Orthopaedic Patients with Lower Limb Vascular Injuries

KARIN BERNHOFF
Vascular injuries in lower limbs are rare but serious events. If not detected and managed correctly and timely they can lead to permanent functional impairment and even limb loss. The increasing number of orthopaedic interventions, worldwide, makes awareness of this problem among orthopaedic surgeons important.

The overall aim of this thesis was to describe lower limb orthopaedic injuries with associated concomitant arterial injuries, especially to the popliteal artery. Epidemiology, mechanisms of injury, management, outcomes and the patient perspective were all addressed. The research questions were generated from clinical praxis.

Vascular injuries are rare events, but by using as the National Patient (NPR) and National Vascular registries (Swedvasc) a relatively speaking large cohort was studied. Deep interviews with qualitative study method were used to investigate the patients’ perspective.

In papers I and II iatrogenic popliteal artery injuries (PAI) in knee-replacements, and in non-knee-replacements, were investigated. The number of knee arthroplasties in Sweden increased 1987-2008, but not the frequency of iatrogenic PAI. The most common mechanism of injury was sharp, directly to the artery. One third of the injuries resulted in pseudo-aneurysms. This was an unexpected and important finding, since these patients were often diagnosed late, resulting in poor outcome.

Paper III. The interviewed patients narrated substantial functional, cosmetic and psychological impairments, 4-17 years after their accidents, yet they described their lives as “normal”. Patients with saved limbs reported a need for better interpersonal support in their rehabilitation and adaptation back to “normal” life.

Paper IV. Popliteal artery injury is feared in knee dislocations and fractures. The proportion incidence of vascular injury was previously reported to be 2-60%. In this large population-based study, the incidence proportion in knee dislocations was 3.4-8.2%, depending on the definition of dislocation/ligamentous injury. In knee fractures the incidence proportion was lower, only 0.2%. The dominating cause of arterial injury in knee dislocations was fall, in knee fractures it was motor vehicle accidents. Amputation- free survival after arterial injury was inferior in knee fractures compared with knee dislocations.

In conclusion, PAI is a serious injury but on sequences can be limited by awareness and timely action.

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To John, Kara and Tore
List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.


III. Bernhoff K, Björck M, Larsson J, Jangland E. Patients’ experiences of life years after severe civilian lower extremity trauma with vascular injury. (Submitted manuscript)

IV. Bernhoff K, Björck M, Michaëlsson K, Gedeborg R. Incidence and outcome of popliteal artery injury associated with knee trauma A Swedish nation-wide population-based cohort study, Manuscript

Reprints were made with permission from the respective publishers. Paper I and II are preprints of manuscripts.
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## Abbreviations

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<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>CDR</td>
<td>Swedish Cause of Death Registry</td>
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<tr>
<td>DAG</td>
<td>Directed Acyclic Graph</td>
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<td>DSPs</td>
<td>Diagnosis-specific survival probabilities</td>
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<tr>
<td>ICD-10</td>
<td>The International Statistical Classification of Diseases, 10th Revision</td>
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<td>ICISS</td>
<td>ICD-10 based Injury Severity Score</td>
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<td>IVI</td>
<td>Iatrogenic Vascular Injury</td>
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<tr>
<td>KA</td>
<td>Knee Arthroplasty</td>
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<tr>
<td>LISA</td>
<td>Longitudinal integration database for health insurance and labour market studies, Statistics Sweden</td>
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<tr>
<td>LÖF</td>
<td>Landstingens Ömsesidiga Försäkringsbolag (same as SPI)</td>
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<tr>
<td>MONA</td>
<td>Microdata Online Access</td>
</tr>
<tr>
<td>NPR</td>
<td>Swedish National Patient Registry</td>
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<tr>
<td>PAI</td>
<td>Popliteal Artery Injury</td>
</tr>
<tr>
<td>PIN</td>
<td>Personal Identification Number</td>
</tr>
<tr>
<td>SCB</td>
<td>Statistiska centralbyrå, Statistics Sweden</td>
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<tr>
<td>SPI</td>
<td>Swedish Patient Insurance</td>
</tr>
<tr>
<td>Swedvasc</td>
<td>Swedish Vascular Registry</td>
</tr>
<tr>
<td>TKA</td>
<td>Total Knee Arthroplasty</td>
</tr>
<tr>
<td>UCR</td>
<td>Uppsala Clinical Research centre</td>
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<tr>
<td>UKA</td>
<td>Unicompartmental Knee Arthroplasty</td>
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Introduction

The life of an orthopaedic surgeon is joyful, but there are also many fears. An arterial complication is one of the most dreaded complications that can occur performing an orthopaedic surgical procedure. Luckily they occur very seldom, but when they do, outcome may be devastating. Since the complication is so rare, there are only small numbers reported in the literature. An adverse event with an iatrogenic vascular injury, or a knee dislocation with popliteal artery injury, may occur once or hopefully never during the career of an orthopaedic surgeon. Thus, it is impossible to acquire sufficient personal professional experience how to handle these events.

The frequency of arterial injury in orthopaedic surgery and trauma is an estimation not based on robust data,\textsuperscript{1,2} and there are no reliable investigations in the literature. Historically there is documentation from as early as the second century on how to treat arterial injuries by ligation, but this knowledge was lost during the dark ages.\textsuperscript{3} Most of the knowledge regarding treatment of arterial injuries emanates from war experiences, and in recent times there has been an increase in wartime arterial injuries. Surgery during wars is performed under extraordinary circumstances and military doctors also depend upon experience from civilian trauma and research.\textsuperscript{4} During World War I, extremity artery injuries were routinely ligated resulting in a 73% amputation rate for popliteal artery injury.\textsuperscript{5,6} These poor results have been improved with the development of arterial repair strategies and are less than 15% in most contemporary civilian series. Although the amputation rate has improved, there is often persisting long-term post injury symptoms in 20-50% of the patients\textsuperscript{7}.

The popliteal artery is the most frequently affected arterial segment when it comes to vascular injuries in orthopaedic surgery.\textsuperscript{2} It is the only great artery at knee level and when it is injured there are few collaterals. Injury to the popliteal artery has a devastating outcome in most cases, if repair is not undertaken.
Vascular injury

Presentation

Arterial injury may occur at any time and almost always require urgent management. Signs of arterial injury can be divided into hard or soft signs.

*Table 1. Signs of traumatic arterial injury.*

<table>
<thead>
<tr>
<th>Hard signs</th>
<th>Soft signs</th>
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<tbody>
<tr>
<td>- Bleeding observed</td>
<td>- Significant haemorrhage by history</td>
</tr>
<tr>
<td>- Visible spreading hematoma</td>
<td>- Peripheral neurologic abnormality</td>
</tr>
<tr>
<td>- Absent distal pulses</td>
<td>- Diminished pulse</td>
</tr>
<tr>
<td>- Bruit over the area of injury</td>
<td>- Proximity of bony injury or penetrating wound</td>
</tr>
<tr>
<td>- Arterial thrill by manual palpation</td>
<td></td>
</tr>
</tbody>
</table>

The injuries can manifest themselves as open or confined bleedings, thrombosis or an intimal flap dissection with secondary thrombosis, occlusion, impaired circulation and distal ischaemia. The symptoms can initially be mild with a risk of diagnostic delay. Outcome can be poor with loss of muscle and/or nerve function, pseudo-aneurysm or arterio-venous fistulae. Early diagnosis is important to avoid a delay of intervention/surgical correction and to reduce the risk of permanent disability.

A high degree of suspicion, early detection, and timely action is crucial for outcome. Soft signs are sometimes difficult to detect and evaluate.

Figure 1. Normal arteries, MR-angiography
Treatment

The popliteal artery is crucial for the circulation below the knee. There are many different ways to repair the artery and which method used depends upon the mechanism of injury, and the experience of the surgeon. In the last decades endovascular methods have increasingly often been used in the management of vascular injury.\textsuperscript{15}

Open methods for injury to the popliteal artery include:

- **By-pass surgery.** An endogenous venous graft, or less ideally a prosthetic graft, is applied with inflow proximal to the injury and outflow distally. It can be applied from the femoral artery to popliteal artery or branches below or from the popliteal artery itself and connected to more distal branches. –In venous interposition grafting, a shorter segment is exchanged with a reversed venous graft. An important difference between these two approaches is that an interposition graft passes through the injured area, which can otherwise be avoided.

- **Patch.** When a direct suture of arterial defects is impossible due to the extent of the injury, a venous or prosthetic patch can be applied.

- **Direct suture.** Small penetrating defects can be directly over-sewn without risk of narrowing the lumen of the vessel.

