarding mortality rates, prosthetic fitting and how to avoid them. Given that reamputation is a prevalent issue and a substantial number of individuals

undergoing reamputation lose their knee joint, and subsequently face increased challenges in ambulating with a prosthesis, this presents an area where enhanced understanding could significantly impact outcomes. Naturally, by aiming to preserve the knee joint, the incidence of reamputation will be higher. There are areas to explore, such as optimizing patient nutrition and circulation, investigating the efficacy of negative pressure wound therapy, and potentially employing more advanced imaging techniques to assess skin perfusion.

3.4.6 Prosthetic Fitting

An amputation poses a significant challenge, not only for the individual undergoing the procedure but also for the relatives, the healthcare system and welfare. With an increasingly aging population, the consequences of an amputation can be more pronounced compared to younger and more physically active patients. In a Swedish study, almost half of the amputees (43%) were 80 year or older at the time of their first amputation.[8]

Both the presence of multiple comorbidities and advanced age could have an impact on prosthetic fitting rates, but there is disagreement on to what extent age affects prosthetic fitting, and age alone should not exclude individuals from being considered for a prosthesis.[79] Thus, the ability to walk with a prosthesis influences the Quality of Life in a positive way.[80, 81]

Prosthetic fitting rates have a large spread in the literature, indicating different inclusion criteria. For TFA, prosthetic fitting rates are described as 20 to 40%,[12, 82, 83] and corresponding data for KD are 13 to 100%, according to two systematic reviews.[68, 84] In the literature, rates for prosthetic fitting after TTA are 45 to 93%.[8, 17, 85–88] A more proximal amputation has a higher metabolic cost, that is the energy expended to move the body a certain distance.[89] So, it is important to keep the amputation level as low as possible for a higher chance of prosthetic fitting.

3.4.7 Risk Factors for Prosthetic Fitting

Ambulation is the key to maintaining independence. The strongest evidence affecting the prosthetic fitting has been seen for age, comorbidities, amputation level and physical fitness.[79] Preoperative mobility, cognition, and the ability to stand on one leg also seem correlated to prosthetic outcomes.[79]

Geriatric amputees often have many comorbidities, and PAD as well as cardiac disease can have a negative impact on prosthetic rehabilitation.[90] A possible explanation for this could be difficulty meeting the increasing energy demands

of prosthetic ambulation. End-stage renal failure can also hinder prosthetic use,[90] possibly due to stump volume changes, concomitant comorbidities and the frequent time needed for dialysis. Cognitive impairment or dementia also has a negative impact on prosthetic fitting.[82, 91] Elderly patients could more often be chosen for a more proximal amputation levels, and with a proximal level of amputation, fewer patients can maintain their preoperative independent status after the amputation. The high mortality among elderly amputees also poses a challenge to prosthesis fitting and rehabilitation. In a Finnish study, the annual mortality rate was 7.4 times higher than an age- and gender matched population.[41] Still, age alone should not exclude from prosthetic fitting.

3.5 Gender Differences

The cause of amputation differs between genders, where women commonly are older and the indication for amputation is vascular disease without diabetes to a higher extent than for men.[8, 92]

Is there a gender difference in prosthetic fitting? In several studies men were more likely to receive a prosthesis than women,[8, 82, 86, 93] and women were less likely to even receive a referral for a prosthesis.[64] Women seem to be less satisfied with their prosthesis[94] and have a longer time to prosthetic fitting.[95] Even though several of these studies have controlled for known confounders, the impact of gender stayed significant. In contrast, there are studies showing no difference in prosthetic fit rates between the genders.[95, 96] Research on women's perspectives in amputation care is limited. However, a qualitative study revealed that female amputees experienced gender bias, during prosthetic fitting.[97] It remains unclear whether this bias is a general trend or just worse preconditions, such as older age at the time of amputation, for female amputees.

3.6 Clinical Guidelines

Amputation care and management present a complex challenge, primarily because it necessitates collaboration across diverse medical professions and specialties. This complexity is further compounded by the presence of frailty and multiple concurrent medical comorbidities in most patients.[5, 6, 49] The continuum of care can also be sectioned between medical providers like a relay,

lacking an overall responsible person and affecting the patients' experience.[98] An illustration of this relay in a local context can be seen in Figure 5.

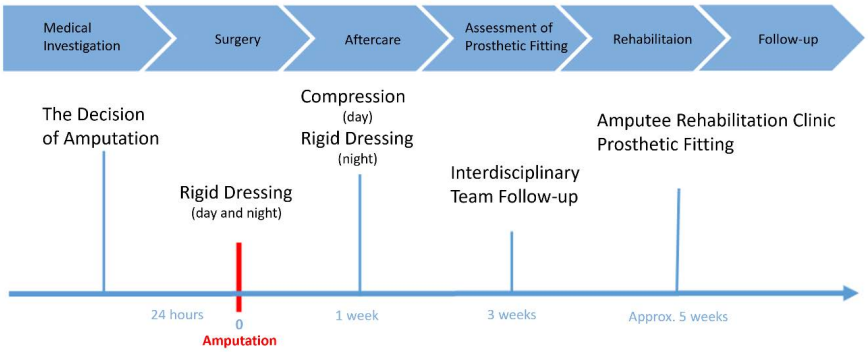

Figure 5. Overview of the amputation care pathway.
Source: Stockholm regional guideline for lower extremity amputation, 2019.

Guidelines of both surgical and medical care of the amputees seem to impact outcomes. A standardized surgical program evaluated at a Swedish hospital resulted in more than half (55%) of the patients being fitted with a prosthesis within a median of 41 days.[85] The surgical program included sagittal flaps, compression treatment with a silicone liner, usage of a rigid dressing, and direct manufacturing prosthetic socket technique. Yet another small study showed a shorter duration of rehabilitation using a silicone liner after TTA.[99] Furthermore, an effect on mortality rates was seen after the implementation of a multidisciplinary treatment and rehabilitation program for amputees in a Danish hospital, where both 30-day and 1-year mortality were markedly reduced.[38]

The planning and time of the surgery also may impact the results. Studies have shown that daytime scheduled surgery could affect both failure and mortality.[47, 61, 73] Hence, scheduled daytime surgery for those who are not in acute need of surgery may be an important part of a guideline for amputees.

The Enhanced recovery after surgery (ERAS) protocol has gained attention in different medical areas, aiming to enhance recovery through an evidence-based perioperative approach.[100] A guideline based on core principles of ERAS showed improvement in long-term ambulation with a prosthesis in a frail population of amputees.[101] In the context of perioperative care for amputations, it is important to note that there is not yet a universally established "gold standard". Instead, healthcare professionals (HCPs) often rely on local preferences and regional

protocols. But, regardless of the aims of mobilization, all patients will need a healed amputation stump.

3.6.1 The Surgical Procedure for Transtibial Amputations

Whether the surgeon is a general surgeon, a vascular surgeon or an orthopedic surgeon differs depending on the country and the local tradition. Regarding the surgical technique for TTA, a Cochrane review compared skew flaps and posterior flap techniques and found no benefit of one technique over the other.[102]

3.6.2 Postoperative Dressing for Transtibial Amputations

The efficacy of rigid dressings compared to soft dressings for TTA has been supported in literature, particularly concerning time to prosthetic fitting and stump maturation, that is when the stump relatively has stabilized in shape and volume.[103-108] However, in a Cochrane review, the conclusion was that due to low certainty evidence it is unclear if rigid dressings are superior to soft dressings.[109] Although a removable rigid dressing (RRD) has not proven to be superior compared to conventional casting,[110, 111] they provide clinical benefits like the possibility of wound inspection and early compression liner treatment.

