Periprosthetic femoral fracture after total hip replacement

Incidence, risk factors and treatment

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«Μέτρον ἄριστον»
“Lagom är bäst”
(Moderation is best)

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ABSTRACT

ABSTRACT

Periprosthetic femoral fracture (PPFF) is the third most common reason for reoperation in Sweden, after a primary total hip replacement. It is associated with poor patient satisfaction postoperatively, increased mortality and high costs. In most cases, the treatment is surgical and the type of surgical method depends on the type of fracture. Although there are a large number of studies on PPFFs, most of them include comparatively few cases, selected fracture types or selected treatment modalities, which means that there is a large risk of bias. This thesis investigates the incidence of surgically treated PPFFs in Sweden between 2001 and 2011, the demography of this population, risk factors that may contribute to its occurrence, and the treatment of these fractures. All four studies in this thesis are observational and are based primarily on material from the Swedish Hip Arthroplasty Register (SHAR) database. This database was linked with data from the National Patient Register (NPR) in two stages and with the Swedish Knee Arthroplasty Register. Data were extracted from both the SHAR database and medical records.

In Paper I, the data link between the SHAR and the NPR revealed a high registration rate for reoperations that include revisions of the femoral stem and low registration in cases where other treatment methods were applied. Fractures distal to the stem of a hip prosthesis were almost four times more common than primarily recorded in the SHAR. The incidence of PPFFs increased in Sweden during the study period, with higher incidence in individuals older than 80 years. Paper II showed that the force-closed design of the cemented Exeter stem was a high risk factor (HR=9.6) for fractures close to a hip stem (Vancouver type B) when compared with the shape-closed Lubinus SP II cemented stem. However, stem design did not affect the risk of fractures distal to it (Vancouver type C). Age, gender, diagnosis and calendar

year at primary THR also influenced the risk of PPFF. The surgical treatment and the outcome of fractures close to a femoral component were studied in Paper III. Vancouver type B1 and interprosthetic femoral fractures (IPFF) ran a higher risk of a poor outcome in cases with cemented stem fixation and primary osteoarthritis at the index operation. The type of plate fixation preferred in B1 fractures did not influence the outcome, whereas the choice of ORIF (open reduction and internal fixation) instead of stem revision in B2/B3 fractures resulted in a poorer outcome. Similar re-reoperation rates were recorded for cemented and uncemented modular or monoblock revision stems in the treatment of fractures close to a loose stem (Vancouver type B2/B3). Paper IV studied the treatment of and outcome for femoral fractures distal to a hip prosthesis. The four most common treatment methods were fixation with one conventional plate, one locking plate, two plates, or an intramedullary nail. Locking plates had a lower re-reoperation rate within two years of the PPFF, when compared with conventional plates in patients without an ipsilateral knee prosthesis. Interprosthetic fractures did not have significantly different re-reoperation rates compared with non-IPFFs. Within two years of the surgical treatment of a Vancouver type C fracture, 24% of the population had died. The re-reoperation rate for all B and all C fractures was 17.3% and 15.2% respectively (Papers III and IV).

In conclusion, periprosthetic fractures treated with methods other than stem revision had a low registration rate in the SHAR. The incidence of this complication increased in 2001-2011. The force-closed design of the cemented Exeter stem involved a 10 times higher risk of Vancouver type B fractures than the Lubinus SP II stem. The presence of an ipsilateral knee prosthesis was a risk factor for poorer outcome in type B but not in type C fractures. The type of plate fixation in B1 and the type of revision stem in B2/B3 fractures did not affect the outcome. Locking plates had a better outcome than conventional plates in the treatment of type C fractures.

SAMMANFATTNING

SAMMANFATTNING (SUMMARY IN SWEDISH)

Fraktur i anslutning till stammen på en höftprotes (PeriProtesFemurFraktur- PPFF) är den tredje vanligaste orsaken till reoperation efter primär total höftprotesoperation i Sverige. Risken för denna komplikation är högst hos äldre individer. Frakturen är förknippad med hög mortalitet, innebär höga kostnader och resulterar ofta i låg grad av patientnöjdhet. Behandlingen är i majoriteten av fall kirurgisk och varierar beroende på frakturtypen. Flera studier av dessa frakturer har publicerats men majoriteten av dem inkluderar jämförelsevis få fall och ofta endast specifika frakturtyper eller behandlingsmetoder, vilket ökar risken för bias. Denna avhandling undersöker incidensen av kirurgiskt behandlade PPFF i Sverige mellan 2001 och 2011, demografi, riskfaktorer samt behandling. Alla fyra studier i avhandlingen är observationella, och primärt baserade på material från Svenska Höftprotesregistrets (SHPR) databas. En samkörning utfördes med Svenska Knäprotesregistret och två med Patientregistret (PR). Dessutom genomfördes en journalgranskning av alla i delstudierna ingående fall.

I Delarbete 1, efter samkörningen mellan SHPR och PR fann vi att SHPR hade en hög täckningsgrad för reoperationer utförda med stamrevision, medan täckningsgraden för frakturer som behandlades med annan metod än revision var dålig. Fraktur distalt om femurstammen var nästan fyra gånger vanligare än vad som primärt registrerats i SHPR. Incidensen av PPFF ökade i Sverige under studieperioden, med högre incidens hos individer äldre än 80 år. Delarbetet 2 visade att patienter opererade med den polerade Exeter stammen (force closed design) hade knappt tio gånger större risk (HR=9.6) att drabbas av fraktur runt protes-stammen (Vancouver typ B) jämfört med Lubinus stammen (shape closed). Frakturer distalt om protesstammen (typ C) var dock lika vanliga i båda grupperna. Ålder, kön, diagnos och kalenderår vid primär höftprotes påverkade också risken för PPFF. Kirurgisk

behandling och utfall efter fraktur runt en protes-stam studerades i Delarbete 3. Vancouver typ B1 och inter-protesfraktur mellan en höft- och en knäprotes (IPFF) hade högre risk för dåligt utfall bland individer som opererats med cementerad stam på grund av primär artros vid indexingreppet. Typ av plattfixation påverkade inte utfallet vid behandling av B1 frakturer, medan val av intern fixation i stället för stamrevision vid B2/B3 frakturer gav sämre resultat. Frekvensen av reoperationer efter en första reoperation på grund av PPFF (re-reopertion) skiljde sig inte signifikant mellan val av cementerad och ocementerad revisionsstam vid behandling av fraktur runt en stam som var lös (Vancouver typ B2/B3). I delarbetet 4 studerades behandling och utfall efter femurfraktur distalt om en höftprotes. De fyra vanligaste metoderna var fixation med en konventionell platta, en vinkelstabil platta, två plattor, eller intramedullär spik. Vinkelstabila plattor hade lägre re-reoperationsfrekvens inom två år från PPFF, jämfört med konventionella plattor hos patienter utan ipsilateral knäprotes. Re-reoperationsfrekvens skilde sig inte signifikant mellan IPFF och icke-IPFF. Tjugofyra procent av populationen med en Vancouver typ C fraktur avled inom två år från frakturdatum. Re-reoperationsfrekvens, under hela observationstiden, för alla B och alla C frakturer var 17,3% respektive 15,2%.

Sammanfattningsvis fann vi att periprotesfrakturer behandlande med annan metod än med stamrevision hade låg registreringsgrad i SHPR. Incidensen av PPFF ökade under perioden 2001–2011. Den polerade Exeter stammen hade knappt 10 gånger högre risk för Vancouver typ B frakturer, jämfört med Lubinus SP II stammen. Samtidig förekomst av en knäprotes på fraktursidan innebar ökad risk för sämre resultat vid typ B men inte vid typ C fraktur. Val av vinkelstabil eller konventionell platta påverkade inte utfallet vid behandling av B1 fraktur. Val av stamfixation påverkade inte heller utfallet vid behandling av typ B2/B3 fraktur. Vinkelstabila plattor hade bättre resultat än konventionella plattor vid behandling av typ C fraktur..

LIST OF PAPERS

LIST OF PAPERS

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

I. Chatziagorou C, Lindahl H, Garellick G, Kärrholm J. Incidence and demographics of 1751 surgically treated periprosthetic femoral fractures around a primary hip prosthesis. *Hip International.* 2019 May; 29(3): 282-288

II. Chatziagorou C, Lindahl H, Kärrholm J. The design of the cemented stem influences the risk of Vancouver type B fractures, but not of type C: an analysis of 82,837 Lubinus SPII and Exeter Polished stems. *Acta Orthopaedica.* 2019 April; 90(2): 135-142

III. Chatziagorou C, Lindahl H, Kärrholm J. Surgical treatment of Vancouver type B periprosthetic femoral fractures. Patient characteristics and outcomes of 1381 fractures treated in Sweden between 2001 and 2011. *The Bone & Joint Journal.* 2019 November; 101-B: 1447-1468

IV. Chatziagorou C, Lindahl H, Kärrholm J. Lower reoperation rate with locking plates compared with conventional plates in Vancouver type C periprosthetic femoral fractures: A register study of 639 cases in Sweden. *Injury.* 2019 December; 50(12): 2292-2300

ABBREVIATIONS

ABBREVIATIONS

AO	Arbeitsgemeinschaft für Osteosynthesefragen
ABP	Angle blade plate
ASA	American Society of Anesthesiologists
BMD	Bone mineral density
BMI	Body Mass Index
CI	Confidence interval
CP	Conventional plate
DB	Double plating
DCS	Dynamic condylar screw
DM	Diabetes mellitus
FHN	Femoral head necrosis
FNF	Femoral neck fracture
HA	Hemiarthroplasty
HHS	Harris Hip Score
ICD	International statistical classification of diseases and related health problems
IMN	Intramedullary nail
IPFF	Interprosthetic femoral fracture
KVÅ	Klassifikation av vårdåtgärder
LCP	Locking compression plate
LISS	Less invasive stabilisation system
LP	Locking plate
NARA	Nordic Arthroplasty Register Association

NCB	Non-contact bridging
NHS	National Health Service
NPR	National Patient Register
OA	Osteoarthritis
OPCS	Office of population censuses and surveys - Classification of intervention and procedures
ORIF	Open reduction and internal fixation
OTA	Orthopaedic Trauma Association
PPFF	Periprosthetic femoral fracture
PR	Patientregistret
PROM	Patient related outcome measures
RA	Rheumatoid arthritis
RCT	Randomized control trial
SFR	Swedish Fracture Register
SHAR	Swedish Hip Arthroplasty Register
SHPR	Svenska Höftprotesregistret
STROBE	Strengthening the reporting of observational studies in epidemiology
THA	Total hip arthroplasty
THR	Total hip replacement
TKR	Total knee replacement
UCS	United classification system

1. INTRODUCTION

INTRODUCTION

Between 2010 and 2015, approximately 16,000 primary total hip replacements (THR) were inserted every year in Sweden.[1] The incidence was expected to increase to 18,000 THRs in 2020 and to 20,000 in 2030,[2] but in 2017 as many as 18,148 primary hip replacements had already been registered.[3] According to the latest annual report, the incidence of THRs in individuals aged 40 years and older was 360 per 100,000 inhabitants.[4] The prevalence of THR in the total US population was 0.83% in 2010,[5] i.e. around 2.5 million individuals had a hip prosthesis that year. It is estimated that the demand for primary THRs in the United States will grow to more than half a million by 2030.[6] One complication of hip replacement surgery is periprosthetic femoral fracture (PPFF), which is a fracture of the femur around or distal to a hip prosthesis. It may occur during the insertion of a prosthesis (intraoperative), or later (postoperative). The majority of postoperative fractures occur after a fall from standing height[7-9] and are mostly seen in patients aged 70-90 years.[7, 10] The treatment of a PPFF is usually surgical and the surgical method depends on the type of fracture.[11] These fractures are associated with high complication and mortality rates.[9, 12-14] A large proportion of patients are unable to return to their previous activity level although the fracture has healed.[15] The level of patient satisfaction is relatively low after the treatment of a PPFF[16, 17] and the costs are comparatively high.[18, 19]

2. BACKGROUND

BACKGROUND

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2.1 Types of total hip replacement

At a primary total hip replacement (synonym: total hip arthroplasty, THA), the hip joint is removed and replaced with prosthetic components. The prosthesis consists of major and minor components. The major components are the cup, which replaces the cartilage surface of the acetabulum, and the stem, which replaces the proximal part of the femur (Fig. 1). The number of minor components can vary depending on prosthetic design. Examples are a modular femoral head, a modular liner, or screws for the additional fixation of a metallic cup shell. In a conventional THR, the major components are fixed to the bone either by using cement or cementless. In the latter type, different methods, such as press-fit fixation, use of a screw-in function, additional pegs or screws or other measures, may be used to achieve primary stability. When cement is used for the fixation of both parts, the THR is called cemented, while uncemented (or cementless) THRs are fixed without cement (Fig. 2a-b). A THR is called hybrid when only the stem is cemented and reverse hybrid when cement is only used for the fixation of the cup (Fig. 2c). Another type of THR is the resurfacing arthroplasty, where only the articular surfaces of the acetabulum and the femoral head are resected, which means that most of the proximal femoral bone can be retained. During the last two decades, this type of THR was exclusively designed as metal-on-metal articulation. Today, this design has been almost completely abandoned because of a higher risk of revision when compared with conventional THRs.[20, 21] In contrast to a total hip replacement, a hemiarthroplasty (HA) is restricted to only one major part – the stem, which can be cemented or uncemented. Hemiarthroplasties are mainly used to treat the oldest and most frail population with femoral neck fractures, although the indications for these prostheses may vary. Hemiarthroplasties are supplied with a fixed or movable head, where the outer diameter should match the inner diameter of the acetabulum, as accurately as possible, to minimise cartilage wear.

In a conventional THR, the stem is placed into the medullary canal of the femur after the surgeon has resected the femoral head. The neck of the stem is either exchangeable (minor component)

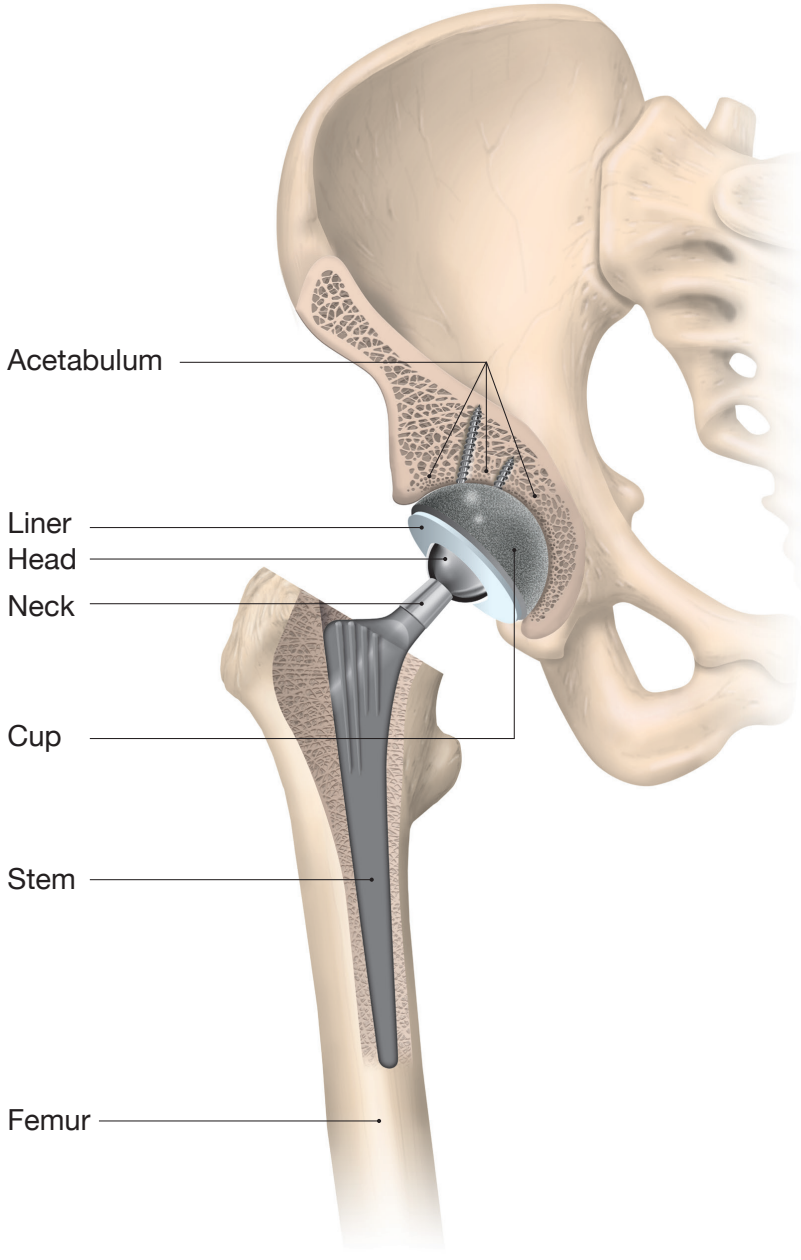

Figure 1. Major and minor components of a conventional total hip replacement.

Figure 2. Types of conventional total hip replacement: **(a)** cemented, **(b)** uncemented, **(c)** hybrid.

or fixed to the stem. Because of higher complication rates with exchangeable (modular) necks,[22, 23] stems with fixed necks are more commonly used in primary THRs. In the vast majority of cases, the femoral head (minor component) is modular, i.e. it is attached to the stem during the operation. A monoblock stem corresponds to an implant, where the femoral head has already been attached to the stem during manufacture. In this thesis, revision stems are labelled modular if the proximal and distal parts of the stem are assembled during the operation (e.g. the MP, Restoration, Revitan stem) and a modular head is fitted to the proximal modular body of the stem. These stems thus have three parts. Solid revision stems with a modular head are called monoblock. The reason for this choice of terminology is that true monoblock stems with a fixed head are no longer used in Sweden.

Uncemented cups are regularly of the modular type with a separate metal shell which is fitted with a liner during the operation. Cemented cups are typically of monoblock design, even if a few modular cemented cups and also a few monoblock uncemented cups are available. Some cups have two articulations, one between the fixed metal shell and a mobile liner and the second between the femoral head and the liner, which are assembled during the operation using a "snap-fit" mechanism. These so-called Dual Mobility cups (also termed Tripolar cups) are thought to be more stable than standard cups and are used for patients with an expected increased risk of dislocation.

2.2 Design of cemented stems

The cemented fixation of the femoral stem has a long tradition in Sweden, with two stem types dominating since the SHAR began prospectively registering primary procedures on an individual basis in 1992. These stems are the Lubinus SP II and the Exeter stem. Together, they

Figure 3. The Lubinus SP II primary hip stem. Anteroposterior view (left) and lateral view (right).

have constantly accounted for more than half the total number of stems that have been used in Sweden since 1992 and, in 2018, they constituted 56% of all stems used in primary THRs.[4] Their design is totally different and they are representatives of two main cemented designs; the composite beam or shape-closed design (Lubinus, Waldemar LINK GmbH & Co. KG, Germany) and the loaded taper or force-closed design (Exeter, Stryker Howmedica, Mahwah, NJ, US). The Lubinus has an anatomic s-shape and is made of CoCrMo (cobalt-chromium-molybdenum) alloy. It is collared and has a matte finish and a 19° built-in anteversion of the femoral neck (Fig. 3). The Exeter stem is a force-closed, straight, collarless, double-wedge tapered, highly polished stem of stainless steel (Fig. 4). These two stems represent two totally different principles of achieving fixation and stability in the femoral canal. Force-closed stems do not bond to the cement and are designed to subside into the cement mantle as a wedge, while shape-closed stems resist rotational stability due to their anatomical shape that fits into the proximal femur and distal migration is restricted because of the collar. While the subsidence of a force-closed stem is a fundamental principle of achieving stability, stability is required for good long-term results in shape-closed stems. The Lubinus is reported to have a mean distal migration

Figure 4. The Exeter Polished primary hip stem. Anteroposterior view (left) and lateral view (right).

of 0.03mm two years after index operation and no further subsidence 10 years postoperatively,[24] while the Exeter stem can be expected to subside 0.7 mm at two years and to continue to subside to a mean of 1.2mm up to 10 years after the primary operation.[25]

2.3 Design of uncemented stems

Several studies have attempted to classify uncemented stems into different design categories.[26, 27] The size of an uncemented design category of stems may vary from very short, which accomplish fixation within the collum-calcar or the metaphyseal region,[28] to stems that ex-

tend as far distal as into the metaphyseal region of the distal femur.[29] Most uncemented stems, however, have a length of about 13 to 16 centimetres for the sizes most commonly used. Uncemented stems are often classified as straight, anatomic, curved, tapered and cylindrical, according to their shape. Stems may be tapered in one, two, or three planes. They can also be classified based on the presence of a cross-sectional rounded, splined or rectangular shape. More complicated shapes are found in the modular stems mainly used in the revision situation. In these stems, the proximal part could be wedge shaped, conical or rounded and the distal part rounded, wedge shaped, straight or slightly curved. A collar support may or may not be used and some designs are available with both options. The surface characteristics of the uncemented stems used today can be roughly divided into porous or grit blasted. These surfaces may be coated with different types of ceramic regularly made up of hydroxyapatite, occasionally mixed with other types of phosphonate.[30]

At the end of 2011, approximately 13% of all primary stems in Sweden were uncemented, with six designs (Corail, CLS-Spotorno, Bi-Metric, ABG-II, Accolade, Wagner Cone) accounting for 93.4% of these stems.[31] The variation in the design of uncemented stems was greater compared with the variation in cemented stems, where only three components (Lubinus SP II, Exeter Polished, MS30) accounted for 97.6% of all uncemented stems. The small number of uncemented stems used in Sweden up to 2011 and the large diversity of uncemented stems would jeopardise a detailed analysis at brand level in this thesis and they have therefore not been studied in depth.