- **Direct anastomosis.** Direct circumferential cuts to extremity arteries can be repaired by direct suturing without a graft.
Venous injuries

Venous injuries are sometimes more difficult to handle than arterial ones. They may cause haemorrhage that can lead to shock and even death, and there is also a risk of thrombosis and pulmonary embolus. Isolated venous injuries are probably underreported. Perkins et al found in a large British study isolated venous injuries in only 13% of all vascular injuries admitted to a large trauma centre between 2005 and 2010.16

The incidence is not known due to several factors. Often venous injury is diagnosed in the context of other injuries and not noted or described as well as the arterial ones.17 Dua et al performed a recent nationwide retrospective study and reported that 14% had an isolated popliteal vein injury out of 2216 patients with injury to the popliteal system. Fifteen per-cent had both arterial and venous injury and 71% an isolated popliteal artery injury. They did not find an increased amputation rate associated with vein ligation.18

Historically the treatment of isolated venous injury has been ligation. This is still a way to manage venous bleeding and may be life-saving.19,20 Since the Vietnam War, however, the reconstruction of venous peripheral injuries has increased and is recommended in isolated venous injuries. It is reasoned that repair and open patency may decrease venous hypertension that could lead to increased perfuse bleeding in blunt soft-tissue injuries.17,21 Repair or not to repair is the question. Timberlake et al. concluded that oedema occurred in venous injuries regardless of repair or ligation and that very few patients developed permanent sequelae after isolated venous injury. In combined arterial and venous injury there seem to be more and more evidence for repairing also the vein. Barros described that restauration of venous flow can help keeping the arterial repair open22 and Perkins et al16 concluded a reduction in amputation rates when both vessels were restored. Gifford.et al concluded the same.23

This thesis has focus on arterial injuries and in the material of study I, II a total of ten (out of 53, (19%)) concomitant venous injuries were mentioned in the case records. All except the arteriovenous fistula in study II were minor and could either be left without intervention, or were sutured directly. There were three documented postoperative cases of venous thrombosis, two were associated with pseudoaneurysms. Venous injuries may give similar impairments as persistent or transient oedema that are described after arterial repair in papers I, II and III.
Orthopaedics

Musculoskeletal conditions are relatively common in Sweden. Approximately 20-30% of all visits paid to primary health care physicians are due to musculoskeletal disorders, such as osteoarthritis, back pain, osteoporosis and rheumatic disease. According to Statistics Sweden’s population survey 2012/2013 (ULF/SILC), updated in 2014, 4.6% of the men and 7.1% of the women reported that they had reduced ambulatory capacity, preventing them from running a shorter distance of 100 meters, entering a bus without difficulty, or walking briskly for five minutes.

The consequences of a musculoskeletal disease for the individual are extensive in terms of reduced health and quality of life. Sometimes it also affects the patient’s socio-economic status. Musculoskeletal diseases put demands on health care services and consume a large part of provided health care. They also account for high societal costs of illness. According to statistics from the national social security office, around 23 percent of the persons on sickness benefit in December 2013 this was secondary to a musculoskeletal disease. Orthopaedic acute trauma is added upon the statistics for disease. Trauma is the leading cause of death among people under 60 years of age in the world and accounts for 16% of the global burden of disease.
When a person suffers a serious trauma to the lower extremity, with combined orthopaedic and arterial injury, at some stage the emergency team has to take the strategic decision if to attempt rescue the limb, or to amputate. This decision may be obvious, but in many cases it is difficult to know which treatment is the best, and if an amputation is not performed in the acute phase it can be difficult to perform later on. Previous studies concluded there was no difference in long-term outcome (2-7 years) regarding physical function between patients undergoing reconstruction or amputation. It should be emphasized, however, that these comparisons are not based on randomization, and may be subject to selection bias, as well as other bias. But what about the personal experience of the patient? We were able to identify only four previous studies investigating this issue.

An important clinical injury that involves orthopaedic surgeons as well as vascular surgeons is knee trauma with concomitant popliteal artery injury. The fourth study is on knee dislocation and knee fractures. The incidence of arterial injury in knee dislocation has been debated. Robertson et al estimated the incidence of vascular injury in knee dislocation to be 19% in a review article. Medina et al concluded 18% in another review. Estimates based on retrospective clinical studies carry a severe risk of selection bias, however. In recent studies, based on larger patient cohorts, the estimated incidence estimates are lower: Natsuhara et al reported an incidence proportion of 3.3% and Sillanpää et al 1.6%. The estimates are dependent on the definition of knee dislocations and fractures, and how they are reported in the patient records. The incidence proportion is also depending on how you define the popliteal artery injury. If only surgically repaired injuries are counted the proportion will be lower. Knee dislocations can be difficult to diagnose, since spontaneous relocation is common and the severity of the injury is often underestimated. MRI can diagnose multi ligamentous injury but is seldom performed in the acute situation. The fourth study aims at trying to make an estimate of the incidence proportion based on different denominators. What happens if all ligamentous injuries are added, are some multi ligamentous injuries missed in previous estimates? Knee fractures, especially severe Schatzker (fracture of the proximal tibia) are clinically associated with arterial and nerve injuries, but there are no reliable estimations of their frequency in the literature. Thus, the incidence of arterial injury in knee fractures is practically unknown.

Traditionally it has been thought that arterial injury related to knee dislocations and fractures is predominantly a consequence of high energy trauma, but recently low energy trauma, such as falls from standing height, has also been identified as a common mechanism for arterial injury in knee dislocations. Fall in the morbidly obese was also identified as a risk factor.

Other risk factors have not been studied. Thus, there are no studies including socio economic status or comorbidity as possible risk factors for PAI. If we could predict which patients are at greatest risk to suffer a PAI it
would improve clinical management of these injuries. As PAI combined with knee-trauma is a rare event a large register based study is probably the only way to address this question.

The importance of emergency management of popliteal arterial injuries has been emphasized including to avoid delays in detection and time to revascularisation. Angiography can be a helpful diagnostic tool but can also delay treatment when arterial occlusion is obvious. Sometimes it is better to perform the angiography in the operating theatre and not in the radiology department. Angiography is also an invasive method. Methods as CT-angiography and MR-angiography are being introduced opening new, faster possibilities for detection of vascular injury.

Rationale for the current investigation

The thesis and its studies are derived from authentic questions asked in clinical practice. The rationale was to enlighten and create awareness among colleagues about arterial injuries and their management in lower limb surgery and trauma.

Orthopaedic surgeons will come across this type of injuries in their lifetime but so seldom that they will not acquire sufficient personal experience how to manage them. This thesis handles various aspects of these injuries.

The number of elective surgical procedures in the knee joint is increasing over time in the world. The life expectancy is increasing in most parts of the world and so are demands on high quality of life. Paper I present popliteal injuries in knee arthroplasty, an area where most previous publications were case reports. The registry based study design enabled a larger and population-based investigation.

More patients will probably benefit from a knee replacement in the future. Even though the surgical techniques are improving, the patient population becomes older with combined pathology and concurrent arteriosclerosis. Elective orthopaedic surgery aims are to reduce pain and restore function. In the case of an accidental arterial injury the outcome may be the opposite. If the orthopaedic surgeon can predict risk factors and/or improve measures to quickly detect a popliteal artery injury, outcome in these adverse events may improve.

In traumatic injuries, we do not know how the patients themselves experience their life after a mangled extremity accident. Most studies are quantitative, measuring functional and health-related outcomes with questionnaires. However, do we ask the right questions? Do we treat this group of patients in the best way? Knowing more about these patients’ own experiences can enable us to improve management, to achieve a better long-term outcome. The fourth manuscript is answering the question about incidence of arterial injury in knee dislocation and fracture. This type of injury has always been frightening for physicians on call and the incidence has
been unknown until recently. The incidence in knee fractures is unknown. Risk factors have been debated but not investigated in a population based nationwide context as in this study.

The collaboration between orthopaedic and vascular surgeons is vital for the patients’ outcome in these rare events.

In this thesis four different aspects of lower limb vascular injuries are described. Arterial injury in elective surgery (I and II), acute surgery (II and IV), epidemiological aspects and incidence (IV) and the long-term effects of the injury from the patients’ perspective (III).
Aims

The overall aim of the thesis is to investigate arterial injury in orthopaedic surgery and trauma, in order to improve management of future patients.

The specific aims are the following:

- Describe the frequency and mechanisms behind iatrogenic arterial popliteal injury in orthopaedic surgery and trauma. Study I and II
- Describe management when popliteal artery injury occurs. Study I and II
- Identify potential preventive strategies in the management of popliteal artery injury. Study I and II
- Describe the lived experience of patients afflicted by lower extremity artery injury. Study III.
- Identify areas of improvement in health care management for patients with severe lower limb trauma. Study III
- Estimate incidence proportion and risk factors for popliteal artery injury in orthopaedic knee trauma. Study IV
Methods

Ethics
Ethical approval for all studies was sought and approved by the Research Ethics Committee in Uppsala/Örebro region. In study III there is also an informed consent from all the participants.

Methodological considerations
This work contains various methodological approaches to arterial injuries in orthopaedic surgery and trauma. All studies are based on national registers. The Swedvasc register has been used in all four studies.

Study I, II and III are combined with information from case-records and/or patient interviews. Study IV is an epidemiological study totally derived from registry data. Patients were identified by injury or surgical procedure and the Swedish personal identification numbers (PIN) was used to combine data with various registers. Both quantitative and qualitative research methods were used to get as broad an understanding as possible of these events.

Personal Identity Number (PIN)
Since 1947 every person who remains in Sweden more than a year receives a unique personal identification number and is entered into the Total Population Register. The number consists of ten digits based upon the date of birth and four added numbers where the last is a calculated control digit. Each PIN is unique for one resident in Sweden.

International Classification of Diseases (ICD)-number
ICD is an international classification system that has been in common use since 1964 (ICD-7). Each disease, condition and procedure are given a number that can be used for epidemiological, health management and clinical purposes. In this work ICD 9 and 10 are used.