3.6.3 Rehabilitation

There is a substantial proportion of amputees in need of in-patient rehab or skilled nursing facilities postoperatively. Inpatient rehabilitation after amputation is associated with better outcomes regarding mortality, function, reamputation risk and prescription of prosthesis.[62, 112]

However, the main factor influencing quality of life after an amputation is the ability to walk with a prosthesis,[80] and a shorter time to prosthesis is associated with higher satisfaction and more frequent usage.[113]

3.6.4 Interdisciplinary Teams

Bringing several health professions together around a patient, evaluating and assessing together to obtain a broader view of the patient, is important in rehabilitating patients and is an essential part of evidence based high quality care.[110] There is a wide range of terms used for describing the collaborative work between professionals; and terms are often used interchangeably. Briefly put, in a multidisciplinary team the professions work in parallel, and the communication is led by the physician, but less communication is done between the other

professions. Team members can draw knowledge from each other but stay within the boundaries of their discipline.[114] Hence, team members can have differing priorities for the patient. However, in an interdisciplinary team, more jointly goals are set for the patient and the team collaborates, analyses, and synthesizes a coherent whole, which is beneficial for complex health problems. In literature, interdisciplinary teams are superior to multidisciplinary teams.[115, 116]

For patients with diabetic foot ulcer, an interdisciplinary approach has been proven effective in reducing amputation rates.[117-119] However, there seems to be a growing interest in extending this approach to the continuum of care for individuals undergoing major LEA.[120, 121] Besides medical advantages in gathering competence, an interdisciplinary team approach could also offer value for both patients and caregivers.[122]

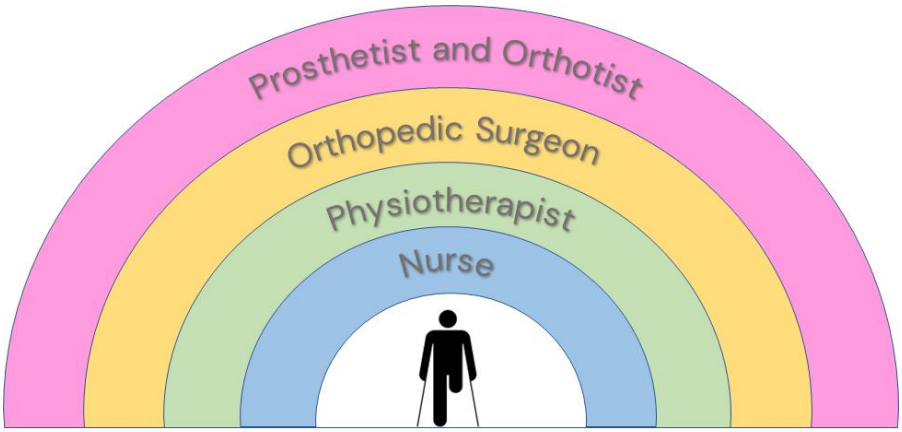

Figure 6. An illustration of the interdisciplinary team around the patient during follow up, three to four weeks after the amputation at Södersjukhuset.

3.7 The Patient

An amputation is a life changing event, and it is important not to lose sight of the patient in the process.

3.7.1 The Patients' Experience

Several studies indicate that the patient experiences a lack of information about the amputation procedure and what to expect from a life with just one leg.[123, 124] A

study on patients with PAD going through amputation also found a severe lack of knowledge about the process, both before and after the amputation, and what to expect in the future.[125] The uncertainty seems to be less prominent if there is a possibility of meeting an already established amputee peer.[126] A peer amputee can also be a way of overcoming the distress patients feel about their new life ahead.[127]

3.7.2 Shared Decision-Making

Shared decision-making (SDM) is defined as a collaborative process between the healthcare professional and the patient. There is a two-way exchange of information, and both parties contribute to the treatment decision that both can agree to implement. This involves exchanging information about treatment options, discussing the potential benefits and risks, and considering the patient's preferences and values. The aim is to reach a mutually agreed-upon treatment plan that aligns with the patient's goals and values.[128, 129] The decision is not solely the patient's or the doctor's; instead, it is taken in the context of the doctor-patient relationship; the choice is made together.[130] Active participation by taking into account the values and preferences of the patient and the treatment planned in consultation with the patient, is also stipulated in the Swedish law.[131] One way to enhance shared decision-making is by using decision aids to communicate risks and benefits.[132, 133] In amputations, for example the AMPREDICT tool compares different outcomes of levels of amputation for patients with diabetes and/or PAD.[134-136]

Why is SDM even important? Shared decision-making can increase patients' satisfaction and be a valuable way of reaching treatment agreements in long-term decisions.[137] There is more work to be done in involving patients in the decision-making process, and maybe a good way to go is to listen to patients' advice to give clear, concise information around the need for amputation and to communicate concern during the discussion.[138]

3.8 Research Gaps

As previously noted, numerous studies include various levels of amputations, including both first-ever as well as reamputations. However, only a limited number of studies specifically concentrate on TFA as a first-ever amputation. Furthermore, there remains uncertainty regarding the impact of diabetes on

mortality outcomes. Another gap is the knowledge of the mortality rate in-hospital, a parameter of clinical significance to surgeons, as the patients are still within the acute hospital setting and amenable to interventions for critical conditions.

Few studies evaluate the mobility or fitting of a prosthesis after a reamputation. Given the prevalence of reamputation procedures, it is of great interest to increase the knowledge of the patient's postoperative ability to ambulate with a prosthesis. This information is important for the patients as well when facing an amputation and presented with various levels of reamputations to consider.

KD is a less common procedure and hence not as well studied as other levels of amputations, especially among elderly patients. There are some advantages to KD that are appealing to the geriatric population and therefore more research could be done in this area.

Guidelines for amputation care and the possible benefit from better care are another area to explore. Except for the influence on the proportion of prosthetic fitted patients and time to prosthesis, the patient's experience of the process and the shared decision-making are important.

4 Research Aims

The overall objective of my thesis was to study various aspects of major lower extremity amputation (LEA); complications such as mortality and reamputation (Studies I-II) and the effect of a new guideline for transtibial amputation (TTA) using both quantitative and qualitative methods (Studies III-IV).

4.1 Study I

The primary aim was to investigate all-cause 1-week and 1-year mortality following a first-ever transfemoral amputation (TFA), with a specific focus on diabetes mellitus, and to contrast these rates with an age-matched Swedish cohort. Additionally, the secondary aim was to investigate the rate of reoperations after the TFA.

4.2 Study II

The primary aim was to assess reamputations levels, TFA compared to knee disarticulation (KD), after a failed TTA, with subsequent reoperations (wound revisions and reamputations) as the primary outcome. Examining rates of mortality and prosthetic fitting were considered secondary aims.

4.3 Study III

The primary aim was to analyze days to prosthesis after a new guideline for TTA was implemented and compare it with a historic cohort. The secondary aim was to examine the rate of prosthetic fitting, difference in prosthetic fitting between genders, and mortality rates.

4.4 Study IV

The primary objective was to investigate the patient's experience of the care trajectory and the given information after the implementation of the new guideline, with the secondary objective being to examine their perception regarding involvement in their care.

5 Materials and Methods

5.1 Ethical Considerations

All studies were carried out in accordance with the Declaration of Helsinki.[139] All four studies were approved by either the Regional Ethics Committee or the Swedish Ethical Review Authority with the following reference numbers: No. 2015-65331, No. 2017-212932, No. 2021-05269 and No. 2023-02580-02.

Studies I, II and III were retrospective observational studies, and the necessity for informed consent was waived. Despite this, it is essential to note that the data incorporated in these studies consists of sensitive personal information and therefore are pseudonymized and presented at the group level to minimize or avoid the risk of identifying individual information.

Before obtaining data from The Swedish Amputation and Prosthetic Registry for the Lower Extremity (SwedeAmp), a separate application for data extraction for research purposes had to be approved.

Participants involved in Study IV were given both oral and printed information, and they signed an informed consent form before participating. Participants were included three to four weeks after surgery and there was a risk they could be affected by anxiety. Due to the potential vulnerability of the participants, details about the study were repeated before the interview to ensure they remained well-informed. Participants were explicitly informed that they retained the right to withdraw their consent to participate in the study at any given time. Each participant was given a code, and the list containing these identification codes was securely stored, distinct from the data files, and transcribed interviews.

5.2 Settings

In this thesis all studies were conducted with adult patients (≥ 18 years) treated at Södersjukhuset, Stockholm, Sweden.

Södersjukhuset is a large acute hospital, with 126 143 unique visits to the hospital's Emergency Departments in 2022.[140] One of the two vascular surgery departments of the regions is situated at the hospital, and in 2015, the Wound Centre opened a regional outpatient clinic for difficult-to-treat wounds. At the

hospital, all amputations are carried out by orthopedic surgeons, however patients depending on ambulatory status and medical conditions, are cared for in different wards, not only in orthopedic ones.

In Studies I-III, the determination of the amputation level and the preoperative classification of the reason for amputation were made by the surgeon.