2.4 The swedish hip arthroplasty register (SHAR)

The SHAR has prospectively collected data on all operations related to THRs since 1979.[32] The SHAR divides the types of surgical procedure into two main categories, the primary or index operation and the reoperation. Primary is defined as the very first operation with a total hip replacement, while reoperation includes all the operations that can be related to the primary THR, irrespective of whether or not the prosthesis or parts of it remain untouched. Revision is a subcategory of reoperation, where at least one component has been extracted or exchanged during surgery. Reoperations were registered in detail from the very beginning, whereas primary THRs, implants and surgical technique were reported for each hospital until 1991. Since 1992, personal identity numbers have also been recorded for primary THRs, as well as age, gender, diagnosis at the time of the primary operation and implant char-

acteristics. Successively, more parameters like surgical incision, antibiotics peri-operatively, type of cement, BMI (Body Mass Index), ASA class (American Society of Anesthesiologists physical status classification system)[33, 34] and patient reported outcome measurements (PROMs) have been included.[35] Complications after hip replacements treated non-surgically are not registered in the SHAR. This means that superficial infections treated with antibiotics, close reductions for hip dislocations, or periprosthetic fractures treated with immobilisation are not registered in the SHAR.

All orthopaedic departments, both public and private, that perform hip replacement surgery report to the register (100% coverage). The completeness (proportion of registered procedures of all procedures performed in reality) was as high as 90% for revisions during the period 1987-1995.[36] The reporting of primary hip arthroplasties is almost complete (98%) and revisions are now registered with a slightly higher completeness than before (93%).[3] The reporting of reoperations has always been poorer.[37, 38] It is not known how many of the reoperations due to a PPFF are registered in the SHAR (completeness). Lindahl et al. assumed that the Vancouver type C fracture was probably specifically underreported, because it might be regarded as unrelated to the implant and therefore not registered by several departments.[7]

2.5 The national patient register (NPR)

The NPR holds information on all in-patient care since 1987 and all out-patient care since 2001.[39] This means that even non-surgically treated fractures are registered. It is expected that the registration of periprosthetic fractures in the NPR approaches 100% and this is certainly better than in the SHAR. This is mostly due to the fact that reporting to the NPR is compulsory. Registration takes place using ICD-9 and ICD-10 codes (International Statistical Classification of Diseases and Related Health Problems – 9th and 10th Revision). In cases where surgical treatment has been performed, the KVÅ (Klassifikation av vårdåtgärder, Classification of health measures) coding system is also used.[40] KVÅ corresponds to the OPCS (Classification of Intervention and Procedures) of the NHS (National Health Service) in the UK.[41] Each department receives various amounts of financial compensation, partly depending on the type of diagnosis and treatment, based on ICD and KVÅ codes. Unreported cases are not compensated, which can result in a significant loss of income, not least for cases treated surgically because of PPFF. One important disadvantage of this register is that laterality is not reported systematically, something that is obligatory for each registration in the SHAR and SFR (Swedish Fracture Register).

2.6 The swedish fracture register (SFR)

The SFR is a relatively new nationwide register, to which all fractures in all extremities and in the spine are reported.[42] This register started in 2011 by registering only tibial and humeral fractures in adults and only at one department, but had in 2018 expanded to cover about 80% of all orthopaedic departments in Sweden. The completeness of each department varies between 75% and 95%.[42] The registration is web based and fractures are classified according to the AO/OTA classification system.[43] Periprosthetic fractures have been registered since 2015 and are classified according to the United Classification System (UCS).[44, 45] Some of the reported parameters are mechanism of trauma, date of trauma and treatment onset, as well as details regarding the treatment method (plate, nail, screw, revision of stem etc.). The unique feature of the SFR is that even non-surgically treated fractures are registered. Periprosthetic fractures around a hip replacement are reported in the SHAR, the NPR and the SFR. In all three of these national registers, each case is registered with the patient's personal 12-digit identity number, in which the first eight digits are the patient's date of birth and the 11th digit indicates the patient's gender. In this thesis, data from the SHAR and the NPR were used.

2.7 The reporting of PPFFs in registers abroad

Although suffering from a certain degree of incompleteness, the reporting of all kinds of reoperation to the SHAR can be regarded as an advantage. Thanks to cross-matching with the SFR and repeated validation processes, the completeness of these recordings can be expected to improve. The reporting of all kind of reoperation and not only of revisions will provide a better and more complete insight into the type of complications that will actually occur. In a review of annual reports from national and regional arthroplasty registers, excluding the SHAR, it is noted that all registers, apart from two, the Norwegian and the Portuguese, report only revisions. The Norwegian Arthroplasty Register started in 1987 and, during the entire period until now, primary and revision THRs were reported. The first and only case of osteosynthesis of fracture was reported in 2014. Since then, 35 reoperations without revision were registered in 2016 and 45 in 2017.[46] The completeness was 97% and 90% respectively, in the registration of primary THRs and revisions. The Portuguese Arthroplasty Register was officially started on 1 June 2009 and the first annual report was published in 2010. Since 2013, no further annual report has been published, while the coverage and the completeness are unknown.[47] Reop-

erations were reported as "other reoperation besides revision", but no specific reference to periprosthetic femoral fractures was made. Apart from national registers, there are many registers that only include a region of a country and registers of institutions. Perhaps the oldest "institutional" arthroplasty register, with a long tradition of publishing studies of periprosthetic hip fractures, is the one at the Mayo Clinic in the USA. This institution does not publish annual reports, but it has prospectively collected data relating to all hip replacements inserted in this clinic and subsequent complications since 1969. Furthermore, there is access to radiographs and to medical charts of periprosthetic fractures treated non-surgically. Reports on periprosthetic fractures have also been published from material based on collaboration between four national joint arthroplasty registers, the Nordic Arthroplasty Register Association (NARA).[48, 49] The participating countries are Denmark, Finland, Norway and Sweden and revision is the main outcome measurement.[20]

2.8 Classification of periprosthetic femoral fractures

2.8.1 Previous classification systems

Several classification systems for postoperative periprosthetic femoral fractures have been presented. The first was introduced by Parrish and Jones in 1964 when they reported nine cases of PPFF.[50] They classified the fractures in relation to the anatomical region of the femur. Ten years later, Whittaker et al. classified 20 fractures depending on their relationship to the trochanteric region (intertrochanteric or distal to the lesser trochanter) and whether the distal part of the stem was inside or outside the medullary canal.[51] In Belgium, van Elegem & Blaimont divided the fractures in relation to their position corresponding to the proximal, mid, or distal third of the femur.[52] The fractures of the proximal third were located around the femoral stem but could also exceed distal to it. During the 1980s, five classification systems were published, with four of them sorting the fractures depending on the location of the fracture in relation to the femoral stem. Johansson et al. classified the fractures into type I, if the fracture was proximal to the stem tip, type II, if the fracture was around the distal part of the stem and extending distal to it, and type III, if the fracture was entirely distal

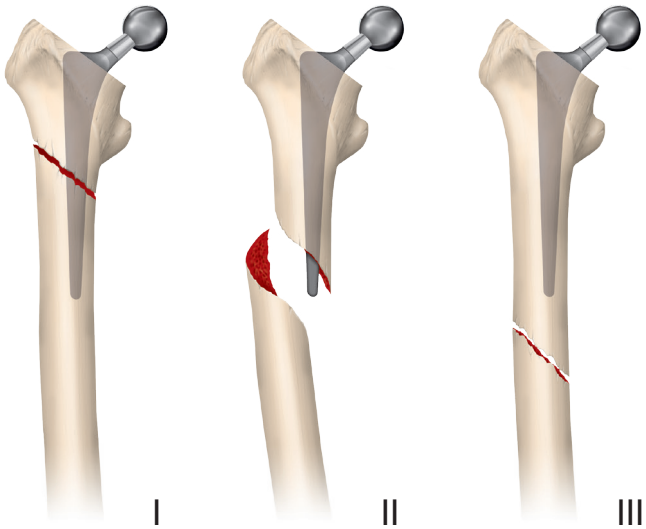

Figure 5. The Johansson classification of periprosthetic femoral fractures.

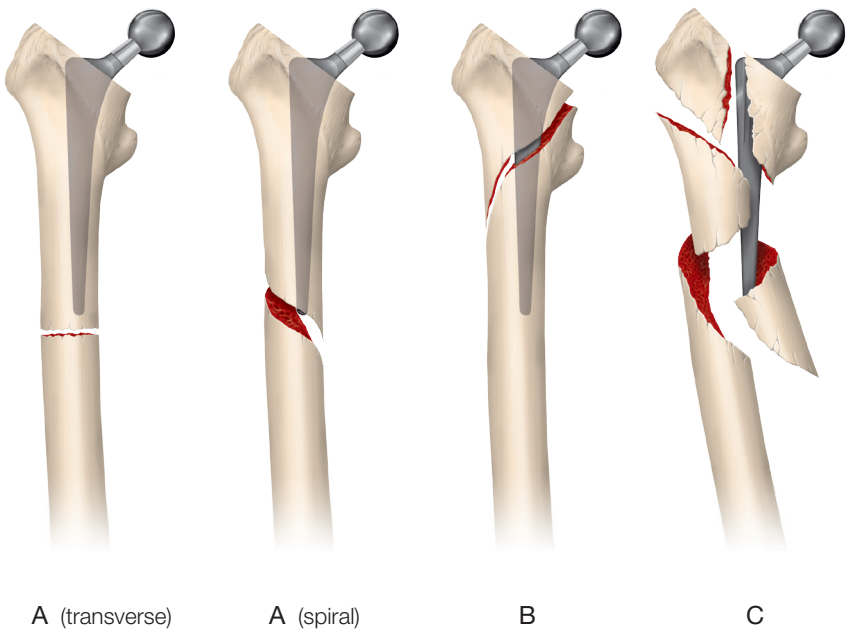

Figure 6. The Bethea classification of periprosthetic femoral fractures.

to the stem (Fig. 5).[53] This classification system was actually used by Jensen et al. who only clarified that type I included fractures around the proximal two thirds of the stem.[54] Interestingly, they focused on the role of stem stability in relation to treatment. The authors suggested revision arthroplasty with a long stem when the stem was loose. Bethea et al.[55] categorised the fractures into type A, when the fracture was at the tip of the stem, type B, when the fracture line extended around the stem, and finally type C, if there was comminution in a fracture proximal to the stem tip (Fig. 6). Six years later, Cooke & Newman published a modification of the Bethea classification system.[56] The authors added a category for fractures entirely distal to the prosthesis (type 4) and divided the fractures into unstable transverse fractures at the tip of the stem (type 3) and stable oblique or spiral fractures around the stem (type 2). Type 1 included comminuted fractures around the stem. The fifth and simplest classification system, published during the 1980s, grouped the fractures into two categories depending on whether the stem was well-fixed or loose.[57] Two classification systems used the location of the fracture in relation to both the stem and the anatomical regions of the femur. The main difference between them is that one has a separate category for comminuted fractures,[58] whereas the other defines two subcategories; one with less than and one with more than 25% disruption of the stem – cement or stem – bone interface.[59] Gonzalez et al.[60] divided the fractures depending on the stability of the fracture and the prosthesis. In type A, both the fracture and the stem were stable, while, in type B, only the fracture was stable. Both the stem and the fracture were unstable in types C and D, with the latter having inadequate bone stock.

2.8.2 The Vancouver classification system

In 1995, Duncan and Masri introduced the Vancouver classification system (Fig. 7).[61] This classification takes account of the fracture site in relation to the prosthesis, stem stability and the quality of the bone around the stem. This system has been validated in both Canada and Europe[62, 63] and it is now used worldwide. It divides the fractures into three types. In type A, the fracture is an avulsion of either the greater trochanter (A_G), or the lesser trochanter (A_L). Most of these fractures are treated non-surgically. Fractures that occur around or just below the stem belong to type B, while fractures that are well below the stem tip are classified as type C. Type B fractures are further divided into three subcategories: B1, B2 and B3. The femoral stem is stable in B1 and loose in the B2 and B3 subcategories. The B2 and B3

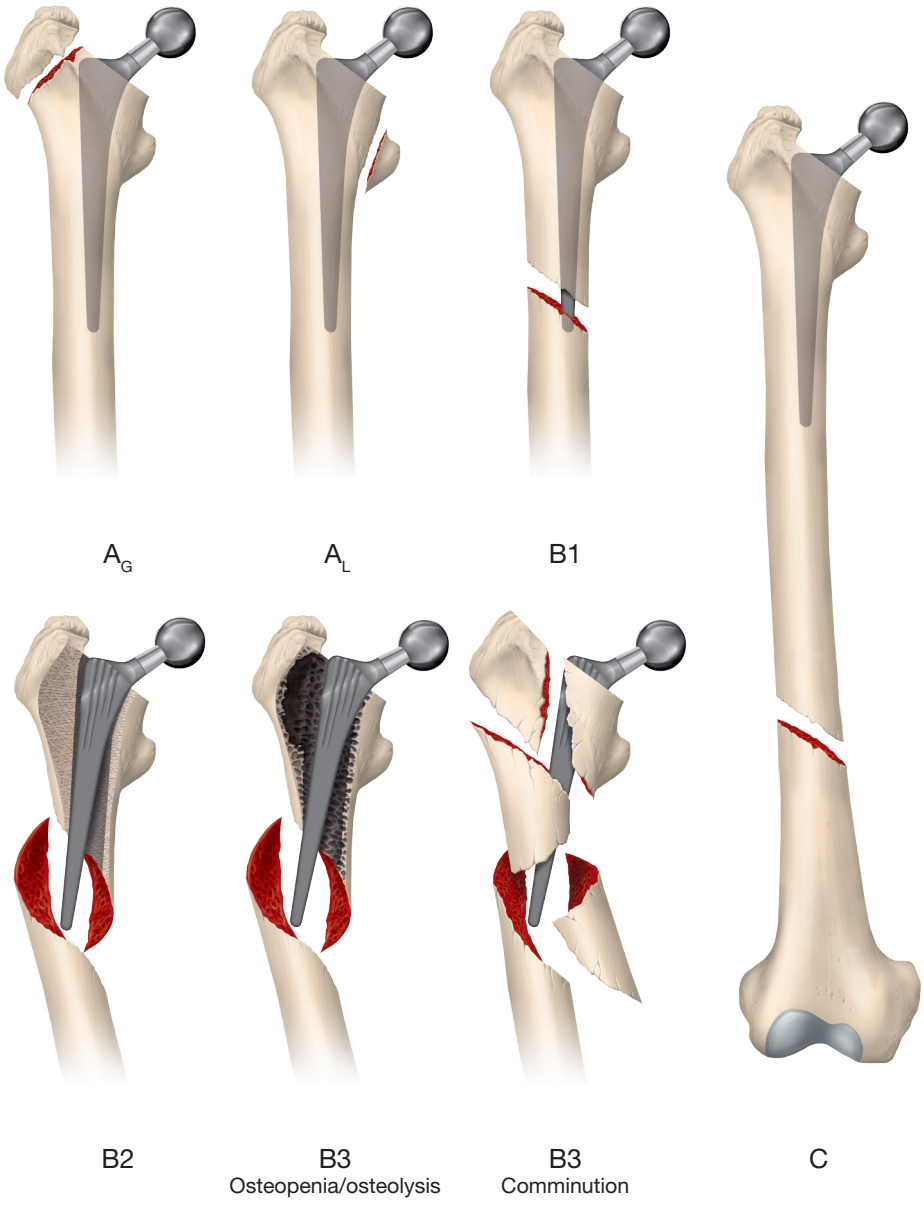

Figure 7. The Vancouver classification system for periprosthetic femoral fractures.

differ in terms of bone loss. In type B2, the bone is sufficient to support a new standard revision stem, whereas, in B3, there is severe loss of bone stock, due to gross osteolysis, osteopenia or fracture comminution. Type B3 fractures often require complex reconstruction with a long, distally anchored revision stem and bone transplantation. Both type B and type C fractures are treated surgically, while, in almost all cases of type C fractures, revision of the stem is not necessary.

The main advantage of the Vancouver classification system is that it incorporates guidelines for choice of treatment. It has some weak points, however. The distinction between a well-fixed stem (B1) and a loose stem (B2), based on the pre-operative radiographs, is not always easy. Corten et al.[64] showed that 20% of the fractures evaluated as B1 pre-operatively proved to have a loose stem during the operation. Moreover, the border zone between adequate and inadequate bone stock surrounding the stem is not well defined. This parameter is partly influenced by the projections and quality of the radiographs and varies between surgeons, depending on their personal subjective estimation. In addition to this, there is no distinct demarcation of the anatomical limit between the B and C fracture types. It is said that type C fractures are so remote from the stem that they can be treated independently from the prosthesis, but this definition can be interpreted differently between surgeons.

2.8.3 Modifications of the Vancouver classification system

Subsequent to the Vancouver classification, some "new" classification systems have been introduced.[65-67] In reality, however, they have mostly attempted to resolve the difficulty in order to determine objectively whether the stem is well-fixed or loose (B1 or B2 fracture type

Figure 8. The "pseudo A_L" or "clamshell" fracture is a B2 fracture that can be falsely classified as a fracture of the lesser trochanter (A_L).

respectively). The "Coventry" classification takes account of the clinical symptoms and pre-operative radiographs, before the fracture occurred.[65] They divide the PPFFs into "happy" and "unhappy" hips and suggest revision of the stem in the latest group. Baba et al.[66] attempted objectively to classify the fractures around the femoral stem, based only on the fracture pattern and the type of the stem. They reported high interobserver agreement compared with previous validations of the Vancouver classification system.[62, 63] According to their classification, the stem has to be loose if the fracture is observed in the femoral region where the stem is expected to have firm bonding. This region is around the coated surface of an uncemented stem and around the cement mantle in a cemented stem. The Unified Classification System (UCS) is a combination of the Vancouver classification for periprosthetic fractures and the AO/OTA classification for fractures in general. [43, 45, 68, 69] The UCS resulted from the aim of developing a common classification system for all periprosthetic fractures in all extremities and for both total and hemiarthroplasties. It extends the Vancouver classification by taking account of the presence of an ipsilateral knee replacement. Houwelingen & Duncan clarified the difference between a type A_L fracture and the "pseudo A_L".[70] The former is an avulsion of the lesser trochanter, while the latter is actually a B2 fracture that begins in the lesser trochanter region and extends medially and distally, involving the medial cortex of the proximal femur (Fig. 8). This type of fracture (pseudo A_L) has also been called "the new B2",[70] or "clamshell" fracture.[71, 72]

A more complicated classification system was proposed by Frenzel et al.,[73] who combined the Mont & Maar,[58] Vancouver[61] and AO/OTA classification systems. The authors took account of six parameters: i) skeletal section, ii) implanted prosthesis, iii) segment, iv) prosthesis stability, v) time point of fracture occurrence and vi) bone structure. So, a Vancouver B3 fracture close to an uncemented revision hip stem would be classified as 3-H-U-1-C-3-L-3-III. Huang et al. extended the Vancouver B category by introducing a subcategory that describes the presence or absence of a femoral stem fracture.[67] Three years later, the authors proposed a modification of the UCS classification system, where they incorporated the stem fracture and the pseudo A_L fracture.[74] Finally, in an attempt to describe fractures related to old cup endoprostheses, resurfacings and thrust plate prostheses, Fink et al. [75] proposed an extension of the Vancouver classification that has not been widely reported in the literature, probably because these types of hip replacement are no longer in use.

2.9 The interprosthetic femoral fracture and its classification

Interprosthetic fractures of the femur (IPFF) are fractures that occur between a hip and a knee replacement (Fig. 9). This category includes not only fractures located in the implant-free part of the femur but also fractures close to either the hip, or the knee arthroplasty, or both. Since the purpose of the Vancouver classification was to describe femoral fractures related to a hip stem, it did not refer to femoral fractures between a hip and a knee replacement. Some authors described these fractures by combining the Vancouver classification with other established classification systems for fractures close to a TKR.[76, 77] The first people to describe a classification system for IPFFs were Fink et al.,[75] by extending the Vancouver classification with the Latin numeral "I", to indicate the presence of an IPFF, and the letters A or B, to denote whether the TKR is a surface replacement (IA) or a stemmed one (IB). In order to specify whether the implants were well fixed or loosened, they added the numbers 1 and 2 respectively. Soenen et al.[78] found that six of eight IPFFs in TKRs with a femoral extension stem had a poor outcome, compared with six IPFFs close to a surface TKR where none failed. They therefore proposed an extension of the Vancouver classification with a D category, which represents the fractures between a prosthesis and a stemmed knee prosthesis. Platzer et al. used a modification of the Vancouver classification in order to describe the treatment of 22 IPFFs.[79] They divided the IPFFs into three main categories to illustrate whether the fracture was adjacent to one of the prostheses (type II), to none of them (type I), or to both of them (III). The subcategories A, B and C were used to demarcate whether both implants were stable (A), unstable (C), or only one of them was loosened (B). Sub-

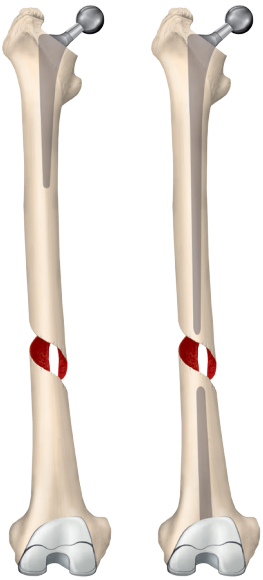

Figure 9. Interprosthetic femoral fracture close to: (a) a primary standard hip stem and a femoral component of a total knee replacement and (b) a long revision hip stem and a TKR with a stemmed femoral component.

type B was additionally divided into B1 (loose hip stem) and B2 (loose femoral component of the TKR). In the author's opinion, this classification system is useful in describing the increasing degree of fracture severity by increasing the category (I to III) and by increasing the subcategory (A to C). Pires et al. classified IPFFs based on the fracture site, the implant stability and the viability of the interprosthetic bone fragment.[80] In spite of this, this classification system demonstrated poor inter-observer agreement (fair to moderate).[81] Last but not least, the UCS classification system,[45, 68] which is a combination of the AO/OTA classification of fractures and the Vancouver classification, uses the letter D to delineate the presence of an IPFF and then describes the fracture separately for the hip and the knee joint.

