ROOPE SARVILINNA

Risk Factors of Periprosthetic Hip Fracture

ACADEMIC DISSERTATION

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Supervised by
Docent Jorma Pajamäki
University of Tampere

Reviewed by
Docent Olli Korkala
University of Helsinki
Docent Hannu Miettinen
University of Kuopio

Distribution
Bookshop TAJU
P.O. Box 617
33014 University of Tampere
Finland

Tel. +358 3 3551 6055
Fax +358 3 3551 7685
taju@uta.fi
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1 LIST OF ORIGINAL COMMUNICATIONS

In the text the original papers are referred to by their Roman numbers (I-IV).

I
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II
R. Sarvilinna, H. Huhtala, J. Pajamäki (2005): Young Age and Wedge Stem Design Are Risk Factors for Periprosthetic Fracture after Arthroplasty Due to Hip Fracture. Acta Orthop Scand; 76 (1): 56-60.

III
R. Sarvilinna, H. Huhtala, J. Pajamäki (2005): Outcome after Re-arthroplasty of Periprosthetic Hip Fracture. Acta Orthop Scand. Submitted.

IV
R. Sarvilinna, H. Huhtala, T. Puolakka, J. Nevalainen, J. Pajamäki (2003): The Incidence of Periprosthetic Fractures Treated by Revision Arthroplasty. An Epidemiologic Study out of 33,154 Hip Arthrosis Patients. Int Orthop 27: 359-361.

2 ABBREVIATIONS

AL	Aseptic loosening of prosthesis
ASA	Classification of anaesthesia risks by American Society of Anesthesiologists
BMI	Body mass index
BMD	Bone mineral density
CI	Confidence interval
COXA	Hospital for Joint Replacement, Tampere
Dexa	Dual energy X-ray absorptiometry
DVT	Deep venous thrombosis
HHS	Harris Hip Score
OR	Odds ratio
p	p-value
PF	Periprosthetic fracture
Q_1-Q_3	Quartiles
RSA	Radiostereometric analysis
TAYS	Tampere University Hospital
THA	Total hip arthroplasty

3 ABSTRACT

Periprosthetic fracture (PF) around the hip joint is a rare complication of hip arthroplasty. The aim of this study was to identify risk factors for periprosthetic fractures and to calculate the incidence of serious, revision-operated periprosthetic fractures.

The dissertation consists of four studies. The first case-control (31 + 31) study was conducted to find any possible risk factors for PF. In the second case-control study (16 + 48) only the risk factors of PF after hip fracture were studied. A third study of 33,154 patients was conducted to calculate the incidence of revision hip arthroplasty due to PF. These hip artrhrosis patients were primarily treated with total hip arthroplasty. Finally, the follow-up study for patients with PF or aseptic loosening (AL) (39 + 83) was done to compare postoperative and late complications between the groups.

Compared to other indications of hip arthroplasty, hip fracture was found to increase the risk for subsequent perisprosthetic fracture. When all indications of hip arthroplasty were included, age, BMI and type of prosthesis were found to have no influence on the risk of PF. However, for the hip fracture patients in Study II, both age under 70 years and the wedge-shaped prosthesis type increased the risk of late PF.

There was no association between the incidence of PF and the type of prosthesis used for hip arthrosis patients. Male gender suggested a tendency towards increased risk of periprosthetic fracture after THA for hip arthrosis patients.

The incidence of the revision hip arthroplasty of PF was found to decline during the years 1990-1999 even though the indications for total hip arthroplasty changed at that time.

The mortality and the complication rate were found to be higher after rearthroplasty of PF than after rearthroplasty of aseptic loose hip prosthesis.

In summary, new risk factors of PF were found. The most noteworthy finding was that hip fracture patients have a higher risk of PF than other arthroplasty patients. For hip fracture patients the wedge-shaped Exeter prosthesis type was found to be an risk factor for PF. This finding needs further studies with larger patient populations. It seems reasonable to suggest that hip arthroplasty registers should also include primary arthroplasties after hip fracture to ensure adequate follow-up for prosthesis types.

4 INTRODUCTION

The development of hip operations is closely associated with general development of surgery. Internal fixation was done for the first time by Langenbeck as early as 1850 and the first attempts at arthroplasty were made in the 1920s. With the improvement of surgical procedures and implant models, arthroplasty changed the treatment of hip fractures and osteoarthritis in the late 20th century. As arthroplasty became more popular, the need for revision surgery also increased.

Over the years, several designs for prostheses were abandoned when they were found to yield inferior results. The trial-and-error culture in orthopedics has been criticised and new methods for systematic design evaluation, pre-clinical testing and clinical trials have been proposed (Huiskes 1993). Dorey and Amstutz (1989) were the first to show that a survival analysis is a valid technique in the long-term evaluation of hip replacement patients, even though patients are lost to follow-up. Additionally, the risk factors for prosthesis complications can be identified even more accurately by combining univariate survival and multivariate statistical analyses (Johnsson et al. 1994).