In Sweden, the healthcare system is publicly funded and accessible to all residents based on their healthcare needs. The Swedish unique personal identity number (PIN) offers a key to link information from different registers to combine data. The PIN plays an important role as an identifier within health care systems and other sectors, as well as linking to different registers for medical research.[141]

5.2.1 Overview of Study Design

The study designs and methods differ between the studies depending on the aims and research questions (Table 1).

Table 1. Overview of study design and methods for Studies I-IV.

	Study I	Study II	Study III	Study IV
Design	Retrospective cohort study	Retrospective cohort study	Retrospective cohort study	Qualitative interview study
Data Sources	Chart review	Chart review	Chart review Swedeamp registry	Semi-structured face-to-face interview
Population	162 first-ever transfemoral amputees	152 reamputations from failed transtibial amputation	432 transtibial amputees	15 participants
Main Analysis Method	Logistic regression analysis	Logistic regression analysis	Mann-Whitney U-test Logistic regression analysis	Content analysis
Ethic Permit	No. 2015-65331 No. 2017-212932 No. 2023-02580-02	No. 2015-65331 No. 2017-212932	No. 2021-05269	No. 2021-05269

5.3 SwedeAmp

The Swedish Amputation and Prosthetic Registry for the Lower Extremity (SwedeAmp) is a national multidisciplinary register for amputations in the lower extremity and the following care trajectory since 2011. Cause and level of amputation, prosthetic fitting, rehabilitation, and patient reported outcome measures (PROMs) are registered.

For surgical data of amputations above the ankle, 15 of 21 regions and 25 of 35 Prosthetic and Orthotic units are connected to the register.

The completeness for transtibial amputation (TTA) in the register for connected regions is 73%. When looking at the completeness of the whole trajectory of care for those who survive 12 months after TTA it shows a completeness of 88%.

For the Stockholm area, completeness for TTA was 35% during 2013-2015 and 42% for 2017-2020 (E-mail S Sanfridsson, SwedeAmp, 2024-03-27).

5.4 Study I

5.4.1 Study Design

Single-center retrospective cohort study

5.4.2 Study Population and Primary Outcome

The goal was to identify patients with a first-ever transfemoral amputation (TFA) between March 1996 and December 2012. A first-ever TFA was defined as the patients' first major lower extremity amputation (LEA), not limited to the index limb. Through a prospective clinical audit and the operation theatre information management system, patients were identified. We found 184 patients in the records and 162 were included in the study. Exclusion criteria were simultaneous bilateral TFA (n = 4), contralateral TFA within the first year after the index procedure (n = 5) and previous contralateral major LEA (n = 13).

The primary outcomes were 1-week and 1-year mortality.

5.4.3 Method and Statistical Analysis

Medical charts were reviewed to collect variables, demographic data as well as information on previous and subsequent major LEA, reoperations and reamputations in the ipsilateral and contralateral limb. With the Swedish unique personal number, mortality data were collected. From the database Statistics Sweden a corresponding 1-year mortality rate was calculated for a Swedish population 1996 to 2012 matching the median age in our study.

Nominal variables underwent testing using Fisher's exact test or Chi-square test and all tests were two-sided. Logistic regression analyses were conducted to evaluate factors associated with postoperative mortality. Independent variables in the model included age, gender, indication for surgery, cardiovascular disease, and diabetes. Initially, in a univariable model crude associations for each variable were examined. Subsequently, a multivariable model for adjusted associations was used. Associations were presented as odds ratios (ORs) with 95% confidence intervals (CIs). Results were deemed significant at $p < 0.05$.

5.5 Study II

5.5.1 Study Design

Single-center retrospective cohort study

5.5.2 Study Population and Primary Outcome

The inclusion criteria were reamputation with knee disarticulation (KD) or TFA after a failed TTA, within one year from the TTA, between 2000 to 2020. Patients were identified through the surgical planning system. Due to reamputation more than one year from the TTA (n = 12), previous inclusion in the study due to their contralateral TTA (n = 3) and lack of Swedish unique personal identity number (PIN) (n = 2), in total 17 patients. After exclusions were made, in total 152 reamputations in 152 patients were included. Reamputation later than one year from the TTA was considered to be a progression of the disease rather than a failed TTA.

The primary outcome was further reoperations, including all reoperations and reamputations separately.

5.5.3 Method and Statistical Analysis

Medical charts were reviewed to find variables, demographic data and ipsilateral reoperations and contralateral amputation within 1 year. In the electronic referral system Tekniska Hjälpmedel Ordersystem (Thord), the date of receipt for the prosthesis was found. All patients were followed for at least 1 year after the amputation or until death and the median follow-up time was 10.1 months. A power calculation was made to detect a 20% clinically relevant difference in reoperation rate between KD and TFA. With 80% power and 5% significance level, we planned to include a minimum of 110 patients.

Nominal variables underwent testing using the Chi-square test or Fisher's exact test, and all tests were two-sided. Means with ranges were presented for normally distributed data. To find factors associated with reoperation, reamputation, and all reoperations separately, univariable, and multivariable logistic regression analysis were conducted. In the model diabetes, age, sex, cardiovascular disease, and reamputation level were tested. For secondary outcomes, previous contralateral amputation and ambulatory status preoperatively were added due to the belief that this could influence the results. The analysis for prosthetic fitting was based on the initial reamputation level, when comparing TFA with KD. The reamputation ratio over time was analyzed by dividing the study period into three seven-year periods: 2000-2006, 2007-2013 and 2014-2020.

5.6 Study III

5.6.1 Study Design

Single-center retrospective cohort study with historical control group

5.6.2 Study Population and Primary Outcome

The inclusion criteria were patients who experienced a TTA between 13 June 2017 – 31 December 2020 (intervention group), and 1 January 2013 – 31 December 2015 (control group). Due to a missing PIN, one patient from each group was excluded, and five patients had already been included in the control group and were excluded from the intervention group. In total 432 patients with TTA were included.

Starting from June 2017, Södersjukhuset in Stockholm has adopted a new surgical and care guideline for TTA. This guideline features recommendations for the sagittal surgical technique, removable rigid dressing (RRD), early liner treatment, and interdisciplinary team follow-up (Figure 6, page 15). Subsequently the Stockholm Health Care Region, in 2019, introduced a regional guideline, necessitating minor modifications for our clinic. Notably, this regional guideline involved the integration of physiotherapists from the Amputee Rehabilitation Clinic into the interdisciplinary team follow-up. However, that change had already been implemented in 2018 at Södersjukhuset.

The primary outcome was days to prosthesis within 12 months from TTA following the new guideline and compare it to a historical cohort.

5.6.3 Method and Statistical Analysis

From medical journals data on gender, comorbidities, mortality, The American Society of Anesthesiologists (ASA) physical status classification system, ambulatory status, reamputations, contralateral amputations and other variables were retrieved. The indications for the amputation were grouped into peripheral artery disease (PAD) and/or diabetes (gangrene, non-salvageable foot ulcers, embolus and critical limb ischemia were included) and other indications (compartment syndrome, necrotizing fasciitis and sequelae after trauma were some of the included indications). Information about prosthetic fitting and the date of receipt for the prosthesis was retrieved from journals of Prosthetic and Orthotic Units and the SwedeAmp registry. A power calculation was made to detect a reduction in time to prosthesis from 120 to 80 days, between the two cohorts. This estimate in time was based on known data from the Prosthetic and Orthotic units' quality assessment and follow-up of prosthetic fitted patients. With 80% power and 5% significance level, the calculated sample size was 90 prosthetic fitted patients in total.

Median and range values were presented for non-normally distributed data, and the Mann Whitney U-test was used. The Chi-square test was used for categorical variables. The tests were two-sided and p-values <0.05 were considered statistically significant. The majority of patients obtain a prosthesis within 12 months; hence the follow-up time was set to 12 months. To evaluate factors associated with prosthetic fitting, logistic regression analysis was used. First, crude associations for cognitive impairment, gender, ambulatory status, and age were tested in a univariable model. Second, to study adjusted

associations a multivariable model was used. The associations were presented as ORs with 95% CIs.