2.10 Intraoperative and postoperative fractures

Fractures that occur during the insertion of a femoral stem are called intraoperative periprosthetic fractures. They may be detected during the primary surgery or on the postoperative radiographs. The decisive difference from postoperative femoral fractures is that these fractures are iatrogenic and occur during the operation. Another important difference is the appearance of the fracture and the treatment protocol. Different classification systems for intraoperative periprosthetic fractures have therefore been proposed.[82] This thesis has only studied postoperative fractures of the femur around or distal to a conventional total hip replacement.

2.11 Risk factors for PPFF

A periprosthetic fracture is a devastating complication, which demands high surgical skills. These fractures frequently occur in the frail elderly who are prone to fall, which could be one explanation of the comparatively high mortality rate. It is therefore important to understand the complexity of these fractures and to study the factors that predispose to their occurrence. This will facilitate any prevention and could optimise their treatment should they occur. The identification of strong risk factors could potentially reduce the incidence of PPFFs by choosing the appropriate surgical method at the primary THR. When this research project started, at the end of 2011, little was known about the risk factors for postoperative PPFF. According to the literature, elderly patients [83, 84] and individuals with a diagnosis of femoral neck fracture (FNF) or rheumatoid arthritis (RA) had a higher share of periprosthetic fractures.[7] Gender was not a clear risk fractor.[83, 85, 86] Higher PPFF rates were noted in cases with a previous history of stem revision than in pa-

tients with a primary stem[7, 84, 87] and the presence of a loose stem was also known to increase the risk of a periprosthetic fracture.[7, 88] The Mayo Clinic reported slightly lower fracture rates in primary uncemented stems,[87] while a register study from New Zealand showed that early periprosthetic fractures were more common in primary uncemented stems than in cemented ones.[89] The design of the stem had also been investigated as a risk factor. The cemented Exeter stem had proportionally more PPFFs than the cemented Charnley,[7] Spectron[90] and Lubinus stems.[7, 90] However, in another large cohort, where 96.5% of all stems were either Exeter (54.3%) or Charnley (42.2%), and with 17 years of follow-up, no association between the incidence of PPFF and the stem design was noted.[83] Since 2012, a relatively large number of studies including large cohorts have been conducted and these results will be discussed below. In general, risk factors can be roughly divided into patient-related and technically related factors, which include surgical method (i.e. surgical approach), surgeon's skills and experience and the implants used during hip arthroplasty.

2.11.1 Technically related risk factors

Only the presence of a hip replacement and/or its effects on bone remodelling are able to increase the risk of someone suffering a fracture at the femur.[91] Katz et al. showed that TKR surgery after a THR increased the risk of a periprosthetic fracture.[92] A fracture during a primary hip replacement increases the risk of suffering a postoperative periprosthetic fracture later in life.[8] There is very strong evidence that uncemented stems entail a higher risk of PPFF, compared with cemented stems. This has been confirmed in both biomechanical studies[93] and clinical studies of THRs[8, 49, 94-97] and of hemiarthroplasties.[98-101] Within the uncemented stems, a higher risk of revision due to PPFF was reported in the anatomically shaped ABG II, compared with the Corail and the Bi-Metric stem.[49] In this register study, the Corail stem, which is a straight stem with a quadrangular cross-section and a distal tapered design,[29] had better survival than the Bi-Metric double tapered stem. The Corail stem is available in two versions, with and without collar support. More recent studies showed a higher fracture risk in uncemented stems with an anatomic shape (when compared with straight designs)[102] and in collarless stems (when compared with collared designs).[103] Another study compared proximally fixed

tapered stems with the ProxiLock uncemented stem (Impex/Zimmer, Warsaw, IN, USA). [104] The ProxiLock stem has a tapered proximal region and a smooth cylinder distal part. The most proximal region has a 14° circumferential flare, while the remainder of the metaphyseal region has a 7° circumferential taper. The authors reported that the risk of the ProxiLock cohort suffering a PPFF was five times higher, but this group included more males and a higher mean age.

In cemented stems, the literature is unanimous in suggesting that polished collarless tapered stems entail a higher risk of PPFF compared with either straight,[10] or anatomic stems.[49] This finding has also been confirmed in cohorts with only hemiarthroplasties,[105] or mixed with both total and hemiarthroplasties.[106, 107] Furthermore, the size of the stem has also been studied as a risk factor. Sawbone femurs broke at a statistically significant lower torque to failure with the shorter cemented Exeter stem (130mm versus 150mm),[108] but in clinical research no difference was noted when comparing two stem sizes of the uncemented TaperLock stem.[109] A smaller size may influence the risk of periprosthetic fracture,[110] or aseptic revision.[90] Another parameter that has been studied is the time to discharge after the index operation. Solgaard et al. noted that the proportion of PPFFs, within six weeks of an operation with a primary uncemented Bi-Metric stem, had increased, since the "fast-track" routine (shorter postoperative hospitalisation) was introduced in their department.[95] Finally, very few studies investigated the surgical approach as a risk factor. Brodén et al. reported no association between surgical approach and PPFF, in primary THRs with the cemented CPT stem.[111] Berend et al. found that an anterolateral approach was associated with intraoperative fractures during primary cemented or uncemented THR.[112] In a mixed material of cemented hemi- and total arthroplasties, Mohammed et al. reported no difference between the posterolateral and the direct lateral approach,[107] while, in another study, patients aged over 85 years and with a hemiarthroplasty ran a two times higher risk of PPFF, if operated with a posterior approach.[101] Recently, a register study from New Zealand showed that cemented THRs with an offset higher than 48mm ran a higher risk of revision due to PPFF.[113] Offset did not, however, influence the outcome in uncemented stems.

2.11.2 Patient-related risk factors

Age at primary THR and gender are two factors that have been investigated in many studies. In general, it could be claimed that the influence of these parameters on the risk of periprosthetic

fracture depends on the study population. For example, in cohorts in which all the patients have a high mean age (>80 years old),[99, 107] age is not a risk factor. One exception is the study by Abdel et al. in which the mean age of patients was certainly lower than 80 years, but age was still not a risk factor.[8] This study is exceptional, because it includes a large number of PPFFs treated non-surgically, whereas the majority of publications only include surgically treated cases. Apart from these studies, many other researchers have reported a higher risk of PPFF with increasing age.[10, 49, 72, 96, 104, 109, 111] Female gender appears to be a risk factor for fractures close to an uncemented stem,[72] or for early PPFFs,[95, 96] which commonly occur close to uncemented stems. Singh et al. also observed a higher risk of females suffering a postoperative PPFF in a population with 63% uncemented fixation.[94] Interestingly, a large register study from four Scandinavian countries showed that the risk of PPFF was higher in females within the uncemented cohort and in men within the cemented cohort.[49] In analogy, several studies found an increased risk in males, where the majority,[99] or all cases,[10, 107] had cemented stems. However, there are also publications in which gender did not emerge as a risk factor.[104, 109, 111, 114]

Another risk factor for PPFF, which interacts with patient age, is the time that has passed since the primary operation with THR. There is an increasing risk of PPFF with a longer period since the index operation, for both cemented and uncemented stems,[8, 84, 94] but there is also a higher incidence during the first months immediately after the operation. In uncemented stems in particular and, to a lesser extent, in polished cemented stems, several studies have reported an increased risk of revision during the first six months after primary surgery,[104, 115] when compared with the situation six to 24 months postoperatively.[49]

Diagnosis at the time of primary THR has also been an important factor for the survival of a hip prosthesis. In contrast to findings by Lindahl et al.,[7] Thien et al. reported that RA did not influence the risk of PPFF.[49] The greatest difference between these studies was that the latter included only revisions, whereas Lindahl et al. also included cases not treated with stem revision. Two other diagnoses have been associated with a high risk of PPFF; femoral head necrosis (FHN)[48, 49, 94] and femoral neck fracture.[49, 111, 115] However, there have been some studies that did not report any correlation between diagnosis and fracture risk. One of them included only uncemented stems[104] and, in the other, cases with FNF were excluded from the study.[96] The quality of the bone stock has been associated with periprosthetic fractures. In a study comprising

87 uncemented Bi-Metric stems, used in THRs due to either OA or FNF, Mann et al. found that only patients from the FNF group (six cases) had sustained a periprosthetic fracture.[115] During a four-year follow-up after the primary THR, the researchers noted a continuous decrease in the bone mineral density (BMD) of the femur, in Gruen zones 1 and 7, and for all patients. Specifically, those six patients with a PPFF had a lower BMD than all the other patients (both the OA and FNF groups), during the first two years of the follow-up. Measurements of their BMD after the two-year control were not available due to the occurrence of the fracture. Gromov et al. noted a higher share of PPFFs in femurs with a cortical index of ≤ 0.5, or in those classified as Dorr type C.[72] In a multivariate regression analysis, they found a fivefold increase in the risk of periprosthetic fractures in Dorr type C femurs and non-significance regarding the cortical index. A cortical thickness index value of 0.4 or lower indicates an osteoporosis investigation.[116] A multicentre prospective observational study showed that patients with medically treated osteoporosis ran an approximately three times higher risk of periprosthetic fracture compared with patients without osteoporosis.[96] This finding, in conjunction with the fact that bisphosphonates prevented BMD loss around hip replacements,[117] led scientists to argue in favour of the benefits of using bisphosphonates in patients undergoing THR. So, bisphosphonates reduced the risk of revision due to aseptic loosening but increased the risk of suffering a periprosthetic fracture.[118] Cross et al. reported a case with a bisphosphonate-induced periprosthetic femoral fracture.[119]

The effect of a high comorbidity status on the incidence of periprosthetic fractures has been barely studied. A higher risk of PPFF was found in patients with a Deyo-Charlson index of ≥ 2 [94] and in patients with a peptic ulcer or heart disease.[120] The association between PPFF and ASA class or cognitive insufficiency is controversial. [93,107, 111] To date, only one study has shown that a high BMI was associated with fractures close to uncemented stems,[102] while several others failed to find any association.[94, 96, 104, 107, 109]

2.12 Incidence

Several factors, such as increasing life expectancy, increasing age at the time of primary THR, increasing numbers of patients undergoing multiple revisions and the increasing use of uncemented fixation, may contribute to a higher incidence of periprosthetic femoral fractures. This has been confirmed in many studies.[7, 49, 86, 87, 94, 121] The annual incidence of PPFFs in Sweden, between 1979 and 2000, varied from 0.05% to 0.13%, with an increase during the final years of the

study.[7] In a larger register study,[49] which included data from four Scandinavian arthroplasty registers, the authors found an increasing incidence of PPFFs between the periods 1995-2002 and 2003-2009. For the whole study period, the incidence was 0.07% for cemented stems and 0.47% for uncemented ones. Abdel et al. reported a 1.7% fracture rate for all primary THRs undergoing surgery at the Mayo Clinic in the USA, between 1969 and 2011.[8] The incidence of PPFFs may differ depending on the study population (primary or revision arthroplasties, cemented or uncemented stems), the length of follow-up and the outcome measurement (fracture, reoperation, revision). Examples are the three large observational studies mentioned above. The outcome measurement in the first study in Sweden was a reoperation due to a periprosthetic fracture after either primary or revision arthroplasty. In the study with data from Scandinavian countries, the outcome measurement was revision within two years of the primary THR, while, in the study from the Mayo Clinic, all fractures, even those treated non-surgically, were included. Another brilliant example is the study by Sköldenberg et al.,[122] who reported a 12% PPFF rate, which is the highest reported hitherto. Their study material consisted of 50 patients (none lost to follow-up), all aged 70 or older, and with a majority of females (72%), undergoing surgery with an uncemented stem due to FNF. This is essentially a study population with the strongest risk factors for PPFF and, in addition to this, an outcome measurement of any kind of fracture, even those treated non-surgically. The incidence of periprosthetic fractures reported in the literature has therefore varied between 0.025% and 3%,[72, 123] with most studies reporting a fracture rate of between 0.5% and 2.1%. A review of register studies and annual reports from arthroplasty registers reported a 0.9% fracture rate.[124] Revisions due to periprosthetic fracture account for 9% to 13% of all revisions for any reason,[3, 10, 125, 126] with the exception of the latest report from the Australian arthroplasty registry, in which PPFF is reported to be the second most common reason for revision (together with hip dislocation), accounting for 17.5% of all revisions.[127] In Sweden, about 300 cases of PPFF undergo surgery every year.

2.12.1 Incidence of various fracture types

The most common fracture type is type B, where type B2 fractures are the most common subgroup in this category.[7-9, 13, 16] The few epidemiological studies reflecting on the incidence and classification of PPFFs relating to the total population of a country are based on arthroplasty registers that do not include non-surgically treated fractures.[7, 16] Other studies

with large cohorts are based on a local hospital register, where even fractures treated non-surgically may be reported.[8] The incidence of type A fractures, the majority of which are treated non-surgically, therefore varies between 1% and 35%, depending on selection criteria for a specific register and the study population. If a register focuses on revisions and especially if only trauma surgeons, with less interest in hip arthroplasty registers, are involved with these patients, the risk of underreporting will increase. In Sweden, for example, revisions were reported at a much higher rate (91.2%) than reoperations, where the hip prosthesis was left untouched (62.6% completeness).[1] Periprosthetic fractures that are only treated with open reduction and internal fixation (ORIF) may therefore be less frequently reported to arthroplasty registers[7] and may present higher proportions at trauma centres.[13] As a result, there are reasons to suppose that type C fractures are underreported because they are frequently treated with ORIF, without any stem revision. This is probably the most important reason why the reported incidence of these fractures has varied widely, between 9% and 30% in several studies.[7-9, 13, 16]

2.13 Treatment

2.13.1 General considerations

A great deal has changed since the first report of a postoperative periprosthetic fracture close to a hip replacement was published.[128] In the beginning, many cases were treated non-surgically with traction, immobilisation and many days in hospital.[51] Fixation with plates in the 1980s could cause the same trauma to patients as revision arthroplasty.[54] Gradually, new types of fixation have been introduced and have replaced old-fashioned methods with poor outcomes. Internal fixation systems like Mennen plates, Odgen plates, Parham's straps, Partridge nylon plates and straps have been abandoned.[11]

The Vancouver classification system is a useful tool in the choice of the treatment. In general, it could be said that Vancouver type B and C fractures are treated surgically, while the majority of type A fractures are treated non-surgically.[8, 129] Another general rule is that, in cases where the femoral stem is loose, the recommended surgical method is to revise the stem and stabilise the fracture.[44]

Figure 10. Close-up view of a cerclage (on the left) and a cable wire (on the right), used for the treatment of periprosthetic fractures.

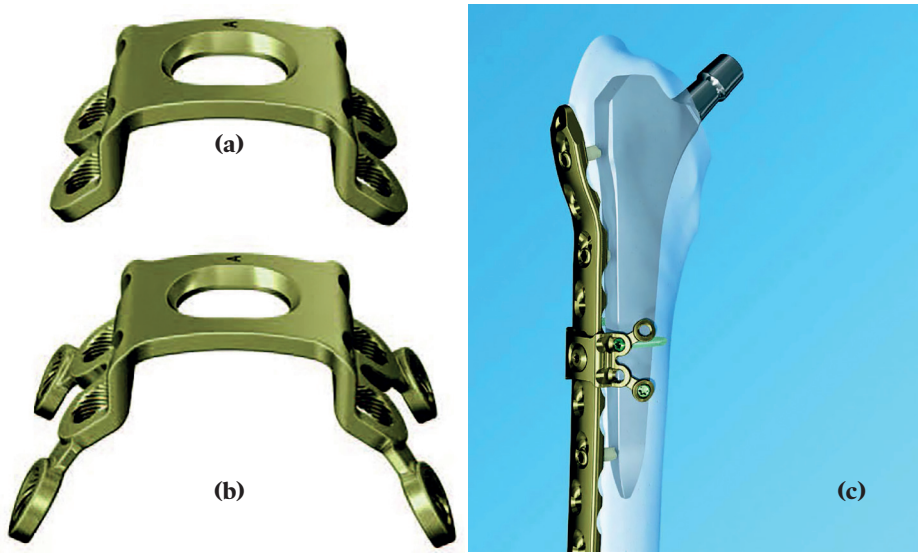

Figure 11. Locking attachment plate (LAP) with four (a) and eight holes (b). LAP applied to a locking plate (c).

2.13.2 Cerclage

The fixation of periprosthetic fractures with cerclage has mostly been used as a supplement to stem revision, plate fixation or fixation with a strut allograft. In the literature, it is reported as the method of internal fixation alone, only in specific fractures and on special occasions, such as some types of intraoperative fracture,[8, 71, 82] undisplaced stable Vancouver B1,[130] and some types of Vancouver A fracture.[8, 129] Historically, various forms and materials for cerclage wiring

have been used. Previous types that are no longer used were wide bands of either nylon (Partridge bands),[131] or metal bands which looked like hose clamps (Parham bands).[51] The most commonly used cerclage fixation today comprises stainless steel monofilament wires (Fig. 10) and multifilament cables of titanium or CoCr (e.g. Dall-Miles, Cable-Ready). They are usually applied around plates at the proximal part of the femur, or for the fixation of strut allografts. The routine use of cerclage or cables is also recommended in revision surgery, in order to prevent intraoperative fractures of the femur.[82] Biomechanical studies have shown better stability with cable than with cerclage.[132, 133] Another type of material is the synthetic cerclage (e.g. SuperCable) made of a nylon core encased in a jacket of UHMWPE braided fibres.[134]

In order to replace cerclage as a fixation tool for the plate to the proximal femur at the level of the hip prosthesis, so-called "locking attachment plates" (LAP) have been developed (Fig. 11). These small plates can be attached to a plate as a clamp-on plate. They have holes for four or eight screws that may be either locking or conventional. They provide an opportunity to insert a screw around the femoral stem and manage bicortical fixation. Biomechanical studies have shown that LAPs are superior to cerclage.[135, 136] There are also some small case series that have reported good clinical outcomes.[137, 138]

2.13.3 Plate fixation

Plates used for the fixation of fractures could be divided in two large categories; locking plates (LP) and conventional plates (CP). The main difference between these two plate categories is the presence of threads at the screw hole or no threads. Locking plates have holes with threads (Fig. 12). When a screw with a threaded screw head (locking screw) is inserted into a threaded hole in the locking plate, it "locks" to the plate. This gives angular stability to the screw and the advantage of not loosening from the plate. One disadvantage is that the angle of the screw in relation to the plate is predetermined by the manufacturer. On the other hand, in CPs, neither the plate hole nor the screw head is threaded and surgeons can place a conventional screw at various angles, in the desired direction. This gives the advantage of avoiding contact with the stem, while inserting the screw, and fixing the screw to the bone beside the stem. With conventional screws, it is possible to draw the bone segments towards the plate and produce interfragmentary compression.