Swedvasc
The Swedish National Registry for Vascular Surgery, started in 1987. The number of hospitals attached to the registry have rapidly expanded and since 1994 all Swedish hospitals with a vascular service report to the register. Thirteen thousand vascular procedures are performed yearly in Sweden and the registry covers approximately 95% of all performed procedures.
Swedvasc has been validated in several previous studies. In a recent validation performed by international independent investigators data contained within the data fields of Swedvasc and hospital data were identical in 97.4% for carotid artery surgery and 96.2% for abdominal aortic aneurysm surgery. Swedvasc is updated each week regarding survival by cross-matching with the Population registry.

The National Patient Register (NPR), also called the Hospital Discharge Register between 1964-2000, includes somatic and psychiatric hospital discharge diagnosis codes. Gender, date of admission, residency and hospital are recorded. Currently it has a coverage for somatic inpatients of 99%. The NPR also include outpatient visits including day-surgery, since 2001.

LÖF/SPI
All Swedish county councils and regions have taken out patient insurance with Landstingens Ömsesidiga Försäkringsbolag (LÖF, the Swedish Patient Insurance (SPI). Approximately 14 000 patient injuries are reported to the LÖF/SPI each year, and around 40 % of the reported injuries are compensated.

LISA (Longitudinal integration database for health insurance and labour market studies.)
The database presently holds annual registers since 1990 and includes all individuals 16 years of age and older that were registered in Sweden as of December 31 for each year. The database integrates existing data from the labour market, educational and social sectors and is updated each year with a new annual register.

Study I
This study was based on cases from the Swedvasc registry database from 1987 until 2011. The method was quantitative and semi-prospective as the cases were included at the time of vascular surgery and not retrospectively based upon outcome. The ICD-9 and 10 codes were also searched in the LÖF/SPI database. Information from the case-records was registered according to age, gender, surgical procedure, time to detection and outcome. Data was systematically collected by protocol and presented in clusters. The study was population based and nationwide.
Study II
Also this study was semi-prospective and cases from Swedvasc between 1987 and 2011. They were identified by searching the variable iatrogenic injury. All case-records were retrieved from hospitals all over the country and studied by protocol. The study is descriptive in nature as the numbers are small in every sub-group. The cases were clustered into two groups.

Study III
A qualitative research method was used, descriptive phenomenological analysis.\textsuperscript{71,72} The analysis was made according to Giorgi.\textsuperscript{73} The descriptive phenomenological method is derived from Hussler’s theories and the text is condensed into essential meanings. Two researchers have made their analysis individually. The qualitative method is investigating the experiences and social contexts of participants and it is influenced by the investigator.\textsuperscript{74} Therefore the preunderstanding of the investigators was considered thoroughly before the study took place.

The qualitative intent is to \textit{understand} how a patient experience a phenomenon, the quantitative research tries to \textit{explain} it.\textsuperscript{75} Phenomenology describes a phenomenon in the context in which it occurs, -in the patients ”life-world”.\textsuperscript{72,76}

Qualitative research has a long tradition in research fields such as sociology, pedagogics and psychology. It aims to deepen the understanding of lived human experiences which is not possible to study and measure with quantitative methods. During the last years qualitative methods have been introduced in medical research as a complement to quantitative research or as a method to generate new research hypotheses.\textsuperscript{77}
Table 2. Quantitative vs qualitative research differences.\textsuperscript{75}

<table>
<thead>
<tr>
<th>Context</th>
<th>Isolated, well defined task</th>
<th>Whole-sighted, taking context in consideration</th>
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<tbody>
<tr>
<td>Aim</td>
<td>Explain/describe issues</td>
<td>Understand what people think and live</td>
</tr>
<tr>
<td>Researchers role</td>
<td>Independent of researcher</td>
<td>Researcher is central, cannot be replaced</td>
</tr>
<tr>
<td>Research plan</td>
<td>Planned in advance, errors are calculated for and avoided</td>
<td>Depends on data collected. Study may change and develop as it proceeds</td>
</tr>
<tr>
<td>Selection of material</td>
<td>Calculated to give significance</td>
<td>Depend on the phenomenon. “Saturation” or “information power” decides when data is sufficient</td>
</tr>
<tr>
<td>Data</td>
<td>Well defined and validated variables</td>
<td>Analysis and condensation, interpretation and searching themes, essences and meaning</td>
</tr>
<tr>
<td>Quality</td>
<td>Reliability, Internal and External Validity, Objectivity</td>
<td>Dependability, Credibility and Transferability, Conformability</td>
</tr>
</tbody>
</table>

Semi-structured deep interviews were conducted by the main researcher. Four interviews were performed at the Uppsala University Hospital and four in the participants’ homes. The interviews were printed verbatim by a secretary.

Open questions were used (see attachment) in order to get as good a description of the persons experience as possible.\textsuperscript{78} One test interview was performed and evaluated to adjust the questionnaire. This interview was than included in the study.

Analysis: analysis was performed developed by Giorgi 1985.\textsuperscript{73,78}

The interview material was condensed in four steps:
1. Intuitive phase without interpretation
2. Identification of units with essential meaning
3. Interpretation of the units
4. Synthesis of the units to find the essence of experienced phenomenon.
The phenomenon was defined “how do persons afflicted by a severe lower limb trauma with vascular injury experience their situation of life long time after reconstruction or amputation”. The units were identified separately by the main researcher (KB) and the main co-author (EJ). The units were then compared, discussed and agreed upon. Two co-authors were added in step four and discussion was held among the three researchers to reach consensus in the essence of the phenomenon.

Study IV

Study design:

By searching ICD-10 codes and surgical procedure codes in NPR and combine them with information in several other registries we were able to study vascular injury in knee trauma in a population of almost 10 million people during a 17-year period (1998-2014). To identify knee injury, admissions with ICD codes indicating knee dislocation, multi-ligament injury and knee fractures were included. All patients in the National Patient Registry between 1998-2014 cases were selected by injury and cause of injury using ICD-10 codes. The first admission-date for injury was used as index-date.

The cases were combined with information from the Swedvasc registry, Cause of death register, and socioeconomic data from Statistics Sweden. Readmissions and admissions for complications were excluded.

One obvious outcome of interest was subsequent amputation and mortality.

Data management was performed in Microdata ONline Access (MONA, http://www.scb.se/Grupp/Produkter_Tjanster/Forskare/_Dokument/Produktblad_MONA.pdf). This is an environment created to enable cross-matching of different registries using PIN, without threatening patient integrity. Data from the different registries were submitted to this laboratory at Statistics Sweden (Statistiska CentralByrån, SCB). The PIN was replaced by anonymous identity codes and cross matching could be performed. Only aggregated data left the laboratory.

Part of the analysis was to identify potential risk factors for popliteal artery injury associated with knee fractures, multi ligament injury and/or knee dislocation. Potential risk factors, as comorbidity, mechanism of injury, injury severity, and socio economy status were added as covariates. The risk factors were discussed upon beforehand and based on clinical reasoning and available scientific data. A DAG was drawn based on potential risks to form the base for the initial analytical strategy. All hypothesised risk factors in the DAG were not investigated in this study but they may be possible to study in the future.
Previous disease and comorbidity was addressed using Charlson index. Charlson index is a validated index for comorbidity, it adds several morbidities into a score and together with age it is possible to calculate risk of mortality within ten years. Critical evaluation of comorbidity indexes has concluded that Charlson comorbidity index is reliable and predicts mortality well. Weighted Charlson comorbidity index was calculated based on hospital discharge diagnosis for the previous five years.

The International Classification of diseases Injury Severity Score (ICISS) was used as a measure of injury severity. This score has been shown to perform well compared to other injury severity scores. ICISS is calculated from international diagnosis-specific survival probabilities (DSPs) for individual injury ICD codes. The ICISS score for the individual patient was calculated as the product of each of the DSPs corresponding to the patient’s injuries. ICISS strata for descriptive purposes were as previously defined to: critical (0–0.219), severe (0.220–0.354), serious (0.355–0.664), moderate (0.665–0.940), or minor (0.941–1.0).

Cause of injury was categorized from ICD-10 codes, using the cause of injury matrix. It is a recommended way to aggregate external causes for injury into groups based on mechanism and used to investigate measures for injury and accident prevention.

The socio economic status was defined by total family income the year before index-date and educational level was defined as the highest educational level for each individual the same year as index date. Information was collected from the LISA database. Educational level was stratified from a seven level scale down to three, elementary school 1-2, high school 3-4 and university degree 5-7.
Educational level

1) Elementary school less than 9 years
2) Elementary school 9 years
3) High school 2 years or less
4) High school 3 years
5) University level less than 3 years
6) University level 3 years or more
7) Research degree

The total family income was stratified into three groups, low income <250,000 SEK/year, medium 250,000-500,000SEK/year and high income >500,000SEK/year.

The LISA database holds information on individual basis from 1990.

Outcomes were death and amputation. Date of death was retrieved from the CDR (Swedish Cause of Death Registry) and date of first amputation was retrieved from the NPR. Survival estimates were conducted calculating time from index date till death, amputation or end of follow up 31st of December 2014. The association was estimated between PAI injury and amputation free survival using Cox proportional hazards regression. Incidences of different orthopedic injuries were calculated as rates per 1,000,000 population per year. Annual population counts were provided by Statistics Sweden. Incidence of PAI was calculated both as incidence proportion of knee injury and as rates per 1,000,000 population per year. Approximate 95% confidence intervals were calculated for incidence estimates.