5.7 Study IV

5.7.1 Study Design

Qualitative interview study with content analysis

5.7.2 Study Population and Primary Outcome

Participants were recruited following the scheduled interdisciplinary team follow-up visit at the Orthopedic Outpatient Clinic, three to four weeks after their TTA. Sixteen patients were asked to participate and 15 accepted and gave informed consent. The inclusion criteria were being 18 years old or older and having undergone a TTA three to four weeks earlier. The exclusion criteria included not being fluent in Swedish and having a cognitive impairment that hindered the ability to give consent. Purposeful sampling and broad inclusion criteria were used to capture various perceptions.[142]

In a qualitative interview study, there is no primary outcome.

5.7.3 Method and Statistical Analysis

To gain a deeper understanding of the patients' perceptions of the care trajectory and provided information after the new surgical and care guideline was implemented, a qualitative methodology with content analysis using an inductive approach was employed, following Graneheim and Lundman.[142, 143] The inductive approach means that codes and themes are derived from the material itself and not from any pre-existing theoretical framework.

The interviews took place face-to-face two to three months after the TTA. A semi-structured interview guide was used, developed within the research team, and based on significant findings from previous research. The interviews were conducted by one researcher, (LS), who was not involved in the patients' care, at a location chosen by the participants. Using only one interviewer reduces the impact of the interviewer and enhances trustworthiness. The interviews began with an open-ended question: "Can you share the details about the first time amputation was mentioned as a treatment option?" Further questions focused on the experiences before, during and after the amputation procedure. After the

first interview, the material was reviewed and discussed within the research team and the interview guide underwent minor adjustments. To increase the understanding and ensure that the participants' comments were correctly understood additional questions were asked for clarification, as well as rephrasing, summarizing, and probing questions.[144]

The interviews were recorded and then transcribed verbatim. The material was analyzed using a latent approach, which focuses on uncovering underlying meanings, interpretations, or concepts that may not be immediately apparent in the data.[143] Following the first 13 interview, an analysis were made. Thereafter, two more interviews were conducted and analyzed, but no new data emerged, suggesting saturation was reached.[145] The transcriptions were read and re-read many times to become familiar with the content and gain a sense of the whole. Thereafter, meaning units corresponding to the aim of the study were identified, then shortened, condensed, and labeled with a code while still preserving the core. This was done by LS with continuous feedback from the last author (ET). The codes were systematically examined and compared for differences and similarities, and subsequently organized into sub-themes and themes. Disagreements in the analysis were discussed until reconciliation was achieved within the research team. The last step of the analysis involved reflecting on and discussing the interpretation of the findings within the research group to reach consensus and increase credibility.

6 Results

6.1 Study I

A total of 162 patients with a first-ever transfemoral amputation (TFA) were included in the cohort. Exclusion from the study was due to simultaneous bilateral TFA (n = 4), contralateral TFA in the first year after the index procedure (n = 5) and previous contralateral major lower extremity amputation (LEA) (n = 13), in total 22 patients.

In the majority of cases peripheral artery disease (PAD) with or without diabetes was the indication for surgery (78%, n = 126). The cohort consisted of 67% (n = 109) females and in 19% (n = 30) of the cases diabetes was present. Comparing diabetic patients to non-diabetic patients, no significant difference was seen between the groups regarding age, The American Society of Anesthesiologists (ASA) physical status classification system, and gender. Among diabetic patients, cardiovascular disease was overrepresented (83% versus 64%, p = 0.04) but there was no difference regarding the consultation of a vascular surgeon prior to amputation.

For diabetic patients, mortality was significantly higher at 1-week (30% versus 8%, p = 0.001) as well as at 1-year (80% versus 57%, p = 0.02) (Table 2). In total, 1-week mortality was 12%, and 1-year mortality was 61%. The corresponding 1-year mortality rate for a cohort of Swedish 85-year-olds, was 12% for men and 8% for women during 1996-2012.[146]

Table 2. Postoperative mortality following first-ever transfemoral amputation.

	Patients with diabetes n = 30	Patients without diabetes n = 132	p-value
1-week mortality; n (%)	9 (30)	10 (8)	**.001**
1-year mortality; n (%)	24 (80)	75 (57)	**.02**

Using a univariable analysis both diabetes and cardiovascular disease were found to be associated with 1-week mortality but in a multivariable analysis only diabetes remained significantly associated. Using a univariable analysis age, the indication for surgery, diabetes, and cardiovascular disease were found to be

associated with 1-year mortality, but in a multivariable analysis, age, diabetes, and indication remained significantly associated (Table 3).

Table 3. Logistic regression analysis to evaluate factors associated with mortality at one week.

			Univariable analysis		Multivariable analysis	
	All n	Mortality	OR(95% CI)	p-value	OR (95% CI)	p-value
Age; n (%)						
<85 years	80	10 (13)	1 (reference)	.76		
≥85 years	82	9 (11)	0.86 (0.33 – 2.25)			
Gender; n (%)						
Female	109	13 (12)	1 (reference)			
Male	53	6 (11)	0.91 (0.34 - 2.64)	.91		
Diabetes; n (%)						
Yes	30	9 (3)	5.23 (1.90 – 14.39)	**.001**	4.45 (1.59 – 12.47)	**.005**
No	132	10 (8))	1 (reference)		1 (reference)	
Indication for surgery; n (%)						
PAD	126	15 (12)	1 (reference)			
Others	36	4 (11)	0.93 (0.29 – 2.98)	.90		
Cardiovascular disease; n (%)						
Yes	109	17 (16)	4.71 (1.05 – 21.22)	**.04**	3.77 (0.82 – 17.44)	.09
No	53	2 (4)	1 (reference)		1 (reference)	

OR = Odds Ratio, PAD = Peripheral Artery Disease.

The overall reoperation rate for the ipsilateral leg was 14% (n = 23), with the majority of being a higher level reamputation (n = 15).

6.2 Study II

We found 152 reamputations in 152 patients following a failed transtibial amputation (TTA); 86 were transfemoral amputation (TFA) and 66 were knee disarticulations (KD) and included them in the study. The indication for the previous failed TTA was in all cases PAD with or without diabetes (including embolus, critical limb ischemia, non-salvable foot ulcers, or gangrene). The indication for the reamputation was a necrotic, non-healed, or infected wound. Comparing groups of reamputation levels, TFA patients were older (82 versus 78, p = 0.02) and more patients suffered from cardiovascular disease (83% versus 68%, p = 0.04). Otherwise, no differences were seen between the groups. Most of the patients (70%, n = 106) were ambulant with or without aid before their transtibial amputation (TTA), with missing data from 2 patients. Ambulation status did not differ between the groups.

The median time from the failed TTA to the index reamputation was 30 days (range 3-345), with the majority (78%, n = 118) reamputated within 2 months of their index TTA.

The indication for further reoperations was a necrotic, non-healed, or infected wound. Further reoperations, including both reamputation and wound or soft tissue revision, in the ipsilateral leg within 1 year were performed in 44 patients (29%). Of them, 37 patients had a reamputation to a higher level. For both reoperation and reamputation, KD had significantly more events compared to TFA.

Using a univariable analysis, the reamputation level was significantly associated with further reamputations (Table 4, page 32). In a multivariable analysis, including factors believed to affect reamputation risk, only TFA was significantly associated with lower odds of reamputation (OR = 0.31; 95% CI, 0.14 – 0.69).

Table 4. Univariable analysis of factors associated with reamputation.

			Univariable analysis	
	All n	**Reamputation** n (%)	**OR (95% CI)**	**p-value**
Gender; n (%)				
Female	78	22 (28)	1.55 (0.73 – 3.28)	.26
Male	74	15 (20)	1 (reference)	
Age (y)			0.99 (0.95 – 1.02)	.44
Reamputation level, n (%)				
TFA	86	13 (15)	0.31 (0.14 – 0.68)	**.003**
KD	66	24 (36)	1 (reference)	
Diabetes; n (%)				
Yes	63	15 (24)	0.95 (0.45 – 2.02)	.90
No	89	22 (25)	1 (reference)	
Cardiovascular disease; n (%)				
Yes	116	26 (22)	0.66 (0.29 – 1.51)	.32
No	36	11 (31)	1 (reference)	

TFA = Transfemoral Amputation, KD = Knee Disarticulation, OR = Odds Ratio.

Regarding the rate of prosthetic fitting, there was a difference, however, not statistically significant, 30% for KD compared to 19% for TFA (p = 0.1). A multivariable analysis showed lower odds for prosthetic fitting for patients with prior contralateral amputation (OR = 0.15; 95% CI, 0.03 – 0.72).