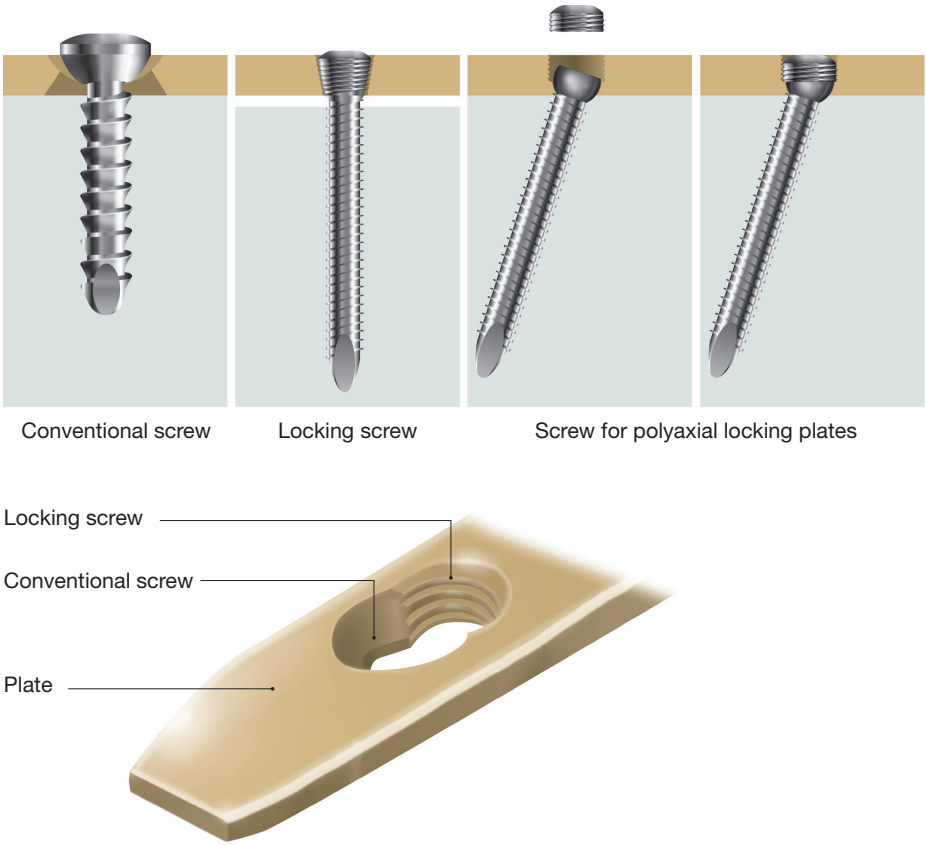

Figure 12. Various types of screw used for plate fixation and close-up view of a plate which is compatible for both conventional and locking screws.

However, if the fixation to the bone loosens, which may happen in osteoporotic bones, conventional screws will also loosen from the plate. This is the greatest disadvantage of CPs compared with LPs, because locking screws remain well fixed to the plate, even when the fixation to the bone has loosened. In LPs, both locking and non-locking screws can be used, but only conventional screws can be used in CPs. LPs (e.g. LCP, LISS) were introduced in Sweden at the beginning of the 2000s and they are now the most commonly used internal fixation system for the treatment of PPFFs. Another advantage of LPs is that they can be inserted using minimally invasive techniques and thus cause less trauma to soft tissues, as well as theoretically reducing peri-operative bleeding and postoperative complications (haematoma, infection). In the middle of the 2000s, a new

subtype of LPs, the "polyaxial locking plate" (Non-Contact Bridging plate, NCB), was introduced.[139] This kind of plate enables the surgeon to insert the screw at the preferred angle up to 30^0 and then lock the screw to the plate (Fig. 12). Another function of this plate is that it can be inserted and fixed without being in contact with the femoral bone, which explains why it is called a "non-contact" plate. The theoretical advantage of this function is that the potential for periosteal damage and impaired blood supply can be reduced. Gradually, more characteristics have been added to LPs, such as the existence of screws that only fix to the distal cortex and not to the near cortex.[140]

Figure 13. Example of a cable plate used for the fixation of an A_G fracture. (Accord cable system by Smith & Nephew, Memphis, USA).

2.13.4 Vancouver type A

Type A_G fractures are usually treated non-surgically.[82] The treatment includes protected weight-bearing for six to 12 weeks and the avoidance of active abduction until the fracture has healed. Indications for surgery are dislocation of the fragment by more than 2 cm, limp, painful nonunion, instability, weakness of abduction and stem loosening.[82, 129] The dislocated greater trochanter can be fixed with either cable plates or tension-band techniques, using wires or heavy braided sutures.[141] Plates can be fixed with wires, screws, or both (Fig. 13). If the stem is loose, it has to be revised. In special cases, where the fracture is the result of proximal femoral osteolysis secondary to polyethylene (liner) wear, it is advised to consider acetabular cup or liner exchange in conjunction with bone grafting and fixation of the trochanter.[82] Type A_L fractures are

rare, usually minor, and do not require surgical treatment. Fragments that involve a large area of the femoral calcar may affect the stability of the stem and therefore require stem revision. These fractures have also been named "pseudo A_L fractures" [70] and should be classified and treated as type B2.[44]

2.13.5 Vancouver type B1

Type B1 fractures are commonly treated with ORIF.[44] Several methods have been described, but they all require fixation with one or more plates. Plate fixation can be combined with the use of cerclage that goes around the plate and the femur. Cable plates can be fixed to the femur with screws and/or cables which are thicker than wires. The use of cortical onlay allografts (strut) in combination with plate fixation is not uncommon, especially in unstable transverse fractures at the tip of the stem.[142, 143] Before the evolution of plate fixation, it had been proposed as an alternative treatment in B1 fractures.[61] In biomechanical studies, the use of a strut in combination with a plate has shown better stability than the use of only one plate.[144, 145] A systematic review of B1 fractures treated with plate fixation, with or without a strut allograft, revealed a significantly shorter time to union in those operated without a strut, but no statistical difference in the union rate or the postoperative infection rate was noted. [146] Neither the use of cerclage nor the type of plate (LP vs CP) affected the results (union, time to union, infection) of type B1 and C fractures treated

Figure 14. Vancouver type B1 fracture treated with the "docking nail" method.

only with plate fixation and without strut allografts. In this review, only four of the 36 studies of B1 fractures comprised more than 30 patients. Another review article, which comprised level IV studies,[147] reported higher nonunion rates for locking plates and an increased risk of hardware failure, when compared with conventional plates, in the treatment of type B1 fractures. The use of one or two plates has been tested in biomechanical studies, revealing an advantage for the double plating (DP) in B1 fractures.[148, 149] It is suggested, especially in transverse or short oblique fractures close to the tip of the stem.[150] This technique is also called "orthogonal plating", because one longer locking plate is placed laterally on the femur with the other shorter plate anteriorly. Good results, with 90% union rates, were reported for the NCB polyaxial locking plate.[139] Pavlou et al. advocated the need for stem revision with a long-stem prosthesis that bypasses the fracture line, in unstable transverse or short oblique B1 fractures at the tip of the stem.[151] Their study reported shorter times to union but not statistically better union rates for seven B1 fractures treated with stem revision, compared with eight femurs operated with ORIF. Finally, the use of an intramedullary nail (IMN) is rarely reported for the treatment of B1 fractures (Fig. 14). With this type of fixation, also called "the docking nail", the surgeon pounds the nail into the tip of the stem.[152, 153]

2.13.6 Vancouver types B2 and B3

Fractures around a loose stem are very difficult to treat and require high surgical skills and experience of both trauma and hip replacement surgery. Although it is generally suggested that these fractures should be treated with stem revision as the main procedure, alternative treatments may be used in some frail patients with reduced general health.[154] Open reduction and internal fixation is usually a shorter surgical procedure, which is easier to perform with less blood loss.[155] Some of these cases may be treated with a two-stage procedure.[156] In spite of this, some authors support ORIF as a viable alternative in B2 fractures, if the fracture can be reduced anatomically and loosening is only present at the stem-cement interface.[155]

The majority of the published studies of revision hip replacement due to PPFF investigate type B2 and B3 fractures as one entity. This may be partly because separating these two types of fracture can be very difficult, especially on the basis of the pre-operative radiographs. Another reason is that B3 fractures have been the less common fracture type, in many cohorts, and it has consequently been difficult to study them as a category on their own.[7-9, 83] Some researchers have also included transverse or short oblique B1 fractures, when investigating the

treatment and the outcome of revision surgery due to PPFF.[151] Implants used for the treatment of fractures around a loose stem are generally divided into cemented and uncemented stems. Tumour prostheses and allograft-composite stems that are only used in type B3 fractures, with severe bone loss, comprise a separate category.[157] It is preferable to use cemented revision stems in older patients with poor bone quality.[157] The extraction of the entire cement mantle around the primary prosthesis, during a revision, is both a time-consuming and perilous procedure, with a high risk of perforation or additional intraoperative fracture. Cementing a revision stem in the previously unfractured cement mantle is therefore suggested in elderly patients with a simple fracture pattern that can be reduced anatomically to preclude cement extrusion (cement-in-cement revision).[158, 159] Cemented stems can be subdivided into long stems that bypass the fracture line and short stems that do not.[160] In a comparison of 89 long and 17 short cemented revision stems, Tsiridis et al. reported a significantly better union rate for the former.[160] Another revision surgery technique, where cemented fixation can be used, is the technique of impaction bone grafting. This method aims to restore femoral bone stock by impacting fresh frozen cortico-cancellous bone chips into the canal, to create a neo-endosteum, prior to implantation of the cemented hip stem. It is mostly preferred in younger patients, in order to restore the bone stock in the event of an eventual future re-revision.[161] Impaction bone grafting can also be used in revision surgery with uncemented stems, by providing sufficient initial stability and scratch fit of the component.

Uncemented revision stems are subclassified as modular fluted tapered stems and monoblock stems that are either proximally or extensively porous coated (Fig. 15). In 2003, Springer et al. reported a higher rate of radiographic loosening

Figure 15. Examples of uncemented revision stems for the treatment of periprosthetic fractures of the femur. (a) Modular MP revision (Link, Hamburg, Germany) and (b) monoblock Wagner (ZimmerBiomet, Winterthur, Switzerland).

and nonunion with the proximally porous-coated stems and suggested the use of extensively porous-coated stems for the treatment of the majority of Vancouver type B fractures.[157] Ten years later, a study from Spain reported 100% fracture healing, with radiographic in-growth fixation of the stem and an increase in cortical bone, in 35 PPFFs (B2 and B3 type) treated with uncemented extensively porous-coated stems.[162] No cortical onlay allografts were used. These stems have been the most commonly used revision stems at several departments, while modular tapered fluted stems were reserved for type B3 fractures with less than 4 cm of diaphyseal fit.[163] After concerns about stress shielding with cylindrical stems (fully porous-coated stems), tapered fluted stems began to gain in popularity in the treatment of type B2 and B3 fractures, with very good results.[163-165] These components gain rotational and axial stability distal to the fracture site, while preserving the proximal femoral bone.[165] In cases of a fixation zone of less than 3 cm in the isthmus, it is possible to improve distal fixation by using interlocking screws at the distal part of the stem.[166] In some other cases, with the insufficient distal press-fit fixation of a modular uncemented stem, cemented fixation may be used for the distal part of the stem alone.[167]

Irrespective of whether or not the revision stem is cemented, it is common to use strut allografts and mesh as a supplement in the treatment of fractures around a loose stem (Fig. 16). Their use is more common in Vancouver type B3 fractures and their role is to enhance

Figure 16. Periprosthetic fracture treated with a long cemented stem and plate fixation with bone grafting and mesh.

fixation and support the impacted bone graft, converting segmental defects into contained defects. Strut allografts provide both biological and mechanical fixation. A review of 71 PPFFs treated with struts concluded that this method provided reliable, safe fixation but with a high complication rate (24% including nonunions, malunions, infections, dislocations and death within six months of the operation).[143] Metal meshes are most commonly used in combination with bone impaction grafting and their use has even been extended to the reconstruction of complete circumferential proximal cortical bone loss.[168] Internal fixation with plates, in combination with stem revision or without, is not uncommon in fractures around a loose stem. A systematic review of Vancouver type B2 and B3 fractures[169] reported poorer results for the patient group treated only with ORIF, when compared with those who underwent stem revision with or without plate fixation.

2.13.7 Vancouver type C

Fractures distal to the femoral stem are probably the least studied complication after a total hip arthroplasty. They are usually described in studies that also include type B fractures, or in studies that investigate interprosthetic fractures. The presented material often constitutes a mix of hemiarthroplasties and THRs, or includes only one type of plate fixation (CP or LP). Most publications that investigate plate fixation in the distal femur are cases with non-periprosthetic fractures (native femoral fractures), and/or PPFFs close to a TKR. The largest material was reported by Molina et al., who investigated the outcome of 580 PPFFs.[170] Of 180 type C fractures, 165 were treated with ORIF and 72% of these had good results. Lindahl et al. reported a 25% reoperation rate in 100 fractures distal to primary or revision stems. ORIF was used in 67% of the cases, while in all other cases revision of the stem (with/without ORIF) was performed.[7] Neither of these two studies described the type of osteosynthesis used in detail. Historically, periprosthetic distal femoral fractures were treated non-surgically, requiring a long hospital stay and resulting in disappointing outcomes.[171] Surgical treatment has shown better results in the treatment of distal femoral fractures.[172] Gradually, plate fixation has become popular. The angle blade plate (ABP) was used for the treatment of supracondylar femur fractures, but with fair or poor results in the beginning.[173] Fixation with a retrograde intramedullary nail (IMN) has also been used as an alternative in the treatment of Vancouver type C fractures. Most published studies of nail fixation due to periprosthetic fractures focus on supracondylar fractures above a total knee replacement. This is a minimally invasive

technique, but with the disadvantage that the nail cannot be very long, due to the presence of the hip stem, and thus subsequently provides less stability to the fracture. Moreover, after the insertion of a nail, the gap left between the proximal tip of the nail and the distal tip of the stem consists of a zone in which stress increases.[174, 175] This increases the risk of fracture in this region, especially if the bone quality is limited,[176] or if the hip stem is loose.[177] Alternatives to fixation with ABP and IMN are the dynamic condylar screw (DCS) system and locking plates (LCP, LISS, NCB, Peri-Lock). These plates enable the conservation of the soft tissue without demanding long incisions. They provide a long fixation from the femoral condyles proximally to the tip of the stem and enable high stability at the fracture site (Fig. 17). In a biomechanical study, Walcher et al. suggested a minimal gap or overlap of at least 6 cm between the proximal end of the plate and the tip of the hip stem.[178] Most publications are case series of just a few patients, with good results.[17, 179-181] The use of locking plates is also described in combination with nail fixation in three Vancouver C fractures.[182]

Figure 17. Vancouver type C fracture (left) treated with a locking plate that overlaps the tip of the stem.

Although locking plates should, theoretically, be superior to conventional plates, this has not yet been proved in clinical studies. Moore et al. reviewed 37 studies published between 1992 and 2012 and reported B1 and C fractures only treated with ORIF (no revision surgery).[146] None of these studies compared LP with CP and the largest material of B1 fractures comprised 182 cases treated with the Partridge plate system, which has now been abandoned. Thirteen studies investigated type C fractures (n=61) and only one of them reported more than 10 cases (n=12). The authors found no significant difference in union rate when they compared LPs with CPs. Another review study reported higher nonunion rates for conventional plates but similar reoperation rates, when compared with locking plates.[183] This material was very mixed, with all types of Vancouver category, hemiarthroplasties, primary and revision THRs. Furthermore, the type of

plate was only known in 46% of the cases. Baba et al. compared 21 locking plates with 19 cable plates for the treatment of 30 B1 and 10 C fractures (6 LP, 4 CP).[184] They found no significant difference in the outcome parameters, operative time and blood loss between these two types of plate fixation. Finally, the use of two plates (double plating) is not uncommon in type C fractures (Fig. 18).[185, 186]

2.13.8 Interprosthetic fractures (IPFF)

The management of interprosthetic fractures follows the same principles as the treatment of fractures around a hip prosthesis. So, if a prosthesis is loose, revision is the treatment of choice, while ORIF is suggested in cases with stable implants. Internal fixation with an intramedullary nail may only be an option in cases where the TKR has an open box design.[187] However, in these cases it is important to be aware of creating an increase in stress, as discussed above. For this reason, plate fixation predominates in this type of fractures. Locking plates offer many advantages by using minimally invasive techniques, achieving stable fixation in the osteoporotic condylar region with locking screws and making

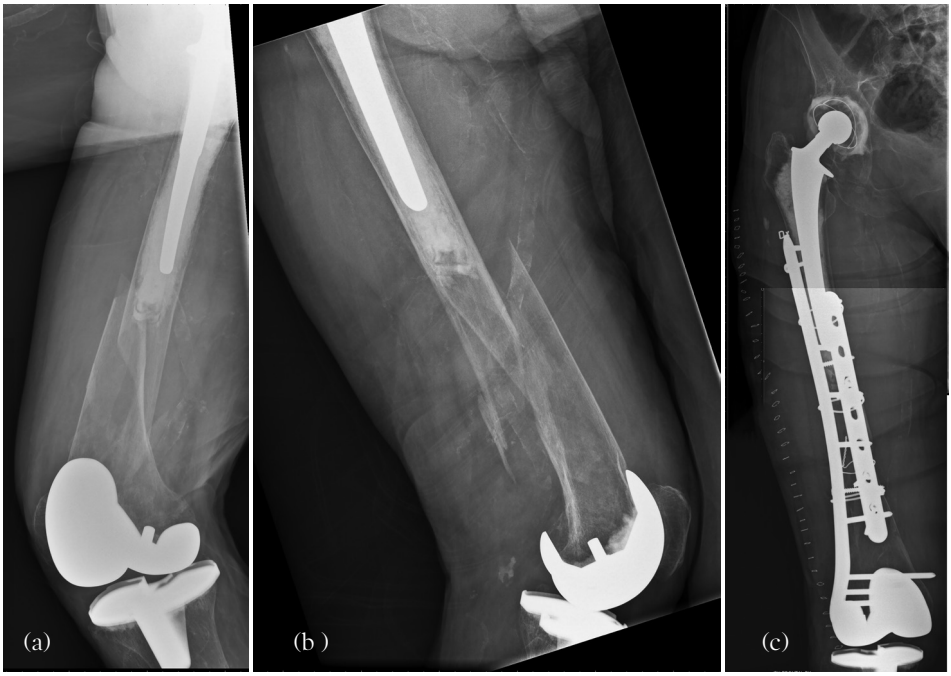

Figure 18 (a-c). Vancouver type C fracture treated with double plating (DP).

it possible effectively to bypass both the fracture site and the tip of the stem. So, in most published studies with the most extensive material, locking plates have been used.[79, 188, 189] Orthogonal plating with good results has also been reported in IPFFs.[76] The most difficult cases of IPFF are those with only a small amount of bone left between a long hip and a long knee stem.[78] The technique of "interposition sleeve" has been described as a salvage procedure in these complex interprosthetic fractures, with additionally poor bone quality.[190-192]

2.14 Outcome of PPFFs and measurement tools

There is a huge variation in the material in studies that investigate outcomes after the surgical treatment of periprosthetic fractures. Most of the studies include fractures postoperatively to both primary and revised stems, while others also include hemiarthroplasties. Patients with a hemiarthroplasty are older[101] and primarily undergo surgery due to FNF, in comparison with THR cohorts where primary OA is the most common diagnosis. It is therefore of great importance to have knowledge of the study population (population at risk), when interpreting the outcome of various treatment methods.

Another variation noted in PPFF studies is the primary outcome measurements that are used to assess various treatment methods. The most common parameters used in the literature are the rate of union (or nonunion), the rate of reoperation (or re-revision), the rate of complications and the functional scores or scores for health-related quality of life. When it comes to complications, they can be divided into medically related complications (renal failure, stroke, deep venous thrombosis) and those related to orthopaedic surgery (wound infection, hip prosthesis dislocation, haematoma and so on). Usually, complications refer to those occurring during the hospital stay, or during the healing process, which is no longer than 12 months. Unions, reoperations and functional scores usually refer to a postoperative follow-up of at least one year.