The incidence of fractures related to osteoporosis, such as proximal femoral fracture, will increase worldwide over the next three decades as the proportion of women over the age 65 increases (Cooper et al. 1992). A total of 7,500 hip fractures were treated in Finland in 1997 and it has been predicted that the annual number of hip fractures will be 19,000 in 2030 (Kannus et al. 1999). A total of 5,900 total THAs, including revision arthroplasties, were performed in Finland in 1999 and the number has also been increasing (Puolakka et al. 2001). Increase in the number of patients undergoing revision arthroplasty and an increase in the number of patients needing more than one such procedure is also raising the prevalence of intra- and postoperative complications, such as PF, in Finland. Periprosthetic fracture is one serious but fortunately not a very common complication of hip arthroplasty. However, to our knowledge, there are no studies showing rise in the age-standardized incidence of PF.

In the present study the incidence and risk factors of revision-operated periprosthetic fracture were studied. Survivals for prostheses were also calculated using the Finnish Arthroplasty Register. Our study hypothesis was that there are still unknown risk factors for periprosthetic hip fracture and some risk factors for hip fracture and PF could be the same. As a study method we used follow-up study, case-control studies and an register-based study. New information on risk factors was found.

5 REVIEW OF THE LITERATURE

5.1 HIP ARTHROPLASTY

Arthroplasty changed the treatment of hip fractures at the 20th century. Themistokles Gluck in 1890 and Hey-Groves in 1927 replaced the head of the femur with ivory, but it was not later used as a material for prostheses (Eynon-Lewis et al. 1992). After that Hey-Groves used glass, then bakelite and finally vitallium prostheses (mold arthroplasty) in arthroplasties done by the anterolateral approach. Later the prostheses were developed to extend more distally in the femur and the use of acrylic hemiarthroplasties was reported Judet and Judet 1949, Moore 1957) Austin, Moore and Bateman developed hemiarthroplasties further during the late 20th century (Freiberger 1986).

Total hip arthroplasties (THA) were created after hemiarthroplasty. The first six total hip arthroplasties were performed in 1938 (Wiles 1958). Metal on metal articulations were introduced by McKee and Farrar (1966). Charnley (1970) and Müller (1967) reported the use of smaller 22 mm or 32 mm diameter prosthesis heads improving the results by reducing the friction. Teflon was used as bearing material in the first prostheses with disastrous outcome and polyethylene replaced it as an exellent counterpart for the metal head. It was Charnley who adopted the use of methyl methacrylate cement introduced by Leon Wiltsie (Charnley 1960). He also adopted the high molecular weight polyethylene instead of teflon as a bearing surface. With Charnley's design, the materials, and the technique of the operation in place, the use of the procedure spread quickly everywhere.

5.2 REVISION HIP ARTHROPLASTY

Treatment options for failed hip arthroplasty include non-operative management, resection arthroplasty or revision arthroplasty. In revision arthroplasty the new components can be fixed with or without cement (Lawrence et al. 1994).

The most common reasons for revision arthroplasty in the study of 75,000 primary or revision THAs in Finland during 1980-1999 were aseptic loosening, dislocation and infection (Puolakka et al. 2001). In some studies fracture has been the second leading cause of revision hip arthroplasty after loosening of the implant and before dislocation and infection (Lewallen and Berry 1997). Johnsson et al. (1994) studied the risk of revision on 799 hips treated for primary osteoarthritis and found male gender, young age at primary THA, the Brunswik and Lubinus snap-fit prostheses compared to Charnley prostheses to be statistically significant risk factors.

The prevalence of revision hip replacement surgery in the United States has increased more than the prevalence of primary hip replacement. In 1992, the number of revision hip replacement surgeries increased by 18%, whereas the number of primary hip replacement surgeries increased by only 9% (Mendenhall 1995). The problem is that hospitals need more resources in revision surgery than in primary hip replacements. In the study by Lavernia et al. (1995), the time spent in the operating room for patients undergoing revision THA was 109% longer than that of patients undergoing primary THA, and patients spent 92% more time in hospital after revision THA. Charges for hip implants were also 25 % higher for revision surgery, and hospital charges were 59 % higher for revision surgery.

During the last decade, the use of cement in revisions has been discussed widely and now both cemented and cementless prostheses are used. Both of these methods have their own advantages and disadvantages (Morrey and Kavanagh 1992, Lawrence et al. 1994, Moreland and Bernstein 1995, Krisnamurthy et al. 1997).

5.3 PERIPROSTHETIC HIP FRACTURES

Periprosthetic fracture is a serious, but fortunately not a very common complication of hip arthroplasty. After several decades of hip arthroplasty, the number of patients living with hip arthroplasties, bone loss and osteolysis has risen. Consequently, a greater proportion of the population is at risk for complications (Berry 1999). A total of 5,900 THAs, including revision arthroplasties, was made in Finland in 1999 and the number has been increasing (Puolakka et al. 2001