Table 5. Ratio of reamputation levels following failed transtibial amputations during the study period.

Years	Ratio KD : TFA
2000–2006	31 : 16
2007–2013	13 : 20
2014–2020	22 : 50
In total	66 : 86

TFA = Transfemoral Amputation, KD = Knee Disarticulation.

Over the course of the study period, there was a shifting preference for reamputation levels. Initially, KD was more prevalent, but over time, there was a transition towards favoring TFA (Table 5).

Overall, 30-day mortality was 17%, and 1-year mortality was 53%.

6.3 Study III

In the intervention group 263 patients undergoing TTA were included between 13 June 2017 – 31 December 2020. The corresponding number for the control group, with a TTA between 1 January 2013 – 31 December 2015, was 169 patients. Exclusion was made due to a missing PIN (one in each group) and being already included with their contralateral amputation in the control group (five in the intervention group). In total 432 individual patients were included.

Median age for the patients was 78 years (range 26 – 102) and 44% (n = 192) were females. The primary cause for the amputation was PAD and/or diabetes, accounting for 93% (n = 400). Between the intervention and control group, there were more patients with renal failure in the intervention group (37% versus 24%, p = 0.008) as well as more patients with an amputation due to other indications than PAD and/or diabetes (10% versus 4%, p = 0.014).

Median time to prosthesis was significantly lower for the intervention group compared to the control group, 76 versus 103 days (p <0.001) (Figure 7). Still,

there was no difference between the rate of prosthetic fitting, 48% versus 46% (p = 0.77).

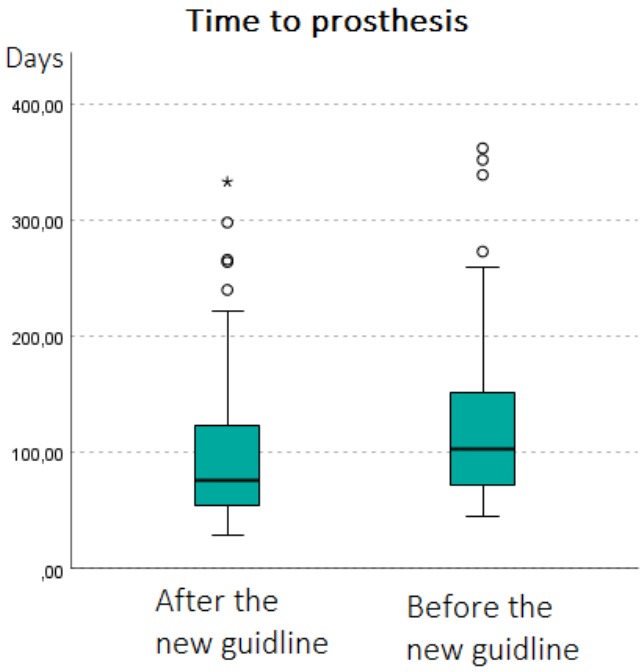

Figure 7. Time to prosthesis fitting within 12 months after the implementation of the new guideline, compared to the historic cohort.

Compared to male patients, female patients were less likely to be fitted with a prosthesis, 34% versus 58% (p < 0.001). With logistic regression, the gender difference persisted after adjusting for confounders. For female patients, the odds for prosthetic fitting are lower than for men (OR 0.47; 95% CI 0.31 – 0.72).

Reoperation rates were higher for the intervention group (27% versus 17%, p = 0.018), however regarding the rates of reamputation to a higher level there were no significant differences, the rate in total was 14%. Mortality at 30-days was 10%, and at 1-year 35%.

Between the cohorts, the preferred surgical technique changed from mainly the long posterior flap (96%) in the control group to the sagittal/skewed flap (79%) (Figure 8). Postoperative dressing changed from plaster (99%) to a rigid vacuum dressing (91%) (Figure 9). A larger proportion of the patients were discharged to a geriatric/rehabilitation facility in the intervention cohort compared to being sent to a skilled nursing facility or home, 69% versus 56%.

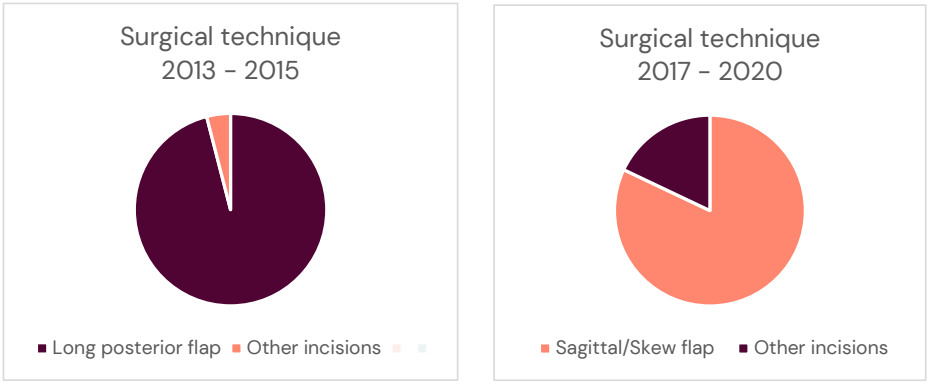

Figure 8. Comparison of surgical techniques before and after the implementation of a new guideline for transtibial amputation.

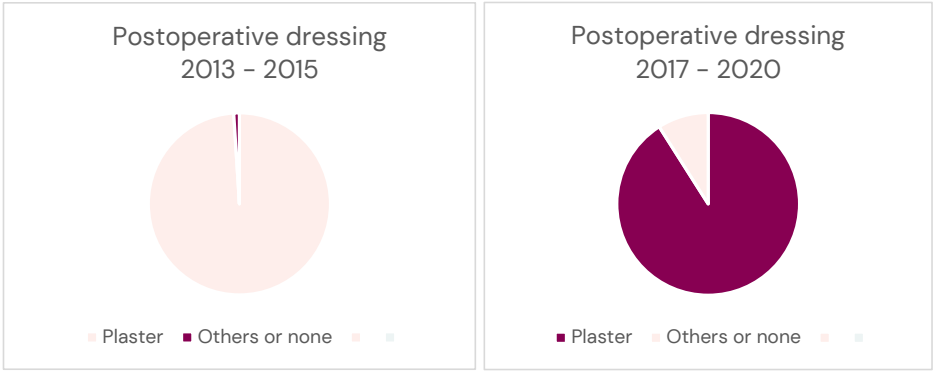

Figure 9. Postoperative dressing practices before and after the implementation of a new guideline for transtibial amputation.

6.4 Study IV

In this study, 15 participants were included with a mean age of 78 years, ranging from 54 to 96. The majority of the participants were men (n = 9), and the majority underwent an amputation due to peripheral artery disease (PAD) and/or diabetes (n = 10). The time between the amputation and the interview was 66 days, in mean. The mean interview time was 40 minutes (range 25 – 67 minutes), and after 15 interviews saturation was achieved and the material considered sufficient to portray the research question.

Three themes and seven sub-themes were identified from the data (Figure 10).