Re-reoperation rates reported in cohorts with PPFFs range between 7% and 32%. This large variation depends on several factors. In general, large cohorts that include all types of fracture and treatment method have reported reoperation rates higher than 15%.[7, 130, 193-195] Lower re-reoperation rates have been reported in studies with implant revision as the outcome measurement,[196, 197] in case series describing one treatment method and in specific fracture types,[151, 198-200] or in type B fractures treated only with revi-

sion.[201-203] One exception may be a review of 118 Vancouver B fractures treated with stem revision, which reported a 24% re-reoperation rate. This was probably due to the different types of stem that were used, the large number of patients, the length of the study (18 years) and the detailed recording of all complications. In contrast, a reoperation rate as low as 4% was reported by Neumann et al., who studied PPFFs only treated with revision using a specific stem and with an unclear end to follow-up.[164] Complication rates are expected to be higher and may vary from 10% to 48%.[18, 151]

The common, general characteristic of PPFFs, regarding the outcome of treatment, is that the majority of patients do not return to their previous activity level. The most common functional score used is the Harris Hip Score (HHS) and the majority of studies report a fair or poor outcome. Few studies have reported a good outcome with an HHS of > 80.[142, 160, 204] It is important to note that these scores refer to patient groups that were free from complications requiring a re-reoperation. According to the literature, more than half the patients undergoing surgery due to a PPFF are unable to walk postoperatively without using walking aids. Many might argue that this is due to a low mobility status pre-operatively. However, several studies reported a reduction in walking ability[15, 202] and quality of life after a periprosthetic fracture,[205] in relation to the pre-operative status. When compared with other reasons for revision, patients undergoing a stem revision due to PPFF had a lower activity level postoperatively.[125]

2.15 Outcome of PPFFs and risk factors

Relatively few studies have investigated factors that may influence the outcome after the surgical treatment of a PPFF. Several studies have reported poorer results with ORIF compared with stem revision,[193, 206, 207] while others were unable to prove any correlation between fracture fixation and outcome.[130, 197, 204] In cohorts where only plate fixation was performed, poorer results were noted when the fracture was not reduced anatomically,[199] or if the stem was spanned insufficiently.[208] Molina et al. reported higher complication rates for the plate fixation of fractures around the proximal two-thirds of the femoral stem.[170] In cases where stem revision was preferred, long stems appeared to have better outcomes compared with shorter stems.[160, 206] Neither the type of stem fixation (cemented or uncemented)[16, 169] nor the design of the revision stem[15] influenced the outcome for PPFF in previous studies. Lindahl et al. reported no relationship between the index stem design (the stem had already been inserted when

the fracture occurred) and the treatment outcome.[206] The influence of the fixation type of index stem has been controversial,[130, 204, 209] and two studies reported that the presence of a primary or a revised index stem was not a risk factor.[193, 206]

Vancouver type B1 fractures were associated with inferior outcomes in a large register study,[206] in contrast to findings from other studies that did not find a correlation between fracture type and outcome.[130, 204] In a review of 33 type B1 and 18 type C fractures, all treated with a locking plate, Hoffman et al. reported higher failure rates in AO/OTA type B fractures and, in the presence of an ipsilateral TKR.[200] Lindahl et al. noted that the risk of failure increased during the first two years after PPFF treatment, after which it decreased.[206] The same study reported a higher risk of re-reoperation in elderly patients, in contrast to another study which did not find any correlation between age at PPFF and outcome.[200] The latter study investigated 49 B1 and C fractures treated with plate fixation, while the material in the study by Lindahl et al. comprised 1,049 fractures of all Vancouver types and treatment methods. Other factors studied, but without any influence on the outcome, are diagnosis at index operation and gender[130, 206] and ASA class,[130, 204] as well as BMI, osteoporosis and diabetes mellitus (DM).[200]

2.16 Mortality and risk factors

The majority of studies report one-year mortality, which varies between 9% and 14%. However, both higher (16%-19%)[9, 107, 199] and lower (3% and 5%)[194, 205] mortality rates have been reported. The inhospital mortality rate has varied between 1.2% and 3.7%,[7, 207, 210] with only one study reporting a much higher rate (11%).[9] Patients suffering a periprosthetic hip fracture have not only higher mortality than THR patients without PPFF[211, 212] but also significantly higher mortality than those undergoing revision due to aseptic loosening.[196, 213] Young et al. reported higher one-year mortality rates after PPFF, if the operation was performed at smaller centres or by less experienced surgeons.[196] In general, patients with a primary diagnosis of FNF[130] and elderly individuals have a higher mortality risk.[130, 211, 214] The majority of studies report no correlation between mortality and delay to surgical treatment (time between admission and surgery).[121, 130, 197, 215] Only one study reported higher mortality rates in cases with a delay of more than five days,[205] while delays of more than two days were a risk factor in a study which also included periprosthetic fractures around a knee replacement.[13] The presence of an ipsilateral TKR or the type of fracture did not influence mortality.[121, 130] The question of whether gender and treatment method (ORIF, revision) are risk

factors is controversial. Some studies report higher mortality in men,[211, 215] while others do not.[130, 197] Patients undergoing stem revision had lower mortality in one study and [202] higher in another,[215] while a third reported no correlation between treatment method and mortality.[197] Other risk factors reported in the literature are ASA class,[121, 130] Charlson index,[197] dementia,[130] dependent functional status[214] and higher comorbidity in general.[215]

2.17 Financial burden

Periprosthetic hip fractures represented 3% of all 90-day re-admissions in the USA and accounted for 5% of the total national hospital costs.[19] According to the same study, PPFF was the third most expensive reason for 90-day re-admissions, after infection and dislocation, in THR patients. The cost per hour of theatre time was approximately the same as the cost per day on a trauma ward in the UK,[216] while ward costs accounted for 80% of the total expenses. The cost increased in cases with further surgeries or deep infections postoperatively. In comparison with other complications of THR, periprosthetic fracture was second (after infection) in implant, theatre and total costs.[18]

2.18 The usual case with a periprosthetic fracture

According to what a wide range of studies of PPFF have reported, more than 60% of the patient population are women and the mean age is over 70 years (usually around 73-76). In cohorts that also include hemiarthroplasties, the mean age can rise to 80 years or more.[107, 111, 216] Most patients have ASA class 3 (severe systemic disease) and a BMI of around 25-27 kg/m^2,[200, 207] which is lower than the BMI in patients undergoing re-operations due to other complications of hip replacement.[125] Their physical activity level is also lower than that of patients reoperated for other reasons.[125] The fracture occurs six to 10 years after the primary THR, with a minor trauma mechanism. Following admission to hospital, it will take two to four days for the patient to be operated on by a senior trauma or senior arthroplasty surgeon. Per-operatively, some 800ml of bleeding is reported [9, 199] and a mean four units of blood transfusion may be needed.[15, 197] The total length of hospital stay is usually two to three weeks and fewer than half the patients are discharged to their homes.[121, 210, 217] Within one year of the periprosthetic fracture, one in five patients will die or undergo a reoperation due to fracture complications.

3. AIMS

3

AIMS

This thesis aimed to study periprosthetic femoral fractures in the Swedish population based on data from the Swedish Hip Arthroplasty Register, the National Patient Register, the Swedish Knee Arthroplasty Register, studies of case records and selected radiographic examinations. The three registers were cross-matched to obtain the best possible completeness, including treatment outcomes. The specific objectives were as follows.

Study I

To study the incidence of PPFF and describe the demographics in this population. The secondary purpose was to investigate the registration of reoperations due to PPFF in the Swedish Hip Arthroplasty Register using the National Patient Register as reference.

Study II

To examine risk factors that predispose to the occurrence of PPFF around and distal to the two most commonly used cemented stems in Sweden.

Study III

To describe the surgical treatment of Vancouver type B fractures and study factors that may influence the risk of further reoperations.

Study IV

To describe the surgical treatment of Vancouver type C fractures and compare different types of internal fixation. To study mortality after reoperation due to PPFF and factors that may influence the risk of further reoperations on type C fractures

4. PATIENTS AND METHODS

PATIENTS AND METHODS

4.1 Study design

This thesis includes register studies based on information extracted from both the SHAR and medical charts. It therefore belongs to the category of observational cohort studies in the hierarchy of evidence. It has both a prospective and a retrospective aspect. All patients undergoing THR and all subsequent reoperations are registered prospectively and non-randomly. However, all hypotheses and scientific questions are posed after the start of data collection. Prospective cohort studies (register studies) are more relevant than randomised controlled trials (RCTs) when it comes to determining the risk associated with prognostic factors, investigating rare complications such as periprosthetic fracture, and studying long-term outcomes of hip replacement and mortality after PPFF.[218] In order to improve the reporting of observational studies, a network of methodologists, researchers and journal editors developed a checklist of 22 items, called the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement.[219] This checklist is not used as an evaluation instrument for observational studies but as assistance when reporting and reviewing articles on this type of research.

4.2 Data sources

The data analysed in these four studies were extracted from the SHAR and cross-matched with the NPR and with the Swedish Knee Arthroplasty Register's database (SKAR). Information about fracture type, treatment of PPFF and details during hospital stay were derived from medical records. Information regarding the presence of an ipsilateral knee prosthesis was extracted from both medical records and the SKAR's database. The SKAR started in 1975 and is the oldest national quality register in Sweden. It collects data from all primary and revision knee replacement surgery and, since 2013, it has also included knee osteotomies.[220]

4.3 Data linkage

Data linkage (or cross-matching) between the SHAR and NPR was performed in two stages. At the first

cross-matching, data from the SHAR, including all primary THRs between 1992 and 2011 were linked with the NPR's database in order to find periprosthetic fractures treated surgically between 2001 and 2011 and not reported to the SHAR. We chose not to include primary THRs before 1992, because the SHAR started to register primary hip replacements on an individual basis (with personal identity number) prospectively in 1992. Two difficulties arose. One was that the ICD-10 code for periprosthetic hip fractures (M96.6F) was rarely used by orthopaedic surgeons in Sweden. The majority used codes for native (non-periprosthetic) femoral fractures, i.e. S72.0 (femoral neck fracture), S72.1 (intertrochanteric fracture), S72.2 (subtrochanteric fracture), S72.3 (fracture of the femoral shaft) and S72.4 (distal femoral fracture). So, at the first cross-matching, we searched for any type of femoral fracture (both periprosthetic and native), except for femoral neck fractures which were not relevant for cases with a conventional hip replacement. The second difficulty we encountered was that laterality is not registered in almost any of the cases in the NPR. This means that a case registered in the SHAR with a primary THR only on the right hip and with no reoperation due to PPFF reported, could be falsely linked in the NPR to a left-sided femoral fracture, despite the fact that this patient had not had a hip replacement on this side. This linkage resulted in 4411 cases, in which it was unknown whether the femoral fracture was ipsilateral or contralateral to the hip replacement. To solve this problem, all medical charts were collected and scrutinised by local secretaries or surgeons at each department, secretaries at the SHAR and two orthopaedic surgeons at the SHAR (HL, GC). Finally, after the exclusion of incorrect recordings and duplicates, 1,041 cases not primarily registered in the SHAR were added to the 2,176 PPFFs already reported. These 3,217 charts were reviewed by the author of this thesis. Data derived from the first cross-matching were used in all four studies.

At the second cross-matching, we linked all these 3,217 PPFF cases to the NPR's database in order to find all reoperations not reported to the SHAR, performed for any reason between 2001-2013 and after the index PPFF operation. This time, the linkage was based on KVÅ treatment codes. Any kind of surgical treatment of fractures in the femur (NFJ) or knee (NFG), hip revision (NFC), amputation (NFQ), excision arthroplasty (NFG), extraction of instrument (NFU), bone transplantation (NFN), arthroscopy/endoscopy or reduction of a dislocated hip replacement (NFH), reoperation due to infection (NFJ) and any other reoperation on the femur (NFW) was derived

from the NPR's database. All the medical records of cases only reported to the NPR were collected, while the medical records of reoperations already registered in the SHAR had been prospectively reviewed by the personnel at the SHAR when the data were entered. The second cross-matching resulted in 422 cases, of which 209 were relevant, while the other 213 were either duplicates or incorrect recordings. Eight hundred and twenty-nine reoperations had already been registered in the SHAR, making a total number of 1,038 reoperations after a PPFF. Data derived from the second cross-matching and the linkage with the SKAR were used in Studies III and IV.

4.4 Classification of periprosthetic fractures in this thesis

Periprosthetic fractures are not classified when they are registered in the SHAR. The optimum method to classify a periprosthetic fracture is to combine information from a patient's medical history and symptoms before the fracture, radiographs both at the time of fracture and after the primary hip prosthesis, and finally from the surgeon's assessment per-operatively. Information from these sources is probably optimal to enable the most correct differentiation of Vancouver type B fractures possible. In this project, the type of fracture was assessed and classified based on information from the medical records. The classification was chiefly based on the surgical notes and secondly on the information from admission and discharge. In many cases, the surgeon classified the fracture by testing stem stability intra-operatively. Cases not classified in this way were classified as B2 if there was a cement fracture, a stem fracture, or a spiral fracture around a polished cemented or an uncemented stem. If the treating surgeon referred to inadequate bone stock, or the fracture was treated with a cortical strut allograft, or alternatively a tumour prosthesis, the fracture was categorised as B3. Fractures distal to the stem with visible cement during surgery were classified as B and not as C. In cases where the description of the fracture diverged between the assessment of the author and the surgeon who performed the operation, the classification made by the surgeon was used. The classification was made by author GC and, when information was unclear or classification uncertain, HL and JK were consulted. If the assessment of the fracture type was still debatable, the patients' radiographs were requested. Fractures judged to be impossible to classify were excluded from the studies. Because this method has not been used previously, it was validated at the beginning of the research project (Study I).

4.5 Distinguishing intra- and postoperative fractures

As previously mentioned, this study project aimed to investigate postoperative fractures and to exclude fractures occurring during the primary THR. There are, however, some cases in which it is difficult to define with any certainty when the fracture occurred, especially cases operated on using an uncemented stem. The most characteristic example is a case where an uncemented stem is inserted uneventfully according to the surgical notes, no fracture line or subsidence of the stem are noted on the postoperative radiographs, the patient is allowed weight-bearing and no problems are reported at discharge. However, one to two weeks after the operation, the patient experiences a sudden pain in the thigh without any trauma and a new radiograph reveals a periprosthetic fracture. In such cases, a fissure, not visible on the postoperative radiographs, might have occurred intraoperatively.

There is no uniform definition of intraoperative fractures in the literature. Several studies have used different "time limits" to distinguish intra- from postoperative fractures. Brodén et al. argued that all fractures in their study were postoperative because none of them had occurred or dislocated within one week of the primary operation.[111] Watts et al. defined intraoperative fractures as those noted either per-operatively or on postoperative radiographs,[104] while two other studies excluded fractures that occurred on the same day as the primary THR.[84, 94] Cottino et al. extended this time limit to one month postoperatively,[102] while Cook et al. chose a time interval of six months.[83]

In the current research project, it was feasible to read medical records from both primary procedures and PPFFs. A fracture was defined as intraoperative if it was mentioned in the surgical notes on the primary THR, or in later notes that clearly referred to a fracture noted on the postoperative radiographs, regardless of whether these notes belonged to medical charts of the index operation or any later recording. Furthermore, there were very few cases in which patients fell and suffered a periprosthetic fracture on the ward during the postoperative course of a primary THR. In these cases, the fracture was defined as postoperative in the presence of comments rejecting the presence of a fracture on the postoperative radiographs exposed before the trauma. All other cases were classified as intraoperative and were excluded from the study.

4.6 Patients

4.6.1 Exclusion criteria

In general, many exclusion criteria were common in all four studies. Hip resurfacings and intraoperative fractures were excluded, because they belong to a totally different type of hip prosthesis, together with periprosthetic fractures. In Study I, cases primarily undergoing a hemi-arthroplasty (n=10) and with known malignant disease at the primary operation (n=3) were included. In the following three papers, however, these cases were excluded to avoid bias and to facilitate the interpretation of the results. PPFFs occurring in infected hips and iatrogenic fractures occurring during closed reduction or knee replacement surgery were excluded for the same reason. Nonunions of trochanteric osteotomies were distinguished from nonunions of periprosthetic fractures and excluded. One fracture caused by sawing (non-iatrogenic) was not included. The incidence and location of fractures close to a revised stem differ from fractures around a primary stem. Moreover, a revision stem is often longer than a standard primary stem and the bone mass of the femur could most certainly have been affected by preceding operations. Patients with a previous history of PPFF treated with methods other than revision were also excluded from the studies. Only first-time reoperations due to a periprosthetic fracture were included and, as a result, only primary arthroplasties. A few cases in which the femoral stem was revised due to perforation, without a complete fracture, were not classified as PPFF. Cases with an unknown implant, date, or hospital either at primary THR or at PPFF, as well as fractures with insufficient information regarding the treatment method and the classification, were also excluded. Periprosthetic fractures treated in two stages were managed differently. In the two first studies, where the index operation was the primary THR and the outcome was the occurrence of a PPFF, only the first session of the two-stage procedure was included. In Studies III and IV, where the index operation was the PPFF and the outcome was a re-reoperation, all two-stage procedures were excluded.

4.6.2 Study I – incidence and demographics of all periprosthetic fractures

In this study, all cases with a primary THR between 1992 and 2011, which underwent a reoperation for PPFF between 2001 and 2011, were analysed. The number of cases included in all four studies is described in Table 1.

Table 1. Time periods and number of cases included in the four studies of this thesis.

Studies	Year of pr. THR	Year of PPFF	Population at risk No of cases	Outcome Year of surgery	Outcome No of cases
Study I	1992 – 2011	2001 – 2011	246.679 pr. THR	2001 – 2011	1751 PPFF
Study II	2001 – 2009	2001 – 2011	79.813 pr. THR	2001 – 2011	465 PPFF
Study III	1979 – 2011	2001 – 2011	1381 Vancouver B	2001 – 2013	239 reoperations *
Study IV	1979 – 2011	2001 – 2011	639 Vancouver C	2001 – 2013	97 reoperations *

Pr. THR (primary total hip replacement), PPFF (periprosthetic femoral fracture)
* Reoperations related to previously treated PPFF (reasons could be nonunion, failure of the fixation, re-fracture, infection, hip dislocation, revision of the stem, pain or technical reasons)

4.6.3 Study II – stem design and other risk factors for periprosthetic fractures

Only cemented total hip arthroplasties with either a standard Lubinus SP II, or a standard Exeter Polished stem were included. Vancouver type A fractures were excluded. We identified factors that influence the risk of a stem, inserted during 2001-2009 and undergoing reoperation due to a periprosthetic fracture between 2001 and 2011. The surgical approach at index operation was studied as a risk factor in a separate sub-analysis.

4.6.4 Study III – treatment of Vancouver type B fractures and outcome

The population studied in this work comprised all Vancouver type B fractures undergoing surgery between 2001 and 2011, close to a primary THR inserted in 1979-2011. This cohort was followed until 2013. Fractures treated with methods other than stem revision or plate fixation were excluded. Cases in which the same primary stem was re-inserted were registered as a stem revision and included in the study. We investigated risk factors for poor outcome after the treatment of type B fractures in patients with a cemented stem and a diagnosis of OA at primary THR. A sub-analysis was performed separately for B1 and for B2/B3 fractures.

4.6.5 Study IV – treatment of Vancouver type C fractures and outcome

This study included all Vancouver type C fractures undergoing surgery between 2001 and 2011, in patients undergoing a primary THR between 1979 and 2011. This cohort was followed until 2013. Fractures treated with methods other than plate fixation or fixation with an intramedullary nail were excluded. A sub-analysis was performed separately for type C fractures treated with either a conventional or a locking plate.

4.7 Sub-analyses in Studies II-IV

4.7.1 Study II

The primary hypothesis in this study was that the force-closed design, represented by the cemented Exeter stem, is associated with Vancouver type B fractures, while the shape-closed design, represented by the cemented Lubinus SP II, is associated with C fractures. The sub-analysis focused on the surgical approach at the primary THR as a risk factor for a periprosthetic fracture around the stem (Vancouver type B). If the surgical approach (lateral or posterior) is able to influence the quality of cementing and stem alignment, it might theoretically affect the risk of a Vancouver type B periprosthetic fracture. This sub-analysis was performed in the group of patients with a diagnosis of primary OA at index surgery, because of almost complete registration of the incision in this group (99.97% of all OA cases with a lateral or posterior approach). Other diagnoses had a considerably larger number of cases with an unknown type of approach. Other surgical approaches in the OA group accounted for only 1.6% of the total cases with OA and were not included in this sub-analysis.

4.7.2 Study III

Apart from the analysis of all Vancouver type B fractures, two further sub-analyses were performed after excluding interprosthetic fractures. The first sub-analysis compared the outcome after the treatment of type B1 fractures with either a conventional or a locking plate and without implant revision or supplementary fixation using other techniques. The second sub-analysis, in fractures around a loose stem (both B2 and B3), investigated the outcome after revision (with or without ORIF), with a cemented, an uncemented modular, or an uncemented monoblock stem. In this sub-analysis, stems used in fewer than 10 procedures during the whole study period, short revision stems (≤150mm length) and four uncemented modular MP stems that were fixed distally with cement were excluded.

4.7.3 Study IV

Population characteristics and the outcome of Vancouver type C fractures treated with either plate fixation or an intramedullary nail were described in this study. Further comparisons between locking and conventional plates were made in a sub-analysis where only one plate had been used, while interprosthetic fractures were excluded. We restricted the follow-up to a maximum

of two years (re-reoperation within two years), because of different mean follow-up times in the two compared groups.

4.8 Outcome measurements

The outcome measurement in Studies I and II was the first reoperation due to a periprosthetic femoral fracture after a primary THR. The follow-up began in 2001 and ended in 2011, or when the patient died, emigrated, or underwent a reoperation regardless of the reason. The outcome measurement in Studies III and IV was the first reoperation after the surgical treatment of PPFF (re-reoperation). The follow-up began in 2001 and ended in 2013, or when the patient died, emigrated, or underwent a re-reoperation irrespective of the reason.

4.9 Statistical methods

All statistical analyses were performed with SPSS statistics (IBM Corp, Armonk, NY, USA). Descriptive statistics were used to describe population characteristics, proportions, mean and median values. P-values were two sided with a significance level of < 0.05. Median and interquartile range, or mean and 95% confidence intervals (CI) of the mean were calculated. For a comparison of proportions between categorical variables, we used the chi-square test (χ^2-test). Student's t-test was applied in the comparison of means between two independent continuous variables, whereas, for the comparison of medians, the Mann-Whitney test was preferred. One-way analysis of variance (ANOVA), with the Tukey test, was performed to compare the means of more than two variables. A Kaplan Meier estimate with a log rank test was used in survival analyses, while Cox regression model for calculating relative risks was used in univariate and multivariate analyses of risk factors. We plotted survival curves for the covariates included and log-log plots to test whether the Cox proportional hazard model was fulfilled. Kappa statistics were used in Study I, to validate the classification process.[221] This method had been used in previously reported validations of the Vancouver classification system and showed substantial agreement.[62, 63] In order to describe the relative strength of agreement, we divided the ranges of kappa, as previously described by Landis & Koch (Table 2).[222]

4.10 Primary outcome measurement and censoring in Cox regression analyses

The primary outcome was defined as any type of reoperation due to a periprosthetic fracture in Study I and due to Vancouver type B or C in Study II. Censored cases in Study II included reoper-

Table 2. Divisions used by Landis & Koch to describe the strength of agreement in kappa-statistics.