The statistical package SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and STATA version 14 (StataCorp, Texas USA) was used for statistical analyses.
Patient selection

Study I and II

From Swedvasc registry all injuries marked as iatrogenic were selected from 1987 to 2011 resulting in 1070 injuries. Then an anatomical selection, the arterial popliteal segment was performed. All case records except five were identified and collected.

![Figure 4. Patient base study I and II](image-url)

- 1070 iatrogenic vascular injuries
  - 115 injuries to the popliteal artery
  - 955 other anatomical locations
  - 57 nonorthopaedic injuries
  - 53 orthopaedic injuries
  - 5 case records not identified
    - 32 after arthroplasty (Study I)
      - 26 primary total knee arthroplasty
      - 1 unicompartment arthroplasty
    - 21 after other procedures (Study II)
      - 5 revision total knee arthroplasty
Study III

Sixteen persons were asked by mail to participate in semi-structured interviews. Thirteen persons were identified through the Swedvasc registry having an arterial reconstruction attempt while suffering an orthopaedic injury in a lower extremity. Three persons were found through the hospital registry for patients attending the Walking rehabilitation centre after major lower limb amputation.

Inclusion criteria were:

1. History of traumatic injury with associated arterial injury resulting in reconstruction or amputation of the lower limb.
2. More than four years after the injury so the person should have adapted to a regular life.

Exclusion criteria were:

1. Not speaking the Swedish language, dementia or other condition that would make interviews impossible.
2. The researcher had treated the patient.

All persons were contacted with a letter and asked to give their consent. (See attachment.) The ones who did not return the consent form were contacted by telephone. Nine persons accepted to participate. Four persons did not answer and did not have an updated telephone number, and thus could not be reached. Three did actively not want to participate. The patients who either did not answer or did not want to participate were contacted again with a questionnaire about the reason why they could not or did not want to participate. Only one person responded, however, that due to psychological fatigue he could not participate.

A great proportion (4/7) of those excluded were excluded because of difficulties in getting in contact with the patient, which is natural several years after surgery. A validation was performed regarding the frequency of amputation within one year (that was present in the Swedvasc registry), and only one of the seven patients that did not participate had undergone amputation within one year, compared to three of the nine who were interviewed.

Study IV

All patients in the National Patient Registry between 1998-2014 cases were selected by injury and cause of injury using ICD-10 codes and surgical procedure codes (Nomesco). The Swedish National Patient Registry (NPR)\textsuperscript{92}
and the Swedish Cause of Death Registry (CDR) were linked using the unique personal identification number provided to all Swedish citizens. All injury hospitalizations from 1998 to 2014 were defined as hospital admissions with a principal diagnosis S00–T80 but excluding T78 (allergy) as listed in ICD-10. Readmissions were excluded on the basis of a validated prediction model.

The first inclusion from NPR was broad, containing all possible surgical procedure codes as well as ICD-10 codes for ligamentous injuries, fractures and popliteal arterial and venous injury. The search was then performed with different settings to see if there was a difference in results for different inclusions.

Figure 5. Case selection study IV

Swedvasc was searched for additional PAI. Swedvasc was upgraded in 2008 and data between 1998–2008 could be searched in Swedvasc version one. During 2008 Swedvasc was divided into several modules. Cases for this study were sought in the modules “Miscellaneous arterial procedures” and “Infrainguinal procedures”. The first selection was by trauma indication. Then they were all identified by anatomical location of reconstruction using “in-flow and “out-flow” as inclusion criteria. (see Appendix 2 study IV)
Results

Study I

Thirty-two patients with iatrogenic popliteal injuries during KA procedures were identified through Swedvasc. (See figure 4). There were 26 primary procedures, 5 revision arthroplasties and one uni-compartment knee arthroplasty (UKA). The overall proportion revision TKA during 1987 and 2011 in Sweden was 7.6%, ⁹⁶ compared to 5/32 (15.6%) among those with PAI.

The median age was 68.8 years (range 48-84) at the time of the orthopaedic operation. There were 23 women and nine men, 18 right and 14 left knees. Eleven of the patients (34.5 %) were described as overweight or obese in the patient records but without a calculated BMI.

There were no immediate deaths and one amputation. All KAs were done by fully qualified surgeons. A tourniquet was used in 23 cases but in several case-records this information was missing.

Figure 6. Number of KAs performed compared with popliteal artery injury.
The presentation of injury varied. All from acute bleeding, compartment syndrome or pseudoaneurysm formation. The most frequent mechanism was penetrating, direct injury to the popliteal artery.

The patients were divided into three groups: immediately detected, in the Operating theatre, detection within 24 hours or detection after more than 24 hours. Seven patients did recover fully, five of these in the group detected and repaired in the OR during the same procedure.

All the others had some sort of sequels at one-year follow up. The most common were sensation of swelling, altered sensation or drop foot.

Study II
There were 21 PAI injuries detected in the Swedvasc patient selection, associated with other orthopaedic surgery than KA. They were divided into two groups: elective and inevitable surgery (trauma and tumours).

Four elective procedures clustered: Arthroscopy, high tibial osteotomy, cruciate ligament reconstruction and tibial tuberosity osteotomy. Mechanism of injury and treatment varied, but best outcome had the patients with immediately detected injury and direct repair of the artery.

In the acute/inevitable group there were different indications for orthopaedic surgery. In this group the mechanism of cerclage wire around the popliteal artery clustered. Patients who had a rapid diagnosis and repair had better outcome. Nine patients had a fasciotomy performed. One patient had an amputation. Six patients recovered fully, four of whom had their injury detected intraoperatively, and repaired by vascular surgeon in the same hospital.
Table 3. Elective orthopaedic procedures.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Age</th>
<th>Type of injury</th>
<th>Repair</th>
<th>Time to repair</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACL</td>
<td>24</td>
<td>Sharp, pseudo-aneurysm</td>
<td>Coiling</td>
<td>7 days</td>
<td>Excellent</td>
</tr>
<tr>
<td>ACL</td>
<td>54</td>
<td>Sharp</td>
<td>Direct anastomosis</td>
<td>7 hours</td>
<td>Pain, loss of sensation</td>
</tr>
<tr>
<td>ACL + PCL</td>
<td>36</td>
<td>Sharp</td>
<td>By-pass</td>
<td>Immediate</td>
<td>Excellent</td>
</tr>
<tr>
<td>ACL screw extraction</td>
<td>32</td>
<td>Sharp</td>
<td>Interposition graft</td>
<td>2-7 hours</td>
<td>Sensory loss</td>
</tr>
<tr>
<td>Tib. tuberosity osteotomy</td>
<td>15</td>
<td>Sharp</td>
<td>By-pass</td>
<td>3 hours to shunt</td>
<td>Excellent</td>
</tr>
<tr>
<td>Tib. tuberosity osteotomy</td>
<td>22</td>
<td>Sharp</td>
<td>Interposition graft</td>
<td>6 hours</td>
<td>Sensory loss</td>
</tr>
<tr>
<td>HTO</td>
<td>42</td>
<td>Sharp, pseudo-aneurysm</td>
<td>Direct suture</td>
<td>30 days</td>
<td>Drop foot, sensory loss</td>
</tr>
<tr>
<td>HTO</td>
<td>40</td>
<td>Sharp</td>
<td>Interposition graft</td>
<td>48 hours</td>
<td>Drop foot, sensory loss</td>
</tr>
<tr>
<td>HTO</td>
<td>63</td>
<td>Sharp</td>
<td>Patch</td>
<td>Immediate</td>
<td>Excellent</td>
</tr>
<tr>
<td>Arthroscopy</td>
<td>44</td>
<td>Sharp, pseudo-aneurysm</td>
<td>Trombin injection</td>
<td>52 days</td>
<td>Excellent</td>
</tr>
<tr>
<td>Arthroscopy</td>
<td>55</td>
<td>Sharp</td>
<td>Patch</td>
<td>26 hours</td>
<td>Nerve injury, sensory loss</td>
</tr>
<tr>
<td>Arthroscopy</td>
<td>52</td>
<td>Sharp, pseudo-aneurysm</td>
<td>Patch</td>
<td>4 days</td>
<td>Swelling, sensory loss</td>
</tr>
<tr>
<td>Arthrodesis</td>
<td>48</td>
<td>Sharp, AV-fistula</td>
<td>By-pass</td>
<td>23 years</td>
<td>Wounds healed</td>
</tr>
</tbody>
</table>

ACL = Anterior Cruciate Ligament  
PCL = Posterior Cruciate Ligament  
HTO = High Tibial Osteotomy  
AV = Arterio-Venous
Table 4. Acute or inevitable procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Age</th>
<th>Type of injury</th>
<th>Repair</th>
<th>Time to repair</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tibial condyle fracture, reop</td>
<td>83</td>
<td>Blunt</td>
<td>By-pass</td>
<td>12 days</td>
<td>Unknown</td>
</tr>
<tr>
<td>Distal femoral fracture</td>
<td>75</td>
<td>Cerclage wire</td>
<td>By-pass</td>
<td>25 hours</td>
<td>Dead within 2 months</td>
</tr>
<tr>
<td>Distal femoral fracture</td>
<td>85</td>
<td>Cerclage wire</td>
<td>By-pass</td>
<td>Immediate</td>
<td>Excellent</td>
</tr>
<tr>
<td>Intramedullary nailing tibia</td>
<td>39</td>
<td>Sharp, pseudo-</td>
<td>By-pass</td>
<td>6 weeks</td>
<td>Sensory loss</td>
</tr>
<tr>
<td>Resection of sarcoma</td>
<td>12</td>
<td>Intimal tear</td>
<td>By-pass</td>
<td>14 days</td>
<td>Necrosis, impairment</td>
</tr>
<tr>
<td>Resection of sarcoma</td>
<td>21</td>
<td>Sharp</td>
<td>By-pass</td>
<td>Immediate</td>
<td>Amputation</td>
</tr>
<tr>
<td>Tibila fracture external fix</td>
<td>53</td>
<td>Sharp</td>
<td>Interposition graft</td>
<td>12 hours</td>
<td>Pain, loss of sensation</td>
</tr>
<tr>
<td>Pathological sub troch fx</td>
<td>67</td>
<td>Sharp</td>
<td>By-pass</td>
<td>1 hour</td>
<td>Dead within 6 months</td>
</tr>
</tbody>
</table>

Study III

Sixteen patients with experience of severe lower limb injury with associated arterial injury were asked to participate in an interview. Nine accepted and participated in individual deep-interviews. One was later excluded due to a registration in Swedvasc for an arterial injury occurring several years before the lower limb trauma he was interviewed for.