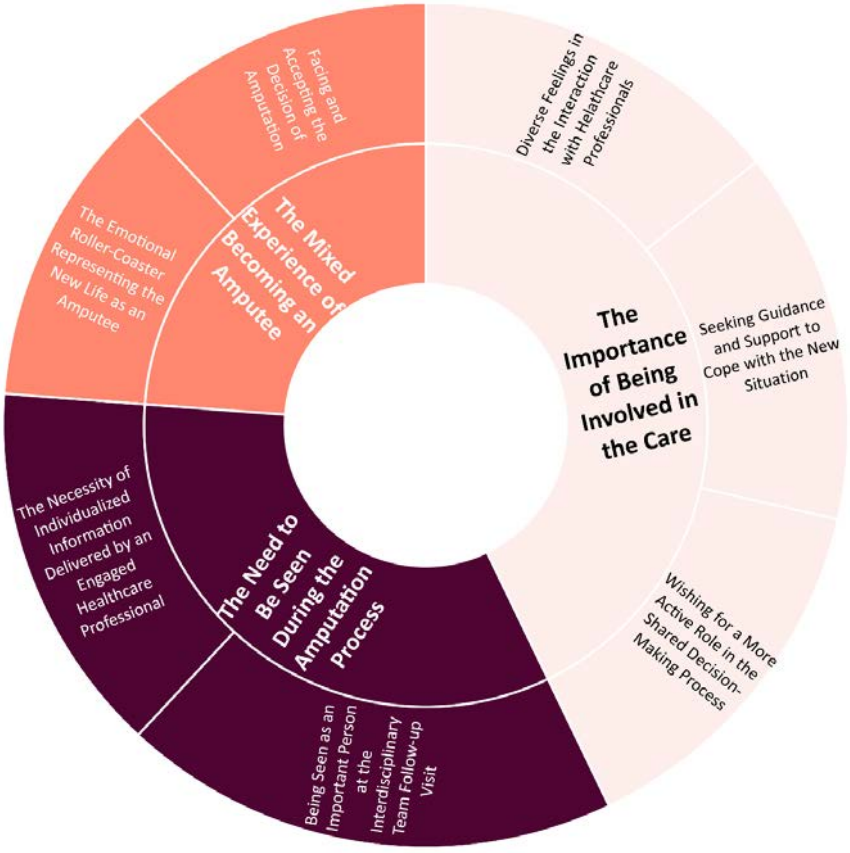

Figure 10. Overview of the main categories and sub-categories emerging from the content analysis in the qualitative study that explores patients' experiences of the care trajectory, given information and involvement in the care after a new guideline.

6.4.1 The Mixed Experience of Becoming an Amputee

Participants' experiences of the period preceding the amputation, the decision-making process and adaptation to their new life varied significantly.

Facing and accepting the decision of amputation was a challenge for the participants. The decision was described as a life-altering event, eliciting feelings of despair, depression, or even shock for some.

Although the duration from the onset of illness to the decision of amputation varied among participants, many expressed a sense of inevitability regarding the procedure. This anticipation came from either a belief that the foot could not be salvaged or previous discussions with healthcare professionals (HCPs) mentioning the possibility of amputation. Despite being aware of the risk for some time, many participants struggled to fully comprehend the need for amputation. Some participants approached the prospect of amputation with a degree of acceptance, viewing it as a necessary step following rapid deterioration, severe illness, or resolution of a profoundly infected foot.

> *I don't know if I am weird, but I have understood all the time, and I think it was best to do (the amputation) rather than having pain and doing wound revisions. (Participant 7)*

While the majority acknowledged the need for amputation as part of their continuum of care, some experienced strong negative feelings such as disappointment, anxiety, self-pity, or grief. Conversely, others were thankful for their continued survival and relief that their pain had diminished.

> *But I could not get my leg back. If it is gone, then it is gone and then you will have to learn to live with it, immediately. Otherwise, you will have a tough time, I think. (Participant 4)*

Participants described a period filled with mixed feelings, like an emotional roller-coaster representing the new life as an amputee. The period was challenging for some, expressing concerns about their future daily life and mobility with only one

leg. A minority of participants described an unforeseen existence marked by physical inactivity and a notable reliance on assistance.

However, participants who had undergone rehabilitation at the Amputee Rehabilitation Clinic felt an evident sense of direction and newfound optimism. Others anticipated challenges in adjusting to ambulate with prosthesis or feared potential complications.

6.4.2 The Need to Be Seen During the Amputation Process

The second theme included the patients' experience of the trajectory of care and the given information, after the new guideline was implemented. The importance of receiving accurate information from engaged HCPs and being seen as a person was emphasized. Patient-centered care and shared decision-making at the interdisciplinary team follow-up visit was an example.

The necessity of individualized information delivered by an engaged healthcare professional was stressed. Participants revealed that oral communication was most important given the gravity of the subject, and they valued the printed information as a helpful supplement. Participants had contrasting experiences regarding the amount of printed information received; some were overwhelmed by the information, while others felt they received none. However, although they received information about the amputation process, they noted a lack of engagement and two-way communication with the surgeon.

Participants felt they had a satisfactory understanding of the level of amputation; however, they received limited information about different amputation levels and potential complications. They also emphasized the need for clear and concise information, easy to understand, particularly for individuals without a medical background.

> *They did not tell me where they would place the incision and why they placed it there. Instead, I had to guess that they made the best choice. (Participant 9)*

Being seen as an important person at the interdisciplinary team follow-up visit was evident to the participants. The purpose of the team follow-up visit was clear to most participants. Overall, participants perceived the visit as providing

high-quality information and an individualized plan for the future, describing it as an efficient process marked by the delivery of excellent information.

> *I thought it was great. That everyone was gathered, that is perfect. (Participant 10)*

The follow-up visit fostered a positive and supportive atmosphere, with many participants appreciating the involvement of multiple professions. Compared to earlier stages, participants felt a greater sense of involvement during the team visit, and for the first time perceived that they were being addressed as an individual.

6.4.3 The Importance of Being Involved in the Care

In various stages of the process, the participants perceived different extents of support and involvement, but the lack of continuity with the surgeon affected the whole experience. After discharge, it was hard to understand how to contact the hospital.

Participants wished for a more active role in the shared decision-making process. Participants exhibited varying degrees of involvement in the decision-making process. Some were well-informed and aware of the pros and cons of different options and actively engaged in the decision-making process, while others adopted a more passive stance, relying on expert recommendations. There was a powerful desire among participants to play a more active role in the decision-making process, yet many felt excluded from discussions and believed that decisions were made without their meaningful input.

> *I was so affected by my illness that I did not care about the information. (Participant 2)*

Various obstacles, such as medications, comorbidities, and emotional distress, stopped the participants from being actively involved in the decision-making, while others cited a lack of information as a barrier to a fruitful discussion. .

The continuity was identified as a substantial challenge, with many participants not knowing or meeting their surgeon before the amputation and desiring more information about the procedure's outcome.

Seeking guidance and support to cope with the new situation was common among the participants. The value of individualized support throughout the process was pronounced.

> *I had no one to turn to, but whoever I told my story to, felt bad for me, but that did not help me. (Participant 4)*

Some were offered the opportunity to connect with a peer amputee and almost everyone was offered contact with a counselor, but not all participants were interested. Those who were interested primarily sought practical advice on adjusting to life without a limb. Some wanted to process the limb loss by themselves first, before seeking external support. Most participants were alone when they faced the decision of amputation. However, some engaged in discussions with and found support from relatives during the decision-making process. Friends or family with previous experience with amputees or healthcare backgrounds were particularly valued as sources of information and support.

Participants expressed uncertainty about how to contact the hospital after discharge. Additionally, they recommended the appointment of a contact nurse to support, coordination with various care providers and to facilitate easier communication channels.

Diverse feelings in the interaction with the healthcare professionals during the acute phase were described by participants. Some felt uninteresting to the doctors and reported scarce interaction with them. Conversely, others had positive experiences with doctors, with many highlighting the importance of humor in doctor-patient relations.

> *I had great trust in my doctor, but why is hard to define. He was focused and concentrated… and then he was really fun! (Participant 5)*

Some participants felt alone and neglected during their hospital stay, experiencing healthcare staff as overburdened and their support as inadequate. However, a greater number of participants described nurses and assistant nurses as engaged, welcoming, and empathetic, and reported positive interactions with them.

7 Discussion

7.1 General Discussion

As an orthopedic surgeon, you encounter a wide range of patients, from children to the elderly and from top athletes to patients with multiple comorbidities. You may not save lives every day, but in amputation surgery, you can indeed save patients' lives. Major lower extremity amputation (LEA) carries high morbidity and mortality. With an aging population, amputation care represents both a significant challenge and a call for improvement.

The aggregated work of this thesis, including four studies, aimed to examine various aspects of major LEA: exploring different levels of lower extremity amputation highlighting complications, the impact of new guidelines, and finally – the perspective of the patients.

7.2 Mortality

Major LEA carries a high postoperative mortality risk, with proximal amputations associated with higher mortality rates compared to distal ones.[37, 53] The 1-year mortality rate in Study I, which examined transfemoral amputation (TFA), was 61%. In Study II, which examined both TFA and knee disarticulation (KD), it was 53%, and in Study III, which examined transtibial amputation, it was 35%, illustrating this correlation.