Kappa Statistic	Strength of Agreement
0.00 – 0.20	Slight
0.21 – 0.40	Fair
0.41 – 0.60	Moderate
0.61 – 0.80	Substantial
0.81 – 1.00	Almost Perfect

ations for reasons other than Vancouver type B and C fracture, death, emigration or end of follow-up on 31 December 2011. In Studies III and IV, the primary outcome measurement was re-reoperations related to previously treated Vancouver B or Vancouver C fractures respectively. These could be any reoperation due to hip dislocation, stem loosening, infection, pain, other technical reasons and "nonunion". "Nonunion" included cases with pseudoarthrosis, re-fracture and fixation failure. Censored cases were re-reoperations with cup revision only (due to cup loosening), transfemoral amputation (due to arterial insufficiency), death, emigration, or end of follow-up on 31 December 2013.

4.11 Ethics

All the studies were approved by the Central Ethical Review Board in Gothenburg (entry number: 198-12, date: 2012-04-05). Three supplementary approvals were obtained due to an unexpectedly higher number of cases in the first cross-matching (date: 2013-05-27), the extension of follow-up from 2012 to 2013 in Studies III and IV (date: 2015-06-03) and linkage with the SKAR for Studies III and IV (date: 2016-05-24).

5. RESULTS

RESULTS

5.1 Validation of the classification process

A comparison between a classification based on a review of medical charts and radiographs revealed agreement in 78 of the 103 cases analysed (76%). The observed agreement between these two methods is shown in detail in Table 3. The Cohen's kappa value was 0.66 (SE=0.06), corresponding to substantial agreement, according to Landis & Koch. The inter-observer agreement between the authors who assessed the radiographs was 0.61 (SE=0.05) at the first review and 0.60 (SE=0.06) at the second. The intra-observer agreement for author HL was 0.82 (SE=0.05), while it was 0.83 (SE=0.04) for author JK, between the first and the second review of the radiographs.* Figure 19 illustrates examples of periprosthetic fractures included in this validation process.

5.2 Registration of periprosthetic fractures in the SHAR

Study I revealed that only 55% of all first-time periprosthetic fractures, treated surgically between 2001 and 2011, were registered in the SHAR. A significant difference was noted in the registration rate between PPFFs treated with stem revision (96.8%) and those undergoing surgery with methods other than revision (26.2%, $p<0.001$).* This also

Table 3. Classification of periprosthetic fractures based on radiographs, compared with classification based on information derived from medical charts (unpublished data).

Classification based on medical charts	"Gold standard" classification based on radiographs						
	AG	AL	B1	B2	B3	C	TOTAL
AG	**2**	0	0	1	0	0	**3**
AL	0	**0**	0	0	0	0	**0**
B1	0	1	**8**	2	0	1	**12**
B2	0	0	7	**26**	6	0	**39**
B3	0	0	0	2	**5**	0	**7**
C	0	0	5	0	0	**37**	**42**
TOTAL	**2**	**1**	**20**	**31**	**11**	**38**	**103**

*Unpublished data

Figure 19 (a-f). Pre-operative radiographs of periprosthetic fractures included in Study I, at the validation of the classification process. **(a)** Vancouver type AG, **(b)** Vancouver type AL, **(c)** Vancouver type B1, **(d)** Vancouver type B2, **(e)** Vancouver type B3, **(f)** Vancouver type C. In all the types illustrated here, apart from the AL, there was agreement between the "gold standard" classification and the classification based on medical records.

meant that the population characteristics of the PPFF cohort after the linkage differed significantly compared with those primarily registered in the SHAR. The compiled cohort consisted of older patients (p=0.016), more females (p<0.001) and more Vancouver type C fractures (p<0.001) than recorded in the original SHAR database. The registration rate for each Vancouver category was: A=79.4%, B1=41.7%, B2=89.6%, B3=93.8%, C=16.7%.

In comparison with the registration of first-time periprosthetic fractures, the reporting of reoperations after a PPFF (re-reoperations) was better only for B1 and C fractures (Studies III and IV). The registration rate for each category was: B1=82.4%, B2=81.4%, B3=87.5%, C=73.1%. Stem revisions after previously treated Vancouver type B fractures (Study III) showed a high level of completeness (95.4%), whereas the completeness of re-reoperations performed without the revision of the femoral component was poorer (72.5%).

5.3 Incidence (Study I)

The incidence of surgically treated periprosthetic fractures in Sweden increased from 1.0 per 1,000 primary THRs in 2001-2002 to 1.4 in 2011. The highest incidence, with the highest increase, was noted in patients aged 80 years and older (Fig. 20). The number of reoperations due to PPFF between 2001

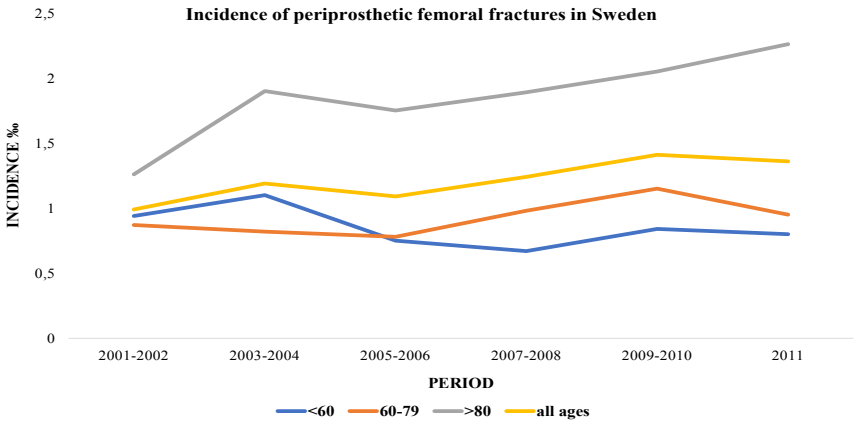

Figure 20. Incidence of periprosthetic femoral fractures per 1,000 primary THRs inserted between 1992 and 2011.

Table 4. Reoperation due to PPFF on the most common primary stems. All primary THRs and reoperations were performed between 2001 and 2011.*

Type of primary stem	Number of primary THRs	Number of PPFFs	Reoperation rate %
All cemented	**121,928**	**664**	**0.5**
Lubinus SP II	67,554	193	0.3
Exeter Polished	34,498	330	1.0
Spectron	8,328	37	0.4
MS30 Polished	6,026	26	0.4
Charnley	3,230	19	0.6
CPT	2,292	59	2.6
All uncemented	**22,552**	**129**	**0.6**
CLS Spotorno	8,054	33	0.4
Corail	5,936	30	0.5
Bi-Metric	5,389	39	0.7
ABG I or II	3,173	27	0.9

* Unpublished data
PPFF (periprosthetic femoral fracture), THR (total hip replacement)

and 2011 in relation to numbers reported for the most commonly used primary stems during the same period is shown in Table 4.

5.4 Age

At the time of primary THR, the mean age of patients that subsequently suffered a periprosthetic fracture varied between 68 and 72 (Studies I, III, IV). Patients who suffered a PPFF around a Lubinus or an Exeter stem were significantly older at primary THR (mean age 74.6 years, CI: 73.7-75.4, $p<0.001$) than those without a reoperation due to PPFF (mean age 71.6 years, CI: 71.5-71.7).* In the entire population (Study I), patients with uncemented stems were approximately 12 years younger at index operation (60.5 years, CI: 58.6-62.3) than those with cemented fixation (72.1 years, CI: 71.6-

*Unpublished data

72.7). Females were significantly older than males (72 versus 70) and patients with Vancouver type C fractures had a higher mean age at the time of primary THR than those with type A, B2 and B3. In Study III, where only Vancouver type B fractures were studied, patients in the B1 group were older than those in the B2 and B3 groups at primary THR.

At the time of PPFF, the mean age of patients ranged between 77.5 and 80 years (all four studies). Females were significantly older (mean 78.9 years) than males (mean 75.5 years) and individuals suffering a Vancouver C were older than those with a type A or B2 fracture (Study I). Patients reoperated on due to PPFF (median age: 80 years) were older than those reoperated for any reason (74 years, Study II). Women with a type B1 or B2 fracture were older than men with the corresponding fracture types (B1: 80 versus 77 years; B2: 79 versus 77 years, Study III).

5.5 Gender

A higher proportion of females was noted in the total population of PPFFs in Study I (60%) and in Study II (61%). A higher proportion of females was also noted in Study IV (84%), where only type C fractures were included. In Study III, in which we investigated Vancouver B fractures, the gender distribution was almost equal (48% females). Within the subcategories of B fractures, females were slightly more frequent in the B1 group (54%), while the same thing applied to males in the B2 group (54%).

5.6 Fracture types

The two most common fracture types, reported in Study I, were Vancouver type B2 (42%) and C (37%). Type B2 was the most common fracture type in men, in patients younger than 90 years, after an operation with an uncemented stem and among the cemented stems, apart from cases undergoing surgery with a Lubinus SP II. Vancouver type C fractures were the most common type in women and in patients older than 90 years. Study II revealed that 74% of all fractures around a Lubinus stem were type C, while 73% of all fractures related to an Exeter stem were type B. A more complete registration of periprosthetic fractures had a great impact on the percentage of different Vancouver categories (Study I). Fractures of type B1 and C were recorded in higher percentages after the linkage with the NPR (16% and 37% respectively), compared with those primarily reported in the SHAR (12% and 11% respectively). This change also meant that the percentage of fractures classified as B2 and B3 became smaller in the linked database (42% and 3% respectively) than in the SHAR database

before cross-matching (69% and 5% respectively).

5.7 Diagnosis at primary THR

The two most common diagnoses at index THR, in patients with PPFF, were primary OA and hip fracture (all studies). In Study I, where all types of primary stem since 1992 and all types of fracture were included, cases with OA accounted for 64% of all PPFFs. Half these cases were B2 or B3 fractures. Hip fracture (20%), inflammatory arthritis (7%) and idiopathic femoral head necrosis (5%) were less common. The percentage of primary OA was higher in Studies II (83%) and III (72%) and lower in Study IV (55%), where only type C fractures were investigated. Generally, the percentage of different diagnostic groups varied due to different selection criteria in each study.

5.8 Time to PPFF

The mean time between primary THR and the first reoperation due to a periprosthetic fracture was 6.6 years (CI: 6.4-6.9, Study I).* There was no difference between males (6.6 years) and females (6.7 years), but there was a difference between cemented (7 years, CI: 6.8-7.3) and uncemented stems (3.6 years, CI: 2.9-4.3). The mean time to fracture for each Vancouver category, in all studies,

Table 5. The mean time between primary THR and PPFF with 95% confidence intervals (CI).

Vancouver category	Mean time between primary THR and PPFF, years (95% CI) Study I *	Study II	Study III	Study IV
A	6.5 (4.7-8.4)			
B (all)	6.8 (6.5-7.1)	3.3 (3.0-3.6)	9.9 (9.5-10.3)	
B1	6.4 (5.8-7.0)		8.4 (7.7-9.1)	
B2	6.7 (6.4-7.1)		10.1 (9.6-10.6)	
B3	9.5 (8.3-10.7)		13.3 (11.9-14.7)	
C	6.5 (6.1-6.8)	3.5 (3.2-3.9)		7.1 (6.7-7.5)

* Unpublished data
THR (total hip replacement), PPFF (periprosthetic femoral fracture)
Study I: B3 vs B1; p=0.001, B3 vs B2; p=0.002, B3 vs C; p<0.001
Study III: B3 vs B1; p<0.001, B3 vs B2; p=0.001, B1 vs B2; p=0.001
(one-way ANOVA, the Tukey test was used for the statistical analysis)

*Unpublished data

is shown in Table 5. Statistically, type B3 fractures had the longest time to PPFF. As expected, the mean time to fracture was shorter in Study II, which included cases between 2001 and 2011, and longer in Studies III and IV, where primary THRs inserted since 1979 were included. The mean time to PPFF did not differ statistically between Lubinus SP II (3.3 years, CI: 2.9-3.7) and Exeter Polished stems (3.4, CI: 3.1-3.7, Study II).* The diagnosis at primary THR influenced the mean time to PPFF (Study III). Periprosthetic fractures in patients with OA or inflammatory arthritis occurred significantly later (10.4 and 12.1 years respectively) than in patients with a hip fracture (6.2 years) or idiopathic femoral head necrosis (7.7 years) at the index operation.

5.9 Fixation and design of the primary stem

In Studies I and III, 89% of the primary stems were cemented and in Study IV, only including Vancouver C fractures this share constituted 93%. Study II only comprised cemented stems and only two types (Exeter and Lubinus). Three stem designs – Lubinus SP II, Exeter Polished and Charnley – constituted 66% of all the stems in Study I, 65% in Study III and 77% in Study IV.*

5.10 Risk factors for PPFF (Study II)

Risk factors for Vancouver B fractures, in a population with cemented primary Lubinus or Exeter stems, were male gender (HR= 2.8, CI: 2.2-3.6), hip fracture (HR= 3.3, CI: 2.4-4.4), idiopathic FHN diagnosis (HR= 3, CI: 1.9-5) and calendar year for primary THR (HR= 1.1, CJ: 1.1-1.2). The design of the primary stem was a strong risk factor, with the polished force-closed Exeter stem running a 9.6 times higher risk (CI: 7-13) of a B fracture than the matte shape-closed Lubinus stem. In OA patients alone, the insertion of the primary THR with a posterior approach was associated with a 1.6 times higher risk (CI: 1.2-2.2) of a B fracture than if the prosthesis was implanted using a lateral approach.

Stem design and calendar year for the primary THR were not risk factors for type C fractures. Patients with a primary diagnosis of hip fracture and idiopathic FHN ran an approximately four times higher risk of type C fractures compared with OA patients. In contrast to type B fractures, female gender (HR= 2, CI: 1.4-2.8) and inflammatory arthritis (HR=5.6, CI: 3.3-9.6) were risk factors for fractures distal to a femoral stem. Increasing age, especially age ≥ 75 years, was a risk factor for both B and C fractures.

*Unpublished data

5.11 Treatment of Vancouver type B fractures (Study III)

The vast majority of Vancouver type B1 fractures (90.5%) were treated with ORIF. In 85% of the cases, one plate was used and, in 12%, two plates. Other methods used for the fixation of B1 fractures were cerclage wiring (seven cases) and intramedullary nailing (the "docking-nail" method, one case). A comparison between conventional and locked plating revealed that LPs were preferred in females and in elderly individuals. The use of locked plating began in 2005 and, since 2009, LP has been the most common type of ORIF for the treatment of B1 fractures.

Revision of the femoral stem, with or without ORIF, was the preferred treatment method in 86.4% of cases with a type B2 fracture and 98.7% with a type B3. The three main categories of revision stems were uncemented modular (53%), uncemented monoblock (13%) and cemented (34%). Cemented revision stems were preferred in females, in elderly patients and in cases with a B3 fracture. The most common type of stems used for B2 and B3 fractures was initially cemented, but, since 2005, uncemented modular stems were mostly preferred, with half of them inserted between 2009 and 2011 (Fig. 21). A strut graft, as a supplement in treatment, was used in a few cases of B2 (0.1%) and B3 (10%) fractures. Other types of bone grafting were applied in 6% of the B2 fractures and 33% of the B3 fractures.

5.12 Treatment of Vancouver type C fractures (Study IV)

Four main methods of ORIF were used for the treatment of Vancouver type C fractures; fixation with two plates irrespective of the type of plate (DP, 4.7%), intramedullary nailing (IMN, 9.7%), fixation with one conventional plate (CP, 28.8%) and fixation with one locking plate (LP, 56.8%). Double plating was preferred in males, while the IMN cohort included younger patients and a larger share of interprosthetic fractures. Locking plates were used throughout the study period and are the most common type of ORIF since 2006 (Fig. 22). Between 2001 and 2006, the most applied type of fixation was CP, with 84% of those inserted during this period of time. The opposite was noted in LPs. Eighty-four per cent of those were used between 2007 and 2011.

5.13 Outcome in Vancouver type B fractures (Study III)

The re-reoperation rate for all Vancouver type B fractures was 17.3%, with significantly higher rates for IPFFs (30%) compared with non-IPFFs

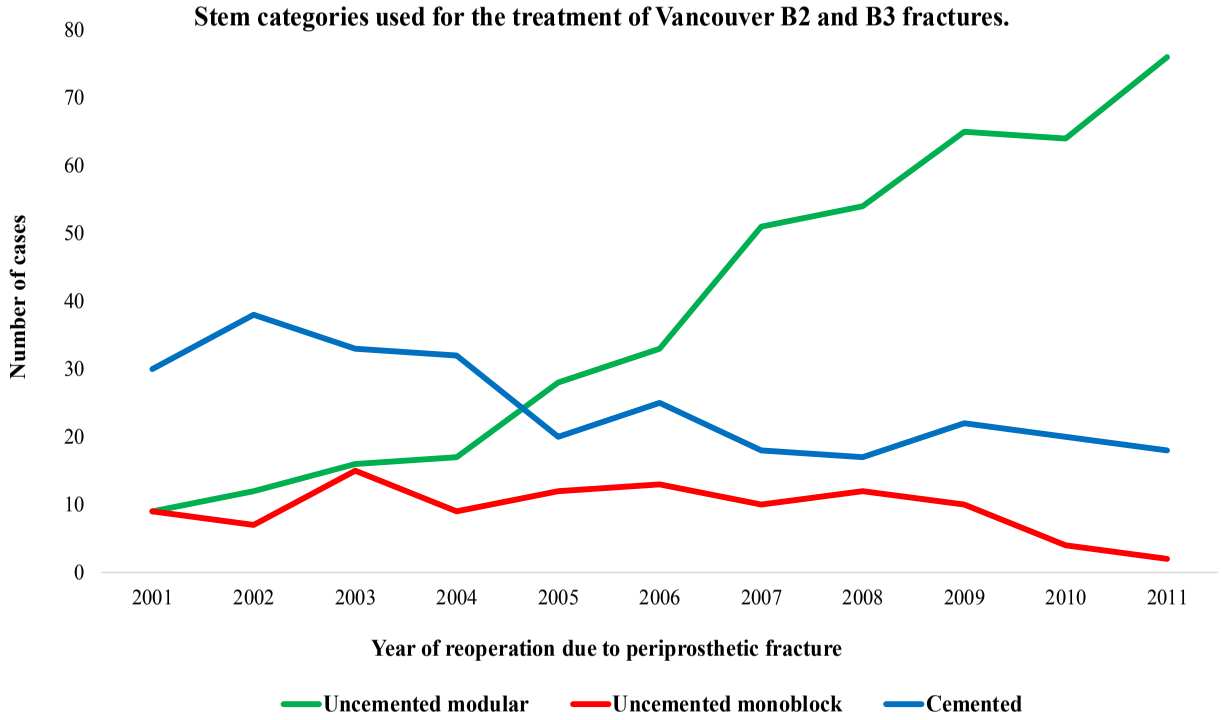

Figure 21. Number of B2 and B3 periprosthetic fractures treated with stem revision, alone or in combination with ORIF (801 cases). Reproduced (and modified) with permission and copyright © of the British Editorial Society of Bone & Joint Surgery [**Chatziagorou G, Lindahl H, Kärrholm J.** Surgical treatment of Vancouver type B periprosthetic femoral fractures. Bone Joint J 2019;101-B:1447-1458].

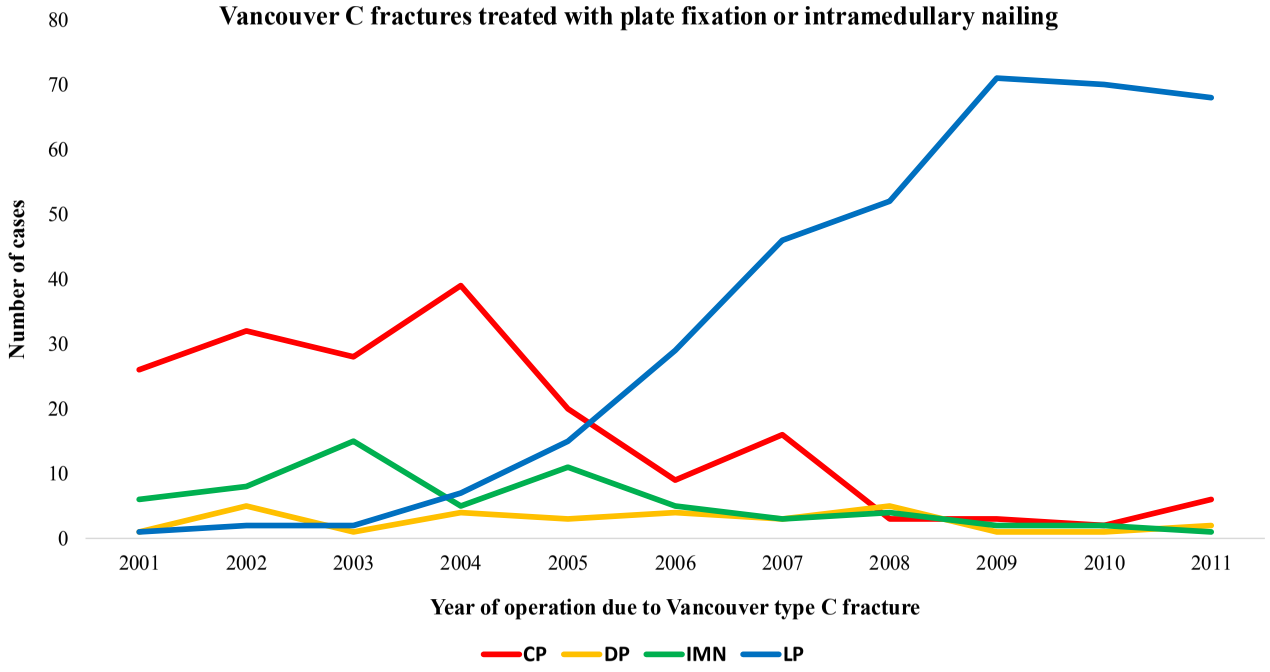

Figure 22. The use of conventional plates (CP), locking plates (LP), intramedullary nails (IMN) and a combination of two plates (DP) for the treatment of Vancouver type C fractures.