Eight interviews with three women and five men were conducted. Three had had their injured limbs amputated and five had a reconstructed limb. Mean age at the time of the injury was 35.5 years. The time since the accident ranged from four to seventeen years. (See table 5).
Table 5. Patient characteristics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age at injury</th>
<th>Mechanism</th>
<th>Reconstruction/amputation</th>
<th>Type of injury</th>
<th>Time since accident</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>49</td>
<td>Motorcycle Blunt</td>
<td>Fem-pop by-pass, fasciotomy</td>
<td>Open tibial condyle fracture, occlusion in popliteal artery</td>
<td>9 years</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>55</td>
<td>Bus Blunt</td>
<td>Fem-distal by-pass, fasciotomy</td>
<td>Open tibial fracture, occlusion in popliteal artery</td>
<td>13 years</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>34</td>
<td>Car Sharp</td>
<td>Ligation, revision of amputation</td>
<td>Traumatic above knee amputation.</td>
<td>15 years</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>37</td>
<td>Bus Blunt</td>
<td>Direct anastomosis + patch, fasciotomy</td>
<td>Multiple soft tissue loss. Intimal tear in popliteal artery</td>
<td>11 years</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>17</td>
<td>Car Sharp</td>
<td>Interposition graft, fasciotomy</td>
<td>Supracondylar femoral fracture, sharp cut of femoral artery and vein</td>
<td>9 years</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>17</td>
<td>Sharp penetrating</td>
<td>A.tib post+ fib ligation, fasciotomy</td>
<td>Severe soft-tissue injury, sharp cut of tibial and fibular arteries</td>
<td>17 years</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>55</td>
<td>Bus Blunt</td>
<td>A.popliteal stent, fasciotomy + amputation,</td>
<td>Multiple tibial fractures and soft tissue injury, occlusion in popliteal artery</td>
<td>4 years</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>29</td>
<td>Motorcycle Blunt</td>
<td>Fem-pop by-pass, fasciotomy + amputation</td>
<td>Multiple tibial fractures and soft tissue injury, occlusion in popliteal artery</td>
<td>15 years</td>
</tr>
</tbody>
</table>

The essence of life after the trauma was described as ‘A life-changing event that foiled existence, daily life and plans, but where disability finally was integrated as part of normal life’. The descriptions that constitute the interviewees’ lived experience resulted in three themes which are presented below, illustrated by direct quotes from the interviews.

1. **An everlasting reminder of physical and cosmetic impairments in daily life with a changed perception of self.**

All of the patients described impaired function in some way. Impairments consisted of fear to fall, pain, numbness, difficulties to fit the prosthesis and worries for the cosmetic appearance.

“I tried to ride my bike when I was in a town with my daughter. We were going to ride to a beach and she had an old bike, but it didn’t work. I got so shaky there was just no way ... that’s hard, too, because I’d really like to do that sort of thing. I used to do it a lot.” (Participant 2)
“I prefer not to wear very short skirts, or shorts – I don’t really want to show my legs. I can’t wear high heels anymore either – before, I practically lived in them – it’s impossible now. Nowadays it’s sensible shoes. I’ve lost a lot of who I was.” (Participant 4)

2. Experiences of decisive encounters, relations and need of interpersonal support

The patients described a change in their close relations. From being independent and maybe even a family provider to be in a wheelchair and in need of daily assistance was a challenge and put relations at stress. Also not being able to take part in for example children and grandchildren’s physical activities was described as troublesome.

“I can’t play with my grandchildren the way I would like to – I can’t run around and play in the woods and fields. I can’t sit down in the sandbox. So certainly I’d like to be more active – you feel like a really old grandma, even though you are not.” (Participant 4)

The patients with reconstructed limbs had wished for more interpersonal support in the transition back to “normal” life. The walking rehabilitation center did provide good support for participants with amputated limbs. Close relatives had to bear a great burden and were not always acknowledged and supported.

“Sometimes I almost think that they took the hard part. At first, when I was in hospital and then, when I came home, before I got the prosthesis – during that period it was almost as if it was worse for them – my partner and her kids – because they’re close by.” (participant 7)

3. The way to ‘normal life’ – and still never the same

Many patients describe a moment or a dialogue that had impact on their recovery or motivation to strive forward.

“First, I was in a wheelchair for a year, and the thing was to get up from the wheelchair. Once I could get up and started to walk, I started to hope that I would be able to go back to work. One orthopaedic surgeon said I could go on working as carpenter. Several doctors in the hospital told me I wouldn’t be able to do that – they talked about all the things I can’t do.” (Participant 1)

Some of the patients described gaining of an insight of fragility of life. Things that had seemed important before the accident had become less important and today’s focus was more on spending time with close family members and fulfill dreams.

“Since then, I’ve developed a new outlook on life: you should seize the day, do fun things, and not just go around and think ‘Should I go there, should I do this or that?’ Yup, and now, I do it. I think about my Dad – he died at 59, and he had so many dreams that he never realized. I have realized many of my dreams.” (Participant 1)
Study IV

We identified 71,310 admissions with at least one of the following: knee dislocation, multiple ligamentous injury, knee fracture, PAI or venous injury requiring hospitalization during 1998-2014. (*ICD and Nomesco codes for inclusion see appendix 2, study IV*). We found 359 admissions with a traumatic popliteal artery injury in NPR. Five more cases were found when merging the Swedvasc dataset with NPR. There were in total 40 registered venous injuries in and 21 were associated with knee trauma. Eighteen were concomitant injuries to both vein and artery.

Two groups of injury patterns were investigated, knee dislocations and knee fractures.

Knee dislocation was addressed by searching all possible surgical procedures and ICD 10-codes associated with ligamentous injury. In total there were 7,308 admissions with possible knee dislocation. It resulted in 49 PAIs. Then the search was narrowed to include at least two combined ligamentous injuries by the Engebretsen definition of knee dislocation, S83.4 and S83.5 combined with the ICD code for knee dislocation S.83.1. It resulted in 46 PAIs. The last search was only the s.83.1 and the same 46 cases of PAI all had this ICD-code.

![Venn diagram](image)

Figure 7. Venn diagram. Proportion of knee dislocations and PAI.

The incidence proportion could be calculated between 3.4% (95% CI 2.5-4.5) to 8.2 (95% CI 6.1-10.8) % depending on the denominator of orthopaedic injuries. (*See table 6*).
Table 6. Incidence of PAI in knee dislocations and fractures

<table>
<thead>
<tr>
<th>Knee injury (definition)</th>
<th>Orthopaedic injury N</th>
<th>Vascular injury N</th>
<th>Incidence proportion % (95% CI)</th>
<th>Incidence/1,000,000/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dislocation only (S83.1)</td>
<td>564</td>
<td>46</td>
<td>8.2 (6.1-10.8)</td>
<td>0.29</td>
</tr>
<tr>
<td>Combination of dislocation and multiligamentous injuries S.83.1 or (S.83.4+S.83.5)</td>
<td>1370</td>
<td>46</td>
<td>3.4 (2.5-4.5)</td>
<td>0.29</td>
</tr>
</tbody>
</table>

Knee fractures

<table>
<thead>
<tr>
<th>Fractures</th>
<th>Orthopaedic injury N</th>
<th>Vascular injury N</th>
<th>Incidence proportion % (95% CI)</th>
<th>Incidence/1,000,000/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal tibial fractures (S.82.1)</td>
<td>25,198</td>
<td>39</td>
<td>0.2 (0.1-0.3)</td>
<td>0.25</td>
</tr>
<tr>
<td>Distal femoral Fractures (S.72.4)</td>
<td>11,283</td>
<td>21</td>
<td>0.2 (0.1-0.3)</td>
<td>0.13</td>
</tr>
</tbody>
</table>
For fractures there were 64,257 admissions with possible knee fracture related IDC-10 codes or surgical procedure. There were 114 arterial injuries. When looking at only ICD-10 codes for proximal tibial fracture (S821) and distal femoral fracture (S724) there were 25,198 and 11,283 respectively in each group. The overlap (both codes) between the groups was 360 admissions (0.6%) that had both codes. The number of PAI was 39 and 21 respectively in each fracture group. The incidence proportion was 0.2% (95% CI 0.1-0.3) for both fracture types.