However, the influence of diabetes on mortality has been inconclusive. Study I focused on patients with high mortality, specifically first-ever transfemoral amputees, and found that diabetes significantly increased the risk of death at 1 week and 1 year. Another study has confirmed the impact of diabetes on 30-day mortality and also highlighted that the median time of death was 6 days.[52] One-week mortality is not often expressed but has clinical implications and relevance since patients are often still at the acute hospital or geriatric clinic care and could be accessible for interventions. In our study, the 1-week mortality for patients with diabetes and first-ever amputation was 30%. Similarly high mortality rates, 20%, were shown in a recent study examining in-hospital mortality rates for diabetes patients with transfemoral amputation.[6] Likewise, a vastly increased in-house mortality has been observed for patients with hyperglycemia following vascular surgery in the lower extremity.[147]

The reason for increased mortality in diabetic patients is not fully understood but may be due to the presence of more advanced vascular disease affecting renal and coronary arteries. Renal failure is associated with increased mortality[148] and one of the most common causes of death following a major LEA is cardiac events.[52, 149] Interestingly adopting aggressive cardiovascular risk management to patients with diabetic foot ulcers, has shown to decrease mortality and could be a way to affect this population at-risk.[150]

Study I provide valuable insights into the complex interplay of factors influencing postoperative mortality following transfemoral amputation (TFA). Patients with diabetes, especially those undergoing TFA, represent a high-risk cohort. These findings emphasize the importance of pre- and postoperative enhancement of diabetic treatment, early evaluation, personalized risk assessment, and proactive management strategies to improve outcomes for patients undergoing major LEA. In addition to medical improvements, logistical factors should also be considered. Whenever possible, immediate daytime surgery should be chosen to minimize further risks of mortality and reamputations.[47, 61, 73]

The high mortality also presents a dilemma for the surgeon. It is necessary to evaluate the need for surgery with the patient and relatives; in some cases, palliative non-surgical treatment may be a better choice. For these types of ethical discussions, shared decision-making with the patient or relatives is preferred.

Comparing mortality data between our study and previous research on major LEA is challenging due to the heterogeneity of study populations and inconsistencies in data presentation. For instance, in many studies, it is unclear whether the TFA was performed as a first-ever amputation or as a secondary procedure after a failed distal amputation. Additionally, discrepancies in inclusion criteria, such as distinguishing between first-ever amputations and re-amputations, may have influenced the results. These findings underscore the importance of standardized inclusion criteria to accurately evaluate mortality outcomes.

7.3 Reamputation

Beyond mortality, other complications of amputation have a significant impact on patients – namely reamputation and prosthetic fitting. Reamputation and

reoperation are relatively common and feared complications after major LEA. Although there are studies on reamputation rates and risk factors, there were no studies comparing different levels of reamputation after transtibial amputation (TTA) and few studies examining prosthetic fitting after reamputation.

Study II aimed to explore further reamputation or reoperations after the first reamputation (TFA or KD) following a failed TTA. The study found that TFA was associated with a reamputation rate of 15% compared to KD, which presented a rate of 36%. In comparison, in Study I, the reamputation rate after TFA was 9% and in Study III, the reamputation rate after TTA was 14%. TFA compared to KD, as a reamputation level after a failed TTA, was associated with significantly lower odds of reamputation when adjusting for age, gender, cardiovascular disease, and diabetes. Comparison with literature shows higher reamputation rates in Study II, as most studies do not exclusively examine reamputations, instead, the inclusion criteria are mostly for primary amputations, which typically have lower rates of complications.

The difference in prosthetic fitting rates (TFA 19% versus KD 30%) was not statistically significant; however, this suggests there may be a clinically relevant difference. For prosthetic fitting, the only significant variable affecting the likelihood of being fitted with a prosthesis was having undergone a previous amputation on the contralateral leg. Comparisons with literature are challenging due to variations in study design, definitions of mobility, and prosthetic fitting. Studies[68, 82, 83] show a wide range of prosthetic fitting rates, reflecting this variability.

Study II highlights the challenges of stump-healing problems in patients with peripheral artery disease (PAD) and/or diabetes leading to high reoperation rates and limited prosthetic ambulation. Enhancing the assessment of circulation and considering revascularization and optimal amputation level, in collaboration with a vascular surgeon prior to the TTA or the reamputation may have potential to impact the outcomes. Given the situation, it presents an excellent opportunity for shared decision-making with the patient, evaluating the pros and cons of different reamputation levels. It involves considering the goals and wishes of the patients and jointly making a plan and decision of the optimal reamputation level.

7.4 Guidelines for Transtibial Amputation

There is a variation in the incidence of amputation, and in Sweden, there is also a substantial variation in the distribution across amputation levels.[5, 151]

To ensure quality, there is a need for clear evidence-based guidelines. While implementing complex healthcare guidelines presents challenges, collaborative care and focused attention to the patient's needs can facilitate quicker prosthetic fitting.

Study III reveals that a new guideline has the potential to affect the time to prosthesis and shorten it by almost a month (76 days versus 103 days). The rate of patients with prosthetic fitting remained the same, even after implementing the new guideline, and the rates are comparable to other studies examining similar cohorts of patients.[152]

The benefit of a shorter time to prosthetic fitting is twofold, for society and for the patient. Early prosthetic fitting is associated with reduced healthcare costs as well as increased patient satisfaction and usage of the prosthesis.[113, 153]

However, the female gender remains a significant predictor of lower prosthetic fitting rates, indicating the need for further research into underlying factors contributing to this disparity. In previous research, women appear older and have more frequent higher-level amputations,[5, 8] but in Study III, when adjusting for age, ambulatory status preoperative, cognitive impairment, and comparing same-level amputation, the disparity still exists. Could factors beyond these affect the result? Professional biases, psychological barriers, or living alone or not may impact the chance of being prosthetically fitted. There is room and a need for further investigation to make prosthetic fitting equal between genders.

Implementing a guideline in a clinical context can be challenging, but in Study III, it proved to be possible. Evidence of good implementation is also the further development of the guideline locally in the clinic. Scheduling a regular day for amputation surgery, enhancing information material, and the possibility of contacting a counselor have been further developments driven by an interdisciplinary group. A guideline similar to ours was adopted as a regional guideline in the Region of Stockholm,[154] and one could argue that Study III serves, by proxy, as a scientific evaluation of the guideline advocated by the region.

7.5 Patients' Perceptions and Shared Decision-Making

A major LEA is a significant life event for a patient, a procedure with lifelong consequences affecting everyday life. In Sweden, we are obliged by the Patient Act,[131] to involve patients and relatives, making them a part of the decision process of their care. However, it is not clear what the patient's perception of involvement is.

Study IV underscores participants' desire for an active role in the decision-making process surrounding TTA, highlighting the need for in-depth, personalized information from healthcare professionals (HCPs). Despite the introduction of new information material based on previous research insights about amputees lacking information, significant deficiencies in information persisted, and there was a lack of shared decision-making (SDM).

The psychological effect of amputation mirrors the experience of losing a spouse,[155] affecting autonomy and necessitating substantial life adjustments. Establishing robust support systems and facilitating SDM are imperative. The role of a contact nurse (CN) is well-established in cancer care, coordinating hospital visits and providing crucial support.[156] Similar support systems are lacking in amputation care, leading to confusion among participants regarding postoperative contact. Introducing a contact nurse embedded within the interdisciplinary team could improve continuity of care and patient experience. While many participants felt actively involved during interdisciplinary team follow-up visits, barriers to SDM persisted, including limited treatment options discussions and inadequate consideration of participants' preferences. They expressed a desire for tailored communication, preferably oral and accurate information delivery, highlighting the importance of delivery from engaged HCPs.

Continuity of care remains a challenge, with participants often lacking interaction with surgeons and feeling isolated during their hospital stay; a CN could offer the continuity that is now lacking.

Another way to improve and support SDM is to use the interdisciplinary team for a pre-amputation assessment. Besides patients' appreciation of the interdisciplinary team as seen in Study IV, the teamwork has been seen appreciated by participating HCPs.[122]

8 Conclusions

8.1 General Conclusions

The combination of qualitative and quantitative studies on the implementation of a regional guideline (Studies III-IV), in a normal clinical setting, gives valuable feedback for future amendments.