Table 6. Revision stems used for the treatment of B2 and B3 fractures, and included in the sub-analysis.

Type of revision stem	Number of PPFFs (re-reoperations)	Re-reoperation rate %
Uncemented modular	**425 (61)**	**14.4**
MP revision stem	215 (43)	20.0
Revitan	114 (13)	11.4
Restoration	96 (5)	5.2
Uncemented monoblock (Wagner)	**103 (13)**	**12.6**
Cemented	**273 (34)**	**12.5**
Lubinus SP II	103 (19)	18.4
Exeter Polished	79 (7)	8.9
Spectron	44 (3)	6.8
CPT	19 (1)	5.2
Charnley	16 (3)	18.8
RX 90-S	12 (1)	8.3
TOTAL	**801 (108)**	**13.5**

PPFF (periprosthetic femoral fracture)
The numbers in the parentheses refer to PPFF-related re-reoperations.
 [**Chatziagorou G, Lindahl H, Kärrholm J.** Surgical treatment of Vancouver type B periprosthetic femoral fractures. *Bone Joint J* 2019;101-B:1447-1458]

(16%, p=0.001). Type B1 fractures had a statistically poorer outcome (22.1%) than B2 fractures (15.6%, p=0.002), while 20% of B3 fractures underwent a second reoperation (re-reoperation) in relation to previously treated PPFF. The re-reoperation rate for B1 fractures treated with stem revision (17%) was lower than for those treated with ORIF (23%), but this was not statistically significant. The sub-analysis of B1 fractures revealed no significant difference in the re-reoperation rate after ORIF with CP (26%) compared with those treated with

LP (19%, p=0.3). However, 55% of re-reoperations in the CP group included stem revision, compared with only 17% of B1 fractures treated with LP (p=0.016). So, if the outcome measurement, after the treatment of B1 fractures, had been revision of the stem, the rates would have been 14.5% for the CPs (18/124 cases) and 3.4% (3/88 cases) for the LPs, which is statistically significant (p=0.009).* The two groups that were compared were not statistically similar. The CP group had more males and a longer follow-up. Patients treated with CP were three years older at PPFF, but this was not statistically significant. The two most common reasons for re-reoperation were nonunion (13.2%) and loosening of the stem or the stem and the cup (4.4%), while the rate of infections was 2.8%.

In type B2 fractures, the two most common reasons for re-reoperation were nonunion (5.3%) and hip dislocation (4.2%). Dislocation of the hip prosthesis was more common in B3 fractures (8%). Nonunion and loosening of the femoral component each accounted for 4% of the re-reoperations after a B3 fracture. Infections that required re-reoperation were reported in 3.4% of B2 and 1.3% of B3 fractures. A significantly higher re-reoperation rate was noted in B2/B3 fractures treated with ORIF (22%) compared with those treated with stem revision (13.5%, p=0.015). The three revision stem categories differed significantly regarding gender, age, fracture type and time of follow-up. The most common reason for re-reoperation was nonunion in cemented stems (6%) and hip dislocation in uncemented modular (5%) and monoblock (7%) stems. Statistically similar re-reoperation rates were noted between uncemented modular (14.4%), uncemented monoblock (12.6%) and cemented stems (12.5%, Table 6). If the outcome measurement had been a second stem revision after previously treated B2/B3 fractures with stem revision (re-revision), the total re-revision rate for all three categories would have been 5.4% (43/801 cases).* Re-revision rates within the three stem categories were 3.3% in cemented (9/273 cases), 3.9% in uncemented monoblock (4/103 cases) and 7.1% in uncemented modular stems (30/425 cases).* A significant difference was noted in the comparison between cemented and uncemented modular stems (p=0.042).*

5.14 Outcome in Vancouver type C fractures (Study IV)

The re-reoperation rate after the open reduction and internal fixation of Vancouver type C fractures was 15.2%. Fractures between a hip and knee prosthesis (IPFF) did not have a significantly different re-reoperation rate from fractures in cases with only a

*Unpublished data

hip replacement. This was noted both in the entire fracture population and after subgrouping into treatment groups. The majority of all re-reoperations (86%) were performed during the first two years after the PPFF and the two most common reasons for re-reoperation were nonunion (10.5%) and pain/technical reasons (2.2%). Re-reoperations due to infection were recorded in 1.4% of the cases. Only five stems underwent revision after the treatment of Vancouver C fractures (0.8% revision rate). Higher re-reoperation rates were noted in the IMN (24%) and CP groups (23%) than in the LP (10%) and DP groups (7%). The incidence of re-reoperations after type C fractures decreased from 9.1% in 2001-2002 to 1.8% in 2011. The sub-analysis of cases treated with only one plate (IPFFs excluded) showed that conventional plates ran a 2.4 times higher risk of re-reoperation compared with locking plates. The two groups that were compared were similar in terms of population characteristics and follow-up time, which was two years after a PPFF. Approximately 8% of LPs (20/259) underwent a re-reoperation within two years, compared with 18% of the CP group (27/152, p=0.003). Mean survival at two years was 79.9% (SE 3.5%) for conventional plating and 91.3% (SE 1.9%) for locked plating (log rank test p=0.002).

5.15 Risk factors for re-reoperation after a PPFF

Risk factors for re-reoperation were studied with Cox regression analysis and only published for type B fractures in Study III. This analysis was performed in cases with cemented primary stem fixation and the diagnosis of primary OA. Risk factors for re-reoperation were decreasing age, B1 fracture type and the presence of an ipsilateral knee prosthesis. Gender and year of operation due to PPFF were not risk factors (Table 7). A Cox regression analysis of the sub-analysis between CP and LP in Vancouver type C fractures showed that neither age nor gender was a risk factor for poor outcome (Table 8).

5.16 Time to treatment, mechanism of injury, weight-bearing, discharge and mortality

The mean time interval between the surgical treatment of a PPFF and re-reoperation varied between one year in type C fractures (Study IV) and 1.6 years in type B3 fractures (Study III). The most common mechanism of injury recorded in all studies was a fall from standing height. This parameter was investigated and only published in Study III (84.1%), but a low-energy injury was also the main reason for PPFF in Study I (86.8%), Study II (89.7%) and Study IV (92.8%).

Table 7. Risk factors, hazard ratios (HR), and 95% confidence intervals (CI) for reoperation after the surgical treatment of Vancouver type B periprosthetic fracture. Only cases with the diagnosis of primary OA and cemented stem fixation at primary THR are included.

Risk factors	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
TKR ipsilaterally		
No (reference)	1	1
Yes (IPFF)	2.0 (1.1-3.5)	2.2 (1.2-3.8)
Type of PPFF		
B2 or B3 (reference)	1	1
B1	1.5 (1.1-2.2)	1.5 (1.1-2.2)
Gender		
Females (reference)	1	1
Males	0.9 (0.6-1.2)	0.8 (0.6-1.2)
Mean age at PPFF	0.977 (0.959-0.996)	0.973 (0.955-0.992)
Year of PPFF surgery	0.99 (0.94-1.05)	0.99 (0.94-1.05)

TKR (total knee replacement), IPFF (interprosthetic femoral fracture) PPFF (periprosthetic femoral fracture)

Postoperatively, partial or full weight-bearing was allowed, depending on the type of fracture and the treatment. In general, higher percentages of permitted weight-bearing were recorded in type B fractures treated with a stem revision than in those cases treated with ORIF alone (Study III). Weight-bearing was allowed in 64.5% of Bl and 65.5% of B2/B3 cases treated with ORIF alone, compared with 93.1% ($p=0.001$) and 86.7% ($p<0.001$) respectively, treated with a stem revision (with or without ORIF).* Cases with a Vancouver type C fracture were allowed to bear weight to a lesser degree (48%).

Some 25% of the patients with Vancouver B fractures (Study III) and 20% of those with Type C fractures (Study IV) were discharged to their homes. The mortality

*Unpublished data

rates after the treatment of Vancouver type B and C fractures are illustrated in Table 9. In Study IV (Vancouver type C fractures), patients older than 80 years had higher two-year mortality (35.2%) compared with those aged 80 years and less (12.9%, p<0.001).

Table 8. Risk factors, hazard ratios (HR) and 95% confidence intervals (CI) for reoperation within two years after the surgical treatment of Vancouver type C periprosthetic fractures. Interprosthetic fractures were excluded.

Risk factors	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Type of plate		
LP (reference)	1	1
CP	2.4 (1.4-4.4)	2.4 (1.3-4.3)
Gender		
Females (reference)	1	1
Males	0.9 (0.4-2.1)	0.7 (0.3-1.8)
Mean age at PPFF	0.98 (0.96-1.001)	0.98 (0.96-1.002)

LP (Locking Plate), CP (Conventional Plate)

Table 9. Mortality rates after the surgical treatment of Vancouver type B and C fractures.

Vancouver type	Mean age at PPFF Years (95% CI)	Gender Males (%)	Mortality rates %		
			Inhospital	1 year	2 years
B all	78.2 (77.6-78.8)	52.0	2.4	13.8	20.0
B1	78.5 (77.2-79.8)	46.0	2.5	11.7	18.7
B2	78.1 (77.4-78.8)	54.4	2.3	14.4	20.2
B3	78.8 (76.6-81.1)	45.9	2.7	13.5	23.0
C	79.2 (78.3-80.1)	16.0	1.6	15.7	24.2

PPFF (periprosthetic femoral fracture)
All calculations for this table were based on the number of patients and not on the number of cases. (Data not included in Papers I-IV)

6. DISCUSSION

DISCUSSION

6.1 The material in this thesis

Large epidemiological studies that describe PPFFs close to a primary THR have previously been published.[7, 8] What makes the present material unique is the exclusion of cases that could bias the results, and the high level of completeness by data linking between two national registers in two steps. In a previous thesis, Lindahl focused on periprosthetic fractures in Sweden between 1979 and 2000.[223] The current thesis deals with PPFFs treated during the following period and up to 2011. During this period, orthopaedics in Sweden underwent substantial changes relating to the implant selection used in primary THRs and the treatment of PPFFs. The use of uncemented primary stem fixation, in our material, increased from 3.9% in 2001 to 29.4% in 2011. Around the middle of the study period, there were two transitions relating to the surgical treatment of periprosthetic fractures. One was the shift from conventional plates to locking plates in B1 and C fractures (Studies III and IV) and the other was the increasing use of uncemented modular stems instead of cemented stems for treating B2 and B3 fractures (Study III). These transitions facilitated comparisons of methods that have now been more or less abandoned (conventional plates), in addition to those still in use (e.g. locking plates, uncemented and cemented revision stems).

6.2 Validation of the classification process and the Vancouver classification system

The comparison of the classification based on a review of medical charts with the classification based on radiographs revealed substantial agreement (k=0.66), which is similar to previously reported validations of the Vancouver classification system.[62, 63] This finding allowed us to continue conducting research (Studies II-IV) based on the information from the charts. Misclassification might, however, have occurred due to methodological limitations, as discussed later in limitations, and even due to weaknesses in the Vancouver classification itself.

According to the description of this classification system,[61] there is no distinct limit regarding the division of PPFFs into B and C fractures. Duncan & Masri stated that “type C fractures are so distal to the stem that the presence of

the femoral component may be ignored and the fracture can be treated by conventional methods".[61] This definition of type C fractures enables different interpretations to be made and, as a result, a fracture just distal to the tip of the femoral stem can be classified as type B or type C by different authors. One example is the work by Leonidou et al. and Caruso et al..[224, 225] A fracture at the tip of the stem was classified as type C by Caruso et al. (Fig. 23) but as type B by Leonidou et al. The latter study defined type B fractures as those that had their most distal end two femoral diameters distal to the tip of the stem. In our research project, fractures distal to the stem tip were classified as type B if the cement mantle (cemented) or the tip of the stem (uncemented) was visible per-operatively. In Study I, we recorded the highest percentage of Vancouver type C fractures (37% of all types), compared with previous reports. This was probably due to the high level of completeness in our material, even including fractures treated with methods other than stem revision, and the small number of type A fractures registered in the SHAR because they are usually treated non-surgically.[8]

The distinction between B2 and B3 fractures is also debatable. According to previous descriptions of the Vancouver classification system, a B3 fracture requires complex reconstruction, proximal femoral replacement, or a tumour prosthesis and it is no longer capable of supporting a standard revision stem.[61, 62] According to the

Figure 23. Fracture at the tip of a femoral stem, classified as Vancouver type C by Caruso et al.
Reproduced with permission and copyright © of Springer Nature [Caruso C, Milani L, Marko T, Lorusso V, Andreotti M, Mssari L. Surgical treatment of periprosthetic femoral fractures. Eur J Orthop Surg Traumatol. 2018 Jul;28(5):937, Fig. 6]

recommendations by Balkissoon et al., these treatment alternatives may be used in femurs classified as Paprosky type IV regarding the bone stock, while primary stems could be used in Paprosky type I and II femurs.[226] The use of a long revision stem that bypasses the fracture has been advised in type B2 fractures.[82] This means that these stems are suitable if there is a loose primary stem surrounded by a bone stock corresponding to Paprosky I or II. However, there are studies that classify cases with bone loss according to Paprosky I and II types as B3,[16] as well as studies with a relatively high proportion of type B3 fractures treated with standard revision stems.[204] Moreover, it is common to treat both B2 and B3 fractures with uncemented modular stems,[164, 165] uncemented monoblock stems,[15] or cemented revision stems.[160] The classification of fracture type should therefore not relate primarily to the type of stem used to treat the fracture. Despite the absence of radiographs, we attempted to be concise regarding the criteria used for the classification of periprosthetic fractures as presented in Study I.

The proportion of type B3 fractures varies in the literature, with most of the studies reporting an incidence between 9% and 11%.[8, 13, 83, 130, 193] Fewer studies have reported proportions higher than 17%,[154, 204, 205] or lower than 5%.[7, 111, 121] The relatively small percentage of B3 fractures in our material (2.7%, Study I) was partly the result of the improved recording of fractures treated with ORIF. Another reason may be the classification criteria used by us. One of the criteria was the use of bone grafts which was recorded in relatively few cases in Study III. So, if a surgeon did not mention the status of the bone stock and the fracture was not treated with supplemental bone grafting, it could be that B3 fractures might have been misclassified as B2 to a certain extent. Previous publications based on a Swedish population reported proportions of B3 fractures similar to those reported in Study I.[7, 111] This may indicate that Swedish surgeons use less bone grafting, especially strut grafts, or have more demanding criteria when it comes to defining the bone stock as inadequate, or both. Vancouver type B2 was the most common type of PPFF (Study I), which is in line with most previous reports. Only a few studies have reported type B1 fractures as the most common fracture type.[121, 204, 205]

6.3 Validation of the SHAR database and the impact of data linking

Every type of reoperation after hip replacement surgery is supposed to be reported to the SHAR. However, reoperations without stem revision

had a significantly lower registration rate (26%) than revision surgery (97%). Furthermore, type B1 fractures, where ORIF is a very common treatment method, had better completeness (42%) than type C fractures (17%). This is presumably because B1 fractures were more commonly treated with stem revision than type C fractures. Further, trauma surgeons who operate on periprosthetic fractures with ORIF did not report to an arthroplasty register during our study period. Today, there is a link between the SHAR and the Swedish Fracture Register, which will address this problem. The compiled data on all PPFFs after the linkage revealed that the patient population with type C fractures was substantially larger than originally observed in the SHAR, they were also older and included more females (Study I).

The improved completeness of re-reoperations after previously treated Vancouver B (82%, Study III), or Vancouver C fractures (73%, Study IV), compared with the registration rate for first-time reoperations due to PPFF (55%, Study I), could be explained by two factors. A second reoperation relating to a THR is often more complicated and hip replacement surgeons are almost always involved in these cases. Arthroplasty surgeons in Sweden may report to the SHAR with greater completeness than trauma surgeons. Another explanation is that, during the first linkage, all consecutive reoperations, not only the first one after a primary THR, were extracted from the NPR. This means that the compiled data that resulted after the first linkage also included any second reoperations that had not primarily been reported to the SHAR. After inclusion in the SHAR, these cases were marked as "already registered" at the second linkage with the NPR.

6.4 The incidence of periprosthetic femoral fractures

Study I revealed that not only the number of periprosthetic fractures but also the incidence of new cases of PPFF in relation to THRs at risk increased between 2001 and 2011 in Sweden. This was probably due to the increased use of uncemented stems in both men and women, together with the increasing use of uncemented stems in the elderly population. Previous reports have shown an increased risk of PPFF when using uncemented stems, especially in elderly patients.[49, 96] Another explanation could be the reduction in reoperations due to stem loosening and a longer time in situ, which can increase the risk of periprosthetic fractures.[3] The number of elderly patients (≥80 years) with a hip replacement has increased during the last few decades, due to both an increasing number of individuals

undergoing arthroplasty surgery and an increase in life expectancy. Study I showed a much higher incidence of fractures in patients older than 80 years.

Previous studies have referred to the incidence of PPFFs as an accumulated risk (or incidence),[7, 123] as an incidence per 10,000 or 100,000 person-years,[85, 92] as a cumulative probability,[8] or as the rate of periprosthetic fractures in relation to the total number of arthroplasties performed (most of the studies). The incidence we reported in Study I was the proportion of new PPFFs in relation to the number of primary THRs in patients that are still alive. The true incidence of all types of PPFF in Sweden is certainly higher, because fractures treated non-surgically and fractures around a revised stem were excluded from this thesis.

6.5 Patient characteristics

Previous studies have shown that patients with PPFF are older and have a lower BMI and a higher ASA score than patients who did not suffer a fracture close to a hip prosthesis.[10, 125] In the selected cohort of only Lubinus and Exeter stems (Study II), we observed a higher mean age in fracture patients compared with those who underwent a reoperation for other reasons. In our material, we also noted demographic differences within the Vancouver categories. Patients with B1 fractures were, demographically, closer to the Vancouver C group (higher age, more females), than to the B2 and B3 subtypes (younger, more males). Women with periprosthetic fractures were older than men at both primary THR and PPFF, but they had a similar time interval between the index operation and fracture (Study I).

6.6 Risk factors for PPFF around a cemented primary hip stem (Study II)

6.6.1 Age, gender and diagnosis

A higher risk of males suffering a fracture around a cemented stem (Lubinus or Exeter) was observed in Study II. This is in accordance with previous reports that reported a higher risk in men undergoing a revision due to periprosthetic fractures around cemented stems.[10, 49] In contrast to fractures around the stem, females and patients with inflammatory arthritis ran a higher risk of type C fractures (Study II). Distal femoral fractures, and thereby type C fractures, are associated with osteoporosis[227, 228] and it is reported that patients with rheumatoid arthritis run a higher risk of osteoporotic fractures.[229] In general, distal femur fractures are more common in women.[230] The finding that the diagnosis of idiopathic FHN and hip fracture at primary THR were risk factors for both B and C fractures is

in line with previous reports.[48, 49, 94, 111, 115] Finally, increasing age was a risk factor for both B and C fractures, as has also been reported by a large number of previous studies.

6.6.2 Force-closed versus shape-closed stem design

Comparisons between force-closed and shape-closed designs of cemented stems have previously been published, but with unknown stem parameters.[7, 49] Study II included only stems of the same length (150mm) and only hips with cemented cup fixation. Furthermore, the analysis could be made separately for type B and type C fractures, including all types of reoperation (stem revision and or ORIF). This fact allowed us to draw valid conclusions as regards the risk of periprosthetic fracture using the shape-closed design (Lubinus SP II) when compared with the force-closed design (Exeter Polished). The latter design showed a risk that was almost ten times higher than that of Vancouver type B fractures when compared with the Lubinus design. However, there was no statistically significant difference between them concerning the risk of suffering a femoral fracture distal to the stem.

6.6.3 Posterior versus lateral surgical approach

The surgical approach as a risk factor for periprosthetic fracture has been only remotely studied. Two reports reported no association between surgical approach and PPFF,[107, 111] one found a higher risk of intraoperative fractures during THR using an anterolateral approach,[112] while another reported a higher risk of PPFF using a posterior approach in hemiarthroplasties.[101] All four studies were based on different materials. Our hypothesis was that, if the lateral approach affected the thickness of the cement mantle,[231] the alignment of the stem[111, 232] and the risk of aseptic loosening,[233] it could potentially influence the risk of a fracture around a cemented stem (Vancouver type B). To our surprise, we found that the posterior approach (or posterolateral) involved a 60% higher risk compared with the lateral approach for type B fractures, in patients with primary OA and a standard Lubinus SP II or Exeter Polished stem (Study II). The posterior approach can result in increased internal rotation of the hip joint[234, 235] and less anteversion of the femoral stem in relation to the femur.[234, 236] Two in-vitro studies revealed that torsional forces around force-closed stems resulted in type B fractures.[91, 108] Minor movement in a stem with suboptimal stem-cement contact might

facilitate the build-up of local stress raisers when the stem is subjected to rotational forces. So, from a theoretical point of view, it could be that the choice of incision causes a slightly different rotational position of the stem in relation to the longitudinal axis of the femur, thereby resulting in a position subjected to higher torsional forces and/or with less resistance to torsional forces before failure.