In total there were 359 traumatic popliteal artery injuries. There were 216 injuries due to other cause than dislocation or knee fracture by our definition.

Fall was the most common cause of PAI injury in knee dislocations and Motor Vehicle Accidents for PAI in knee fractures.

There PAIs with fracture had a more severe trauma according to ICISS. They also had an inferior amputation free survival outcome. (See figure 8.)

Figure 8. Kaplan–Meier curves for amputation or death in the set of 259 patients with popliteal arterial injury by type of injury. The blue line represents non-ligamentous and non-fracture knee injuries, the red line represents fracture injuries, the green line represents the combination of fracture and ligamentous injuries and the interrupted line represents ligamentous injuries alone.
Discussion

The knowledge about popliteal artery injuries in orthopaedic surgery and trauma is limited. In the literature there are only case reports and small case series. The injury is so rare that it is difficult or even impossible to gather many patients and events in one single hospital or region. Thus, registry based studies is the only possibility to create new knowledge in this field.

Paper I and II

The primary aim of the two first studies was to describe the mechanisms behind iatrogenic popliteal artery injuries and to identify possible strategies to prevent poor outcome.

Predisposing risk factors in patient demography were not conclusive. Although in study I eleven patients of 32 had a comment of overweight in their case records, these data were not robust enough to establish obesity as a risk factor for PAI. Since 2009 the Swedish Knee Registry is reporting BMI and this will be interesting to follow in terms of adverse events in the future. Generally speaking, morbid obesity is a risk factor for adverse events after many surgical procedures, and it would expected that this could be case also after knee surgery, as also indicated in a previous study. 99

It has been suggested that a thorough preoperative examination could prevent PAIs. In none of the patients identified in the two studies a preoperative status of the peripheral arteries was performed. It may be possible to detect severe chronic lower limb ischaemia with a preoperative examination, and may be of value to determine whether to perform surgery or not. On the other hand, it is difficult to see how it could prevent injury. Once the injury has occurred, however, the preoperative status is of importance, when evaluating weak or absent pulses. Postoperatively routine control of peripheral pulses when a tourniquet is deflated could probably also be of value, and may enhance the detection of a vascular injury.

In both studies I and II, delay in diagnosis and treatment correlated with poor functional outcome. It seems that when the injury is obvious peroperatively, the long-term prognosis improves. The findings leave no doubt that there is an arterial injury and action is taken. Soft signs and occult bleeding are more difficult to detect. Explanations as arterial spasm may exist delaying the diagnosis.
Traumatic spasm is very rare and the data from this investigation support the conclusion that spasm should not be the first diagnosis when circulation is compromised. In both studies I and II long term outcome was inferior when the patient had to be referred to a nearby hospital.

Sharp injuries dominate in both studies, a finding that is supported by some previous studies, and contradicted by others. Some studies implicate that the use of a tourniquet may inflict arterial injury and should not be used. In these two studies, however, there was not a single observation supporting this theory.

Angiography is a diagnostic possibility when an arterial injury is suspected. It may delay treatment and compromise the outcome, however. In most cases the anatomical position of the injured artery is known, and an angiography may be unnecessary. When it is performed it should preferably be performed within the operating theatre, since moving the patient to the radiology department results in great time loss.

An unexpected large group of patients with pseudoaneurysms were found in study I. They were all detected late and often after several revisits to the out-patient clinic. It seems that the knowledge about the possibility of pseudoaneurysm formation needs to improve among orthopaedic surgeons.

Paper III

Rigour or trustworthiness in qualitative research has been questioned and debated. For many researchers working mainly with quantitative methods the hermeneutic approach is difficult to understand. The methodology was developed in the early 18th century as a response to the mathematically oriented positivism dominating the field of research. The question of rigour in qualitative research must be addressed differently than in quantitative research. Qualitative research aims at a deeper understanding of a phenomenon, not to confirm or reject a hypothesis. Reliability, validity and objectivity will have different meanings in these two research approaches.

Reliability has even been questioned never to be possible to achieve while the study cannot be repeated by other research teams. The term is replaced...
by dependability. Solidity in the analysis, revised by more than one researcher to take in count changes in the study environment.\textsuperscript{107}

Internal validity has been replaced by the term credibility, data shall be transparent, described and findings credible to the reader. External validity is strived for in quantitative research to generalize the results to a broad population. In qualitative research this may not be possible but the equivalent is called transferability. The context of the study is thoroughly described and reader can decide whether the results are relevant in other contexts.\textsuperscript{108,109} (See table 2)

In this study we concluded that great physical and cosmetic impairments are affecting daily life even several years after the initial injury. Long time after the accidents, however, patients described their lives as “normal”.

There are many papers on decision making and outcome, in severe lower limb trauma. Scores as MESS (mangled extremity severity score) are designed to help in the acute situation whether to amputate or save a limb but when validated they are concluded not very helpful in the acute management.\textsuperscript{110,111} Quality of life and outcome after severe lower limb injury has been investigated and poor results even long time after the incident were reported\textsuperscript{31,33} We found only two previous studies in the literature where the patients themselves state their situation.\textsuperscript{34,36}

Many studies on quality of life may report exaggerated negative results, however, due to their design and scales.\textsuperscript{112} Shauver et al\textsuperscript{36} also concluded the paradox that despite severe impairments, the participants express satisfaction with their lived lives. This study confirms that observation.

One of our main findings was the lack of inter-personal support in the post hospitalization phase, that many of the patients experienced. This matter is dealt with in other areas of medicine such as among survivors after trauma or cancer.\textsuperscript{113,114} In the acute phase of injury the focus is on physical, which is adequate, but as the time passes the persons are left on their own to adapt to a new life.\textsuperscript{115} We found that the patients with follow up at the Walking rehabilitation centre stated better inter personal support in the transition back to normal life. Even though qualitative research does not claim to draw conclusions of comparison between two groups, this finding may result in better follow up routines for patients with reconstructed limbs.

The sample size in qualitative research has been debated\textsuperscript{116} and we stated that “saturation” was achieved after eight interviews. No more vital essence changing information was thought to be added by adding more interviews.

The participants with amputated limbs expressed satisfaction with the decision taken to amputate their limbs, and the persons with reconstructed limbs were glad their limbs had been saved. Regardless of treatment all participants had some sort of physical impairment such as pain, balance problems, recurrent pressure wounds from the prosthesis and/or cosmetic issues. Although the decision helping score tools does not seem to work, we think we know in clinical praxis quite well when to amputate and when not to.
This study may help to defuse the great anxiety regarding the decision making process. Irrespective of the chosen treatment, it is important to follow a decided path and provide sufficient support in rehabilitation and transition back to “normal” life.

Paper IV

The incidence proportion of PAI among knee dislocation patients in our study ranged from 3.4% to 8.2% depending on how a knee dislocation was defined. Natsuhara et al\textsuperscript{39} reported a similar frequency while Sillanpää et al reported an incidence proportion of 1.6%.\textsuperscript{40} The incidence of arterial injury following knee dislocation has been debated. Robertson et al estimated the incidence of vascular injury in knee dislocations to be 19%,\textsuperscript{37} and Medina et al concluded the incidence to be 18%.\textsuperscript{38} There may be selection bias as previous studies often are conducted in trauma referral centres. The estimates are dependent on the definition of knee dislocations and fractures, and how they are reported in the patient records. We tried to include all diagnosed PAIs, partly explaining the higher incidence compared to Sillanpää’s estimation. One important methodological problem is the difficulty in defining knee dislocation. We hypothesised that there would be a lower incidence when including multiligamentous injuries but this was not the case. Most PAIs associated with ligament injuries in our study were due to falls. Traditionally it has been thought that arterial injury related to knee dislocations and fractures is predominantly a consequence of high energy trauma. This is probably based on the same selection bias as the incidence reports from trauma referral centres. Recently however, low energy trauma, such as falls from standing height, have also been identified as a common mechanism for arterial injury in relation to knee dislocations.\textsuperscript{37,40,117} This is confirmed in this thesis.

The incidence of PAI in knee fractures was low and PAI associated with knee fracture was more frequent in men. Motor vehicle accidents were the dominating cause of PAI in knee fractures and on average more severely injured which may explain the more adverse patient outcomes in terms of survival and amputation after fractures, compared to the outcomes after knee dislocations.

PAI with fall as the primary mechanism was practically unseen which probably depends on the age distribution.

Venous injuries in general

Venous injuries are not high-lighted in the literature. The venous injuries in this thesis, presented in study I and II were identified in patient records and probably represent a correct occurrence. In study IV there were only 40 in
the entire study population. The incidence of venous injuries in trauma has been estimated to be 13% in association with arterial injury. The low numbers in study IV reflects that venous injuries probably are poorly reported and registered.
Strengths and limitations

The main strength of this work is the large population based design, that it is contemporary, and the fact that multiple well validated registries could be used in a cross-linked design, since all of the registries use the same PIN.

The NPR registry is well documented and validated, and the Swedvasc registry contains a large number of patients, and 95% of all vascular procedures are reported. As it started in 1987 the follow-up time is relatively long and the study design is a semi prospective cohort design. Swedvasc has also been validated on several occasions and has been found to have a more than 90% external validity in all those validations.

The limitations are incomplete reporting to the Swedvasc as is the fact that it did not include all hospitals until 1994. The National Patient Registry had a full coverage already in 1987.

Another limitation is the reporting of risk factors in the case records that form the base of study I and II. Preoperative risk factors such as smoking, BMI, etc. are infrequently reported and therefore we could not draw any conclusions regarding these potential risk factors. The documentation of pre- and postoperative information differ and depend upon the individual doctor. The more recent the injury, the better the documentation, old case reports are often very limited in information. This makes the two first studies more descriptive in their nature.

The limitation of the third study is the missing participants. Out of sixteen identified persons only nine were interviewed and one of them later excluded. Only one missing participant answered upon repeated mails and telephone calls. This may result in a selection bias if only persons with a positive attitude or a better functional outcome participated. It was possible, however, to study the number of amputations within one year, using data from the Swedvasc registry, and there was no trend towards more amputations among those not participating, rather the contrary.

Another limitation is that the phenomenon is investigated in a Swedish setting, which may limit the generalizability of the results in an international context. The strength with the third study is the strict methodology and analysis. The fact that all the interviews were performed by one single person also strengthens this investigation. Other strengths are the independent analysis by two researchers with continuous discussion and consensus upon meaning bearing units and the trustworthiness that is validated by the direct quotations.
The limitations of Paper IV are the limitations of all register based studies. The results depend on the reporting and how correct it is. Even though NPR and Swedvasc are well validated we do not know the exact reporting for knee injuries or vascular injuries. When we merged the datasets from Swedvasc and NPR and correlated the operation date with index date in NPR there were only five more cases with arterial injury added which means that NPR is very complete. Another limitation is the difficult definition and diagnosis of knee dislocation and how the diagnose or repair is coded in the NPR. This is a problem of everyday orthopaedic surgery, since in the emergency room it may be very difficult to know if the knee was dislocated at the time of injury or not. In order to identify not only the obvious dislocations, but also the spontaneously reduced ones, we also analysed the ICD-codes for combined ligament injuries as well as the possible surgical procedure codes.

Engebretsen et al have defined knee dislocation as the rupture of three major ligaments 43 and in other studies it is defined as rupture of at least two major ligaments. The combination of multiligament injuries used in this investigation covers all multiple ligament injuries.

Another limitation is the amputation outcome. We cannot know if the amputation is performed on the traumatized limb from registry data, since the registration of the side (right/left) is incomplete in the Inpatient registry. It may be assumed, however, that these often young patients had the injured extremity amputated, especially when amputation is close in time after the injury. The longer time has elapsed from the time of accident, the more uncertain this correlation becomes. The study covers a time-period of seventeen years and other reasons such as arteriosclerosis or diabetes can be the underlying reason for amputation later during follow up.
Conclusions

– The frequency of iatrogenic popliteal artery injury has not increased significantly over time despite an increased frequency of elective knee arthroplasties. One third of all popliteal artery injuries in knee arthroplasty consisted of pseudoaneurysms and the most common mechanism is direct penetrating injury to the artery.

– Time to detection and management of acute popliteal artery injury is crucial for outcome. Access to a vascular surgeon close to the location of PAI improves outcome.

– Time can be saved by transferring the vascular surgeon to the patient if injury occurs in a setting without vascular surgeon. Applying a shunt can be recommended when delay in circulatory repair is expected.

– Physical, psychological and cosmetic impairment remain several years after a severe lower limb trauma. Despite this many patients cope with their limitations and describe life as “normal” and are mainly satisfied.

– Among patients with lower extremity trauma with associated vascular injury the interpersonal support in the rehabilitation process can improve. Family members bear a great burden, and should be acknowledged and supported.

– The incidence proportion of popliteal artery injury in knee dislocation ranges between 3.4-8.2% depending on the denominator of included knee injuries. Fall is the most common cause of PAI in knee dislocation, and MVAs in PAI in knee fractures.
Further research

This thesis focuses on lower limb and knee-injuries. There are many other anatomical locations that would be interesting to investigate in the same manner, using large databases and registers. Fractures and fixation of the clavicular bone is one example, vascular injuries during spine surgery is another.

The patient records from the patients with arterial injury from study IV would be interesting to study. This way mechanisms behind the arterial injury, the role of angiography, and amputation as well as other outcomes could be understood.

The patient’s experience of a vascular injury has now been studied but an interesting point of view is what the orthopaedic surgeons in study I and II experience. Iatrogenic injuries are devastating also for the surgeon. Is the outcome dependent of their reactions to the adverse event?

The third study has focus on the lived experience of the injured person. We concluded that family members had to bear a great burden. It would be interesting to investigate their experiences in a qualitative study.
Sammanfattning på svenska

Livet som ortoped är meningsfullt och oftast roligt. Ibland kan man dock behöva handha svåra fall, där en lyckad utgång inte alltid är given. Till svåra fall räknas skelett och ledskador där även kärlförsörjningen är skadad. I värsta fall orsakar man själv en sådan skada när man försöker reparera något annat.

Kärlskador är fruktade och lyckligtvis sällsynta. Men när de inträffar kan de ge upphov till svåra reststillstånd och eller resultera i amputation. Arteria Poplitea ligger anatomiskt i knävecket och är den enda större artär som för blod ner till underbenet. När denna blir skadad stängs underbenets enda tillförande blodförsörjning av och handläggning måste ske skyndsamt.

Eftersom skadorerna är sällsynta finns i den vetenskapliga litteraturen sparsamt med tillförlitlig information om uppkomst, handläggning och resultat. Oftast finns endast enstaka fall rapporterade. Detta gör att det även blir svårt för den enskilda kirurgen att veta hur man bäst tar hand om en kärlskada i benet. Ingen ortoped, hur länge han eller hon än jobbar kommer att kunna få någon egen erfarenhet eftersom antalet fall är så få.

I den här boken försöker jag med hjälp av svenska stora register som täcker in hela befolkningen under flera års tid samla in så stora material det är möjligt att få. Registerstudier är ett bra sätt att undersöka sällsynta sjukdomar och skador på. Sverige har unika personnummer som gör att man kan hitta registrerade skador, sätta ihop olika databaser och register för att kartlägga i detta fall kärlskador.

Avhandlingen behandlar kärlskador i ortopedin ur flera olika vinklar:

‒ Av sjukvården orsakade (iatrogena) artärskador vid planerad och akut ortopedi (delarbete I och II)
‒ Akuta skador med komplicerande kärlskada (delarbete IV)
‒ Patientens eget perspektiv (delarbete III)

Dessutom har jag använt mig av flera olika metoder:
– Beskrivande kartläggning av iatrogena skador med hjälp av journalgenomgång och registerdata från Swedvasc och LÖF
– Epidemiologisk registerbaserad studiemetodik med sammanslagning av många olika register men inga journaler eller kontakter med patienter.
– Kvalitativ metod, djupintervjuer med personer som drabbats av en olycka med kombinerad skelett och kärlskada, lång tid efter olyckan.

Delarbete I

Antalet personer i världen som får en ny knäled (knäprotes) ökar stadigt. En sällsynt men fruktad komplikation är artärskada i samband med operationen. I delarbete I finns beskrivet världens största material av a. popliteaskador i samband med knäprotesoperation. Trettiotvå fall har identifierats ur Swedvasc och analyserats. Slutsatsen var att de kärlskador som upptäcktes och reparades inom några timmar hade bra prognos och att sent upptäckta skador till stor del bestod av pseudoaneurysm, (falskt pulsåderbråck), som uppkommit genom en litet stickhål på kärlen. Detta var ny kunskap som kan ge vägledning åt ortopeder vars knäprotesoperade patienter fortsätter ha besvär med svullnad i knäveck efter operation.

Delarbete II

I Sverige utförs mer och mer planerad ortopedi också i privat regi. Korsbandskirurgi, operation för knäskålssluxation, tittålsoperation i knä och omvinkling av knäleden på grund av artros. I delarbete II har frekvensen av a. popliteaskador i samband med dessa ingrepp kartlagts. Dessutom beskrivs kärlskada i samband med akut eller oundvikliga ingrepp såsom fraktur- eller tumörkirurgi. Denna typ av skada visade sig vara oerhört sällsynt, men med mycket svåra konsekvenser för de flesta patienter som drabbades. Även här handlade det om tid till upptäckt och hur skadan hanterades när den väl påvisats. En lärdom var att återställa cirkulationen med en så kallad shunt visade sig framgångsrikt liksom att skicka kärlkirurgen till patienten istället för tvärtom.

Delarbete III

I denna studie genomförde jag åtta djupintervjuer med personer som drabbats av benskada med komplicerande kärlskada. Fem hade fått sitt ben räddat med olika kärlkirurgiska ingrepp och tre hade fått benet amputerat. Djupintervjuerna analyserades metodiskt enligt deskriptiv fenomenologisk metod utvecklad av A. Giorgi och resultatet beskrevs som tre samlade essenser.
En upptäckt var att alla hade upplevda fysiska hinder i sin vardag av något slag men ändå beskrev sina liv som ”normala”. Den kosmetiska upplevelsen var av större vikt än man kunnat ana särskilt för de som fått behålla benet. De beskrev också en upplevd brist på interpersonellt stöd under rehabilitering och anpassning till livet efter skadan. En lärdom är att längre tids och tätare uppföljning avseende stöd vore av värde för denna grupp och att även anhöriga måste uppmärksamas och stöttas.

**Delarbete IV**

Knätrauma kan ge fraktur men det kan också resultera i att knät går ur led. Dessa skador är allvarliga och kan ge skada på poplitea artären. Dock är det ingen som vet hur vanligt det är med kärlskada vid dessa diagnoser. I studie IV försökte vi fastställa händelseforekomsten (incidensen) genom att kombinera Swedvasc och det svenska patientregistret. Då graden av våld och andra faktorer kan ha betydelse för uppkomst av artärskadan tittade vi också på skademekanism, tidigare sjuklighet, skadegrad i övrigt (skallskada, buktrauma etc) samt socioekonomiska faktorer. Vi undersökte också utfallet efter artärskada i form av död och amputation.

Slutsatserna var:
- Antalet knäproteser ökar men inte antalet kärlskador.
- Det kan vara bättre att skicka kärlkirurgen än patienten vid en upptäckt artärskada på ett sjukhus utan kärlkirurg.
- Pseudoaneurysm (falska pulsäderbråck) utgör en tredjedel av alla artärskador efter knäproteskirurgi
- Sjukvården måste ge bättre medmänskligt stöd under längre tid till personer som drabbats av extremitetsskada med kärlpåverkan.
- Incidens proportionen för kärlskada vid knäledsluxation ligger mellan 3,4 och 8,2 % och fall är den vanligaste skademekanismen. Trafikolycka är den vanligaste orsaken till artärskada vid knäfraktur.
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All participants in study III

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Peyman Bakhshayesh, Västerås
Anders Wykman, Helsingborg
Olle Svensson, Umeå
Ola Rolfsson, Göteborg
Ylva Bodén, Mälarsjukhuset
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Olle Sammeli, Mora
Ingvar Jansson, Mälarsjukhuset
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John, Kara and Tore, my most beloved children. You always contribute with energy, happiness and love. You are the perfect distraction when thoughts are blurred.
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77. al GTe. An open letter to The BMJ editors on qualitative research. *BMJ* 2016;352:i563


Appendix 1 Study III

Interview guide
Life after a severe lower limb injury

1. Please describe how you experience a regular day?
   a. Morning
   b. Evening
   c. Night

2. Can you tell me how you experience life with/without your leg?
   a. Socially, family and friends
   b. Home activities
   c. At work
   d. Hygiene
   e. Hobbies
   f. Sleep
   g. Intimacy

3. What do you remember of your hospitalization, memories?
   - Memories about decision whether to rescue or amputate the leg?
     a. Doctors
     b. Relatives and friends
     c. Someone else

4. Tell me about the time after your hospitalization?
   a. Acute/rehabilitation?
   b. Support?
   c. What would have helped you?
   d. Need of support today?

5. How do you experience your lived situation today?

6. Something else you want to tell me?

7. How does it feel to talk about this?
Information och förfrågan om deltagande i en intervjustudie om detivet efter en extremitetsskada.


Vad innebär studien för dig?

Vad ska resultatet användas till?
Inom sjukvården finns idag god kunskap om hur viss benfunktion kan återskapas genom exempelvis operationer och proteser. Kunskapen är däremot begränsad om hur personer upplever livet efter en omfattande extremitetsskada. Studien kan ge oss vägledning om hur sjukvården kan förbättras både när det gäller de avgörande akuta besluten men också om hur eventuellt fortsatt stöd från sjukvården kan förbättras. Resultatet kommer att återföras i utbildning för läkare och sjuksköterskor och också presenteras i en vetenskaplig rapport.

Deltagandet är frivilligt.

Vilka är ansvariga för studien?

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## Appendix 2 Study IV

**NPR**

<table>
<thead>
<tr>
<th>ICD-10 codes for Knee dislocation</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.83.1  Knee dislocation</td>
</tr>
<tr>
<td>S.83.5  Cruciate ligament in combination with</td>
</tr>
<tr>
<td>S.85.4  Collateral ligament</td>
</tr>
</tbody>
</table>

**Codes for Knee dislocation surgery**

- NGH00  Closed reduction of knee joint
- NGH01  Arthroscopic reduction of knee joint
- NGH02  Open reduction of knee joint

**Combinations**

- NGE21  Arthroscopic suture or replantation of ligament in knee joint
- NGE22  Open suture or replantation of ligament in knee joint
- NGE41  Arthroscopic ligament reconstruction in knee joint without allograft
- NGE42  Open ligament reconstruction without allograft
- NGE51  Arthroscopic ligament reconstruction in knee joint with allograft
- NGE52  Open ligament reconstruction with allograft

**ICD codes for knee and close to knee fracture**

- S72.40  Lower femoral fracture (closed)
- S72.41  Lower femoral fracture (open)
- S82.10  Upper tibial fracture (closed)
- S82.11  Upper tibial fracture (open)

**Codes for knee and close to knee fracture surgery**

- NGJ09  Closed reduction of fracture in knee or lower limb
- NGJ19  Open reduction of fracture in knee or lower limb
- NGJ29  External fixation of fracture in knee or lower limb
- NGJ49  Fixation of fracture in knee or lower limb with cerclage wire, pin or like
- NGJ59  Fixation of fracture in knee or lower limb with intramedullary nail
- NGJ69  Fixation of fracture in knee or lower limb with plates and screws
- NGJ79  Fixation of fracture in knee or lower limb with only screws
- NGJ89  Fixation of fracture in knee or lower limb with other method
- NGB49  Total knee replacement
### Popliteal artery injury from NPR

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.85.5</td>
<td>Popliteal artery injury</td>
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#### Surgery for popliteal artery injury

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>PFH20-29</td>
<td>Bypass from femoral or popliteal artery to lower limb artery</td>
</tr>
<tr>
<td>PEH 30</td>
<td>Bypass from femoral or popliteal artery to below knee</td>
</tr>
<tr>
<td>PEW99</td>
<td>Other surgery on femoral artery or branches to popliteal artery</td>
</tr>
<tr>
<td>PFA10</td>
<td>Exploration of popliteal artery</td>
</tr>
<tr>
<td>PFB10</td>
<td>Ligation of popliteal artery</td>
</tr>
<tr>
<td>PFC10</td>
<td>Suture of popliteal artery</td>
</tr>
<tr>
<td>PFE10</td>
<td>Trombendectomy or embolectomy on popliteal artery</td>
</tr>
<tr>
<td>PFN10</td>
<td>Angioplasty on Popliteal artery</td>
</tr>
<tr>
<td>PFQ10</td>
<td>Endovascular stent in popliteal artery</td>
</tr>
<tr>
<td>PFS10</td>
<td>Endoscopic surgery on popliteal artery</td>
</tr>
<tr>
<td>PFQ19</td>
<td>Other surgery from femoral artery to infrapopliteal arteries and lower limb</td>
</tr>
</tbody>
</table>

### Popliteal vein injury from NPR

<table>
<thead>
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<th>Description</th>
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</thead>
<tbody>
<tr>
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<td>Popliteal vein injury</td>
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#### Amputation

<table>
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<tr>
<td>NGQ19</td>
<td>Amputation below knee</td>
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<tr>
<td>NGQ09</td>
<td>Amputation through knee</td>
</tr>
<tr>
<td>NGQ99</td>
<td>Other amputation at knee or below knee</td>
</tr>
<tr>
<td>NFQ19</td>
<td>Femoral amputation</td>
</tr>
<tr>
<td>NFQ99</td>
<td>Other amputation at femoral level</td>
</tr>
</tbody>
</table>
**Swedvasc:**


| Selection 1 | Indication 1, 2 and 3 | 37, 38 blunt and penetrating injury |
| Selection 2 | ANAINH or ANAINV | 11, 12, 19, 21, 15 |
| Selection 2 | ANAUTH or ANAINV | 20, 25, 26, 28, 36 |

**From Swedvasc 2 (2008-2014) Traumatic Popliteal artery injury**

<table>
<thead>
<tr>
<th>Modul “Övrig artär”</th>
<th>variable</th>
<th>Value</th>
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<tr>
<td>Selection 1</td>
<td>Huvudindik or biindik</td>
<td>19, 20 blunt and penetrating injury</td>
</tr>
<tr>
<td>Selection 2</td>
<td>Inflowdx or Inflowsin</td>
<td>7001, 7011, 7201, 6101, 7101</td>
</tr>
<tr>
<td>Selection 2</td>
<td>Outflowdx or Outflowsin</td>
<td>7301, 7401, 7501, 7601, 7701, 7801</td>
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<table>
<thead>
<tr>
<th>Modul “Infrainguinal”</th>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selection 1</td>
<td>Indik</td>
<td>2 Acute Ischemia</td>
</tr>
<tr>
<td>Selection 2</td>
<td>Proximal</td>
<td>7001, 7002, 7011, 7012, 7101, 7102, 7201, 7202</td>
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<tr>
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<td>Distal</td>
<td>7301, 7302, 7401, 7402, 7501, 7502, 7601, 7602, 7701, 7702</td>
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A doctoral dissertation from the Faculty of Medicine, Uppsala University, is usually a summary of a number of papers. A few copies of the complete dissertation are kept at major Swedish research libraries, while the summary alone is distributed internationally through the series Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine. (Prior to January, 2005, the series was published under the title “Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine”.)