8.2 Study I

There is a high postoperative mortality following a first-ever transfemoral amputation (TFA). Patients with diabetes have an elevated risk of postoperative mortality both at 1 week and 1 year, especially compared to an age-matched cohort of Swedish 85-year-olds. The pronounced mortality rates underscore the importance of a timely and comprehensive assessment of the patient's overall medical status and a reflection on the necessity of the surgery. In selected cases, non-surgical palliative care may be a suitable alternative, although it poses an ethical dilemma for the surgeon. Upon deciding on amputation, avoiding surgical delays, and minimizing medical risks are crucial. Further research is warranted to elucidate the specific factors contributing to and causing early death in amputees and to identify and target at-risk patient populations. We advocate monitoring of blood glucose levels in patients with diabetes and prompt management of infection and cardiac events in the postoperative period.

8.3 Study II

We found a markedly reduced risk of reamputation after TFA compared to knee disarticulation (KD) after a failed transtibial amputation (TTA). No statistical difference was seen regarding prosthetic fitting. Based on our findings, we advocate for TFA as the preferred level of reamputation, particularly when the risk of further reamputation needs to be low. However, it is always necessary for the patient to be an active part of the decision-making process, being able to reflect on options, risks, expectations, and likely outcomes together with the surgeon.

8.4 Study III

The implementation of a new guideline for TTA led to a notable reduction in time to prosthetic fitting, emphasizing the importance of contemporary clinical protocols in improving outcomes in amputation care. Nonetheless, the fact that women experience lower rates of prosthetic fitting underscores a domain necessitating further investigation to understand and address gender-related inequalities.

8.5 Study IV

Participants undergoing TTA demonstrated a pronounced preference for increased participation in decision-making and identified deficiencies in continuity of care. While printed information material was considered of high quality, there was a strong requirement for more direct oral communication and engagement with dedicated healthcare professionals (HCPs). Our results highlight avenues for augmenting both shared decision-making and continuity across the continuum of care. There is a necessary paradigm shift towards more interdisciplinary teams in amputation care and integrating the interdisciplinary team into the decision-making phase, alongside a designated contact nurse, holds promise for significantly enhancing the overall standard of patient care.

9 Methodological Considerations

9.1 Study Design

An important strength of this thesis is the use of both quantitative and qualitative research methods. The quantitative approach is valuable for assessing the incidence and examining treatment options and outcomes in populations (Studies I-III). The qualitative method (Study IV) provides a deeper understanding of individual patients' perspectives and gives voice to the patient. Integrating both methods in this thesis offers a deeper understanding of the amputation population.

9.2 Internal and External Validity

There is a trade-off between internal and external validity; the more you control factors in a study the less chance there is of generalizing the findings to other contexts.

Internal validity was likely high due to the single-center design with standardized definitions, treatments, and similar referral routines for all patients (Studies I-III). The single-center design also provides good insight into the implementation of guidelines and subsequent improvements (Study III).

While the single-center design may reduce external validity, it is important to note that patients from the entire health care region of Stockholm are referred to our center. The large catchment area should increase the ability to generalize the results to other populations. This notion is supported by studies with similar baseline patient characteristics from other settings.[85]

9.3 Sources of Bias

There is a risk of selection bias in Study II, as the level of reamputation was not randomized. Older and non-ambulatory patients could be more prone to transfemoral reamputation than younger, ambulatory patients, due to surgeons' preferences and expectations of postoperative outcomes. However, this pragmatic study is justifiable in a clinical setting, and the results regarding prosthetic fitting and reoperation for patients with reamputation add valuable information to the field.

We tried to limit the risk of information bias by using standardized definitions, including only first-ever transfemoral amputation (TFA), excluding the impact of previous amputations, and focusing on the initial procedure only (Study I). Similarly, only reamputations following a failed transtibial amputation (TTA) were included in Study II.

The studied clinical cohorts were still heterogeneous, including a mix of several types of indications for amputation. Although mixed reasons for amputation are clinically common, the classification of vascular disease is not always clear or thoroughly investigated, thus posing a challenge. However, once it is unequivocally determined that a patient needs an amputation, the classification of vascular disease often becomes irrelevant. In settings where vascular surgeons are responsible for amputations, the cohort is often less diverse and more well-defined in terms of their vascular status or disease. The same applies to the type and treatment of diabetes mellitus.

Confounding bias is the effect of an unmeasured variable associated with both the exposure and outcome. In Study III, patients undergoing amputation from 2016 until the implementation of the guideline in June 2017 were excluded from the analysis, due to the risk of confounding by improvements initiated in 2016. In Studies I-III, we tried to control for confounders using multivariable regression analysis. The identification of potential confounding variables in each study was based on clinical relevance and previous research.

9.4 Random Error

Random error refers to inaccuracies in the data since no measurement system is perfect. We use p-values and confidence intervals (CIs) to quantify random errors. A type I error is the probability of incorrectly rejecting the null hypothesis, with the significance level set at 0.05; this risk is 5%. A type II error is the failure of the hypothesis test to reject a false null hypothesis. This can be affected by a small sample size, and to lower the risk of a type II error power calculations were made to ensure an adequate sample size.

9.5 Qualitative Research

To ensure trustworthiness in qualitative research there are different aspects to address; credibility, dependability, confirmability, and transferability.[157]

Credibility refers to what extent the data addresses the intended focus. To address this in Study IV, an interview guide was developed to correspond to the study aims, and to minimize interviewer bias. Interviewer bias represents a systematic error, which arises from the interviewer's conscious or subconscious influence on subjects' responses or selective data gathering. Recall bias occurs when participants erroneously provide responses based on their ability to recall past events. To minimize recall bias, a short recall period, two to three months, was used. To further address credibility, we chose participants of various ages and gender and kept a dialogue in the research team seeking agreement.

Dependability refers to the stability or consistency of data over time. The participants were included within a year from the start of the study. During that time no major alterations to the guideline of care trajectory were made, making the context fairly stable over time. A rich description of the study methods can also allow others to replicate the study or assess dependability.

Confirmability refers to the extent the results would be confirmed or corroborated by other researchers. By parallel content analysis and continuous discussions within the research group, confirmability can be strengthened. A weakness in Study IV is not using member check, which could further enhance confirmability.

Transferability is the ability to transfer your research findings to other contexts, situations, and populations according to the reader. To enhance transferability, we thoroughly described the patients in Study IV and added quotations to the rich presentation of the findings. The requirement of speaking Swedish could affect transferability, but the rationale for this decision is that the use of an interpreter could compromise validity in qualitative studies.[158]

10 Points of Perspective

National guidelines for amputations are lacking, leading to regional disparities in preferred amputation levels, time to prosthesis, and choice of incision for transtibial amputation (TTA).[5, 159] This discrepancy highlights unequal care for amputees across Sweden.

The development and implementation of a national guideline, grounded in evidence along with reporting to the Swedish Amputation and Prosthetic Registry for the Lower Extremity (SwedeAmp), could promote more equitable care for patients while providing regions with feedback on their own amputee care chain, for continual improvement.

Reducing mortality rates also requires urgent attention. Improvements in logistical factors and the development of guidelines for enhanced pre- and postoperative medical care are crucial in this regard.

Addressing the problem with reamputations is paramount due to the significant negative impact on patients, influencing subsequent reoperations and prosthetic ambulation. Local initiatives utilizing negative pressure wound therapy have demonstrated potential in reducing wound complications after amputation, warranting further investigation.

As the population ages and remains more active, it is essential to consider prosthetic fitting and mobility for older individuals. Age should not automatically preclude eligibility for prosthetic fitting, as age per se should not be an exclusion criterion. Clear and concise guidelines based on physical capabilities, psychological abilities and the patient's wishes and goals, instead of age, are important.

There is an urgent need to examine the gender inequality in prosthetic fitting. Despite various theories, persistent lower rates of prosthetic fitting for women may indicate a problem that reaches beyond patient and surgical factors, and instead reveals a gender bias within health care systems. Possibly, the dissemination of information regarding the requirements for prosthesis use is skewed toward men and may not adequately address the needs of women. A sizeable portion of research conducted in the United States, particularly within the Veteran's Affairs system, primarily involves male cohorts. This presents an opportunity for novel qualitative studies to explore this phenomenon and generate hypotheses for subsequent quantitative investigations.

The most crucial perspective is that of the patient. Much remains to be done to achieve increased participation. Involving patients and their families in shaping future amputation guidelines is essential. As co-creators patients play a vital role in ensuring safe and high-quality care. Informed and empowered patients who actively participate in their care and have opportunities to influence decisions based on their preferences and circumstances can significantly enhance the quality of care provided.

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