6.7 Factors influencing the outcome of surgical treatment of a PPFF (Studies III and IV)

6.7.1 Age and gender

The literature has been in disagreement regarding the role of patient age on the outcome after a PPFF. It has been reported that a poorer outcome was related to higher age,[206] to lower age[195] and that age was not a risk factor.[200] In the Cox regression analysis in Study III, we found that younger age was a risk factor for poor outcome in Vancouver B fractures. The risk decreased by 2.8% for each year an individual aged. The analysis only included cases with cemented fixation of the primary stem due to primary OA and the mean age at the time of PPFF was 81.1 years (CI: 80.5-81.7).* In Study IV, we showed that patients older than 80 years of age had a significantly higher two-year mortality than those aged 80 years and less (35% vs 13%). Our interpretation of this finding is that the clinical relevance of a 3% difference in risk of reoperation per year of increased age could be questioned, because increasing age is also associated with higher mortality and a shorter follow-up. In contrast to age, gender was not a risk factor for poor outcome in Vancouver type B (Study III) and type C fractures.* This is in line with previous reports.[130, 195, 206]

6.7.2 Interprosthetic fracture

Interprosthetic fractures were more common in type C fractures (27%, 172/639 cases) than in type B fractures (7%, 97/1,381 cases). The presence of a knee replacement was only a risk factor for poorer outcome in B fractures. There is little evidence regarding the role of interprosthetic fractures as a risk factor. IPFFs were correlated with higher nonunion rates in 31 type B1 and 18 type C fractures, all treated with plate fixation.[200] In a retrospective study of 121 PPFFs, Füchtmeier et al. found no correlation between the outcome and the presence of an ipsilateral TKR.[130] This study included all types of PPFF and 21 fractures were around a revised stem. Similar complication rates in IPFFs and non-IPFFs were reported in a review study that included hemiarthroplasties, primary and revision THRs and all Vancouver categories.[183] However, peri-

*Unpublished data

prosthetic fractures treated only with a revision of the femoral stem were excluded from the study.

It is difficult to explain why the presence of an ipsilateral knee prosthesis influenced the outcome of B but not C fractures. The presence of a TKR may increase the technical difficulties involved in treating a PPFF with plate fixation and probably more so if the fracture is located around a hip prosthesis (type B) than if it is situated distal to it (type C). Higher complication rates in IPFFs where the TKR had a femoral extension have previously been reported.[78] It could be that there was an uneven distribution of TKRs with femoral extension between patients with B and C fractures in our material, but this remains a matter of speculation since the presence or absence of a femoral extension was unknown. One important principle, when treating a Vancouver type B fracture with a revision of the stem, is to bypass the fracture line. For this reason, longer revision stems are preferred, which means that the distance between the distal tip of the femoral stem and the proximal part of the TKR may be very short. If a plate extending distal to the tip of the stem is used, this interspace becomes even shorter. Soenen et al. showed that, if the stem tip distances become shorter than 11 cm, the risk of fracture increases dramatically.[237] So, in a patient population with an IPFF, individuals that received a long revision stem due to a type B fracture should theoretically run a higher risk of re-fracture or failure, compared with those suffering a type C fracture, in whom the stem was not revised and the space between the components is longer. In our material, we were not able to test this hypothesis because we did not have access to postoperative radiographs.

In Study III, we found that type B2/3 fractures treated with ORIF had a poorer outcome and the percentage of B fractures treated with ORIF did not differ significantly (p= 0.138) between the IPFF group (23.7%) and the non-IPFF group (31.2%).* The Cox regression analysis in Study III revealed that younger age was a risk factor for poorer outcome in Vancouver B fractures. Among all B fractures, the IPFF group was statistically younger (mean age 75.8 years, CI: 73.4-8.2) compared with the non-IPFF group (78.4 years, CI: 77.8-79.0, p= 0.027).* In Vancouver type C fractures, the mean age of the IPFF group was lower (78.1, CI: 76.4-79.8) compared with the non-IPFF group (79.4, CI: 78.4-80.5), but this was not statistically significant (p=0.179).* This observation could be interpreted as meaning that IPFFs were a risk factor for poor outcome in type B fractures and not in type C fractures, because patients with IPFF of type B were significantly

*Unpublished data

younger than those with type B fractures without a TKR. However, in the Cox regression model adjustment for age was done, which at least to a certain extent, should account for any age-related effect. Further research is needed to confirm and explain our findings.

6.7.3 Vancouver category

The re-reoperation rate for all B and C fractures (Studies III and IV) was 16.6% (336/2,020 cases) and this is in accordance with previously reported results.[130, 195] A higher re-reoperation rate was noted in B1 fractures (22%), while it was lower in B2 (16%) and C fractures (15%), whereas 20% of all B3 fractures underwent at least one more reoperation. The influence of Vancouver category on the outcome of treatment after periprosthetic fractures has previously been studied. The majority of these studies did not find any relationship between the type of fracture and the outcome,[130, 195, 204] but one previous report, based on material from the SHAR, showed that B1 fractures ran a higher risk of re-reoperation.[206] In Study III, we found that B1 fractures ran a 50% higher risk of undergoing further surgery than B2/B3 fractures. Unfortunately, we were not able to study radiographs and analyse this finding in depth. We believe that the most possible and strongest explanation is that a significant number of B2 fractures may have been misclassified by surgeons as B1 and treated with ORIF instead of stem revision. Type B2 and B3 fractures had a poorer outcome in our material when treated with ORIF. It could be that ORIF in general has a poorer outcome than stem revision.[193, 195, 207] In our material, ORIF was used in 90% of cases with B1 fractures and in 14% of B2 fractures. Other reasons that could theoretically explain our finding are: i) damage to the bone-cement or cement-stem interface at the time of fracture or when inserting screws during ORIF, ii) the general superiority of stem revision as an "intramedullary" type of fixation in femoral shaft fractures and iii) a possibly higher percentage of transverse or short oblique unstable fractures at the tip of the stem in B1 fractures than in B2 and B3 fractures.

6.7.4 Stem revision versus ORIF

The type of surgical method (ORIF or stem revision) has previously been studied as a risk factor for the outcome of PPFFs. Most of the studies have included all types of fracture, with some of them showing no correlation between the type of treatment and the outcome[130, 204] and others reporting a poorer outcome with ORIF.[195, 206] Similar findings have also been reported in studies that investigated Vancouver B fractures. Zuurmond et al. recorded a poorer outcome with ORIF, while Gitajn

*Unpublished data

et al. showed no correlation between treatment method and oucome.[193, 197] In Study III, we investigated this parameter separately for B1 and for B2/B3 fractures and found that ORIF only resulted in a significantly poorer outcome in fractures around a loose stem.

6.7.5 Locking plates versus conventional plates

There is little evidence regarding the effect of the type of plate fixation on the outcome of B1 and C fractures. Theoretically, locking plates provide many advantages in comparison with conventional plates.[238] Baba et al. compared 21 LPs with 19 CPs in mixed material of both B1 and C fractures, close to 31 hemiarthroplasties and nine THRs.[184] The authors found no difference between the two treatment groups. Three review articles have compared CPs and LPs with different results and different inclusion criteria. Dehghan et al., who only studied B1 fractures, reported lower nonunion rates with CPs but similar re-reoperation rates.[147] Moore et al. studied both B1 and C fractures and reported similar union rates between CP and LP for each Vancouver category.[146] Intraoperative and interprosthetic fractures were excluded, but they included studies with old-fashioned plate designs such as Partridge plates. Stoffel et al. included all types of periprosthetic fracture treated with ORIF.[183] In their material, both hemiarthroplasties and primary and revision THRs were included. The authors reported higher nonunion rates with CPs but similar re-reoperation rates when compared with LPs. In this thesis, the choice of a conventional plate or a locking plate affected the re-reoperation rate for Vancouver type C fractures (Study IV) but not type B1 fractures (Study III). Interprosthetic fractures were excluded in both cohorts. Fractures distal to a hip stem treated with a CP ran a 2.4 times higher risk of re-reoperation within two years compared with those treated with an LP. However, type B1 fractures showed higher rates of stem revision following treatment with a CP compared with an LP.

6.7.6 Stem design

The re-reoperation rate after the treatment of Vancouver type B2/B3 fractures did not differ significantly when we compared cemented revision stems with uncemented modular and uncemented monoblock stems (Study III). However, there were differences in the demography and follow-up time within these three treatment groups. Statistically similar re-reoperation rates in cemented and uncemented revision stems have previously been reported.[16, 169] In a relatively small material, Moreta et al. reported significantly more infections

with an uncemented monoblock stem (Wagner) when compared with an uncemented modular femoral implant (24 Modular-Plus).[15] Springer et al. compared cemented revision stems with fully and proximally coated uncemented femoral components and found a much higher rate of complications in the latter group.[157] However, the re-revision rate was lower for the proximally coated stems (11%), compared with the fully coated (13%) and the cemented revision stems (19%). Interestingly, the result in our study changed when, instead of using any reoperation as the outcome, we only focused on revisions. With a second revision as the primary outcome, instead of a reoperation of any type, we noted a significantly higher re-revision rate in uncemented modular stems (7%) when compared with cemented revision stems (3%). This finding confirms the importance of a distinct outcome measurement and can explain to a certain extent the heterogeneity of results based on an analysis of register data. The small size of the studied material, combined with variations in stem lengths and patient demographics, prevented any reliable comparison between different stem designs (e.g. Lubinus vs Exeter).

Another interesting issue is the influence of the primary stem design on the outcome after the plate fixation of B1 fractures. Lindahl et al. found no correlation between the design of the index stem and the outcome after the treatment of periprosthetic fractures.[206] We found no significant difference in the re-reoperation rate between Lubinus SP II (17.6%, 6/34 cases), Charnley (22.9%, 11/48 cases) and Exeter Polished (27.6%, 21/76 cases). We chose, however, not to publish these results for the same reasons mentioned above for revision stems.

7. LIMITATIONS

LIMITATIONS

The material in this thesis is mainly based on information from medical charts. Radiographs have only been examined in cases with an uncertain classification of periprosthetic fractures and during the validation of the classification process in Study I. The optimal method of classifying periprosthetic fractures is to combine information from patient symptoms before the fracture, type of injury (low- or higher-energy trauma), pre-operative radiographs and surgical findings derived from the surgical notes. Our material lacks information on pre-operative radiographs. This information could be most important in differentiating a type B from a type C fracture, because sometimes surgeons did not describe the most proximal and distal end of the fracture line in relation to the hip prosthesis. In these circumstances, the type of fracture was defined using indirect information from the surgical notes, such as the presence of cement near the fracture line (type B), the type of plate used (type C if a plate with condyle fixation was used), or when a surgeon stated that the most proximal screws were inserted distal or close to the tip of the stem.

However, when it comes to the classification of type B subcategories, the use of surgical notes, instead of radiographs, could be regarded as beneficial. Previous validations of the Vancouver classification used the surgical notes as a reference to assess the validity of this classification system within the B subgrouping.[62, 63] In a review of 106 periprosthetic fractures, Corten et al. reported that 20% of fractures classified as B1 pre-operatively proved to have a loose stem intraoperatively.[64] In our material, the stability of the stem was not always defined. On occasions when a long spiral fracture line, along with an uncemented or a cemented force-closed stem (e.g. Exeter, CPT), was described, the fracture was classified as B2. A fracture of the cement mantle around the stem also indicated loosening of the femoral stem. Surgical notes could also be of value in differentiating between B2 and B3 fractures. Gozzard et al. used the amount of bone deficiency described intraoperatively by the surgeons as a reference to validate the Paprosky classification for bone stock loss in revision hip surgery.[239] However, the use of only medical charts to classify periprosthetic fractures was not reported previously and we therefore validated this method. This validation is described in Study I and showed substantial agreement between the classification based on radiographs and the classification based on medical charts.

The lack of radiographs was also a limitation in the assessment of the outcome, after treatment of a PPFF. Postoperative radiographs were not available and important information about the placement of a plate or screws in relation to the hip prosthesis, the type of fracture (transverse, oblique, spiral), or whether or not the revision stem bypassed the fracture line was not recorded. These are important factors that contribute to a satisfactory fracture fixation and could not be derived from medical charts in all cases. Bone impaction grafting was not registered and the only distinction that was made, regarding bone grafting, was whether or not a strut allograft was used. Furthermore, the type of ORIF method used in conjunction with stem revision in Vancouver type B fractures was not analysed. These factors may have contributed to bias and influenced the outcome of type B fractures.

Another limitation, closely related to the lack of radiographs, is the measurement tool we used for the assessment of outcome, after the surgical treatment of a PPFF. We did not study nonunions and malunions and were unable to see whether a stem had subsided or loosened after a PPFF. In this thesis, we used re-reoperation as the primary outcome and, as a result, some complications related to fracture or hip replacement surgery were not recorded. The choice of measurement tool is crucial and the results may be altered depending on the selected outcome measurement. A very illustrative example of this situation is apparent in the study by Springer et al. quoted above, who reported the outcome of 118 Vancouver type B fractures.[157] Proximally coated stems had the lowest re-revision rate (11%) compared with fully coated (13%) and cemented revision stems (19%). However, when complications such as radiographic loosening, nonunion and malunion were added, proximally coated stems emerged as having the poorest outcome (64% complications). On the other hand, although re-reoperation is a crude measurement tool, we believe that it has significant clinical importance. A reduction in re-reoperation rates in this frail patient category would be of great value from the perspective of both patients and the health-care system, not least in terms of improved quality of life and economy.

In the Cox regression analysis in Study II, cases with a reoperation other than PPFF and patients who died or emigrated were censored. The data link between the SHAR and the NPR was only performed to identify reoperations due to PPFF and not secondary to other reasons. This implies that the true number of censored cases would have been larger in reality and it is not known if this could have influenced the results significantly. We presume that the percentage of "missed"

censored cases would be statistically similar in both the Lubinus and the Exeter groups and the results of the Cox regression analysis would therefore not be significantly different. Our assumption is based on the fact that underreporting to the SHAR is not related to the stem design but to the type of reoperation (minor or major revision, reoperation without revision). As a result, the underreporting of these cases was probably equally distributed between the two groups.

In Study II, we investigated the risk of PPFF close or distal to a Lubinus and Exeter stem. The variables included in the Cox regression analysis were stem design, gender, age, diagnosis at index operation and calendar year for primary THR. The presence of a TKR was not included as a risk factor. Katz et al. showed that femurs with an ipsilateral hip and knee replacement ran a 1.8 times higher risk of PPFF than femurs with only a THR.[92] Two of the most common reasons for replacement surgery in both the hip and knee are primary OA and inflammatory arthritis. In our material, the percentage of cases with these two diagnoses was equally split between the Lubinus and

Table 10. Risk factors, adjusted hazard ratios (HR), and 95% confidence intervals (CI) for reoperation due to periprosthetic femoral fracture (unpublished data).

Risk factors	Vancouver B HR (CI for HR)	Vancouver C HR (CI for HR)
Stem		
Lubinus SPII (reference)	1	1
Exeter Polished	9.6 (6.9 – 13.3)	1.3 (0.95 – 1.7)
Gender		
Males (reference)	1	1
Females	0.4 (0.3 – 0.5)	1.9 (1.4 – 2.8)
Diagnosis at primary THR		
Primary OA (reference)	1	1
Other	2.9 (2.3 – 3.8)	4.3 (3.2 – 5.7)
Age at primary THR	1.05 (1.04 – 1.07)	1.05 (1.03 – 1.07)
Calendar year for primary THR	1.1 (1.06 – 1.2)	1.03 (0.97 – 1.1)

THR (total hip replacement), OA (osteoarthritis)

*Unpublished data

Exeter groups and we therefore assume that it is very likely that the percentage of cases with an ipsilateral TKR was also equally distributed between the groups. Another limitation was the use of many sub-categories for age and diagnosis, which reduced the degrees of freedom in the Cox regression analysis. This situation reduces the power of the test. In a new test, where age was a continuous variable and diagnosis was divided into only two categories (OA and non-OA), the Cox regression analysis revealed similar results for stem design, gender and calendar year for index THR (Table 10).*

Finally, our knowledge of periprosthetic fractures close to uncemented stems is limited, due to the relatively small number of cases recorded in the material in this thesis. The cemented fixation of the stem has traditionally been the most popular fixation method in primary THRs in Sweden.[240, 241] Larger material is therefore necessary to study the influence of different uncemented stem designs on the risk of periprosthetic fracture. This was possible in a study where register data from four national arthroplasty registers in Scandinavia were merged.[49] This study showed that, of the five most frequently used uncemented stems that were studied, Corail and CLS Spotorno stems had the lowest revision rates due to PPFF within two years of the index operation, whereas ABG II stems had the highest. In Study I, we observed similar findings, but a statistical analysis was not performed because there were too few observations during the period that could be studied.

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8. CONCLUSIONS

CONCLUSIONS

Study I

The completeness of PPFFs treated with stem revision and reported to the SHAR is high (97%), but it is poor for periprosthetic fractures treated with ORIF (26%) and cross-matching with the NPR may therefore be needed. The classification of PPFFs based on information present in medical records was just as reliable as the classification based on radiographs and corresponded to previously performed validations of the Vancouver classification system. The incidence of surgically treated PPFFs increased in Sweden between 2001 and 2011. Vancouver type C fractures were almost four times more common than was primarily recorded in the SHAR.

Study II

The force-closed Exeter stem ran an approximately ten times higher risk of Vancouver type B fracture compared with the shape-closed Lubinus SP II stem. In a population of patients with a standard primary Lubinus or Exeter femoral component, stem design did not influence the risk of Vancouver type C fractures. Male gender was a risk factor for type B fractures and female gender for type C fractures. Increasing age and a diagnosis of hip fracture or femoral head necrosis were risk factors for both type B and C fractures, whereas inflammatory arthritis only implied an elevated risk of type C. In patients with primary OA, the posterior approach ran a 60% higher risk of Vancouver type B fractures, compared with the lateral approach.

Study III

Open reduction and internal fixation were preferred in type B1 and C fractures, while fractures around a loose stem (B2/B3) were treated with stem revision in the majority of cases with or without ORIF. Primary OA patients with a cemented primary stem ran a higher risk of re-reoperation after the treatment of a Vancouver B fracture, if it was of type B1 or interprosthetic. Gender did not influence the outcome of a type B fracture. ORIF had poorer results than stem revision in B2/B3 fractures but not in B1 fractures. Re-reoperation rates after the treatment of B1 fractures with a locking or a conventional plate were not statistically different. However, a significantly higher rate of stem revisions was noted after conventional plating. Cemented and uncemented modular or monoblock revision stems had similar re-reoperation rates after the treatment of Vancouver type B2/B3 fractures. One in five patients died within two years of reoperation due to a Vancouver type B fracture.

Study IV

The most common methods for the surgical treatment of Vancouver type C fractures were fixation with one or two plates or intramedullary nailing. The fixation of a type C fracture with a locking plate had a lower re-reoperation rate when compared with a conventional plate. Interprosthetic Vancouver type C fractures did not have a significantly different outcome from non-IPFFs. One in four patients that underwent surgery due to a type C fracture died within two years of the operation.

9. FUTURE PERSPECTIVES

FUTURE PERSPECTIVES

Periprosthetic femoral fracture is a less extensively studied complication after THR than aseptic loosening, dislocation and infection. Most studies have been observational, with basic methodological disadvantages that imply a relatively high risk of bias. Retrospective cohort studies based on material from one institution can provide good quality in terms of fracture classification, treatment methods and outcome measurements, but they frequently lack statistical power and complete follow-up. As a result, many cohorts based on this kind of material include different types of fracture treated with various methods. On the other hand, register-based studies have high statistical power and capture cases that underwent revision surgery elsewhere, but they lack detailed information on fracture classification, fracture fixation and usually also clinical outcome measurements. An extended recording of more variables in arthroplasty registers could result in more detailed data, but this could endanger surgeons' willingness to report, and the completeness of registration.

The classification of a periprosthetic fracture and the type of ORIF are not recorded in the SHAR, but they are in the SFR in which fractures treated non-surgically are also reported. Patient-related outcome measurements have been recorded in the SFR (EQ-5D, SMFA) since 2015 and in all reoperations registered in the SHAR (EQ-5D, satisfaction, pain) since 2017. It would be of great interest and value to link data from the primary database of the SHAR and the SKAR with the SFR. Recently a link between the SFR and SHAR has been initiated. In the future, this has the potential to create a national database with a high level of completeness, including details on fracture type, treatment and the outcome of periprosthetic fractures. The SFR is a new quality register, whose coverage has increased continuously, even if it has not as yet reached 100%.

An interprosthetic fracture treated with the exchange of the femoral component in the knee prosthesis and enhanced with plate fixation should be registered in all three of the above-mentioned national registers. The integration of the information from medical charts into the database of national quality registers would contribute to less administrative time for surgeons and a higher level of registration completeness. In an ideal "register world", pre- and postoperative radiographs would also be available for retrospective review. This would facilitate the performance of high-quality studies and lead to improved knowledge of periprosthetic fractures, as well as facilitating their prevention at least to some degree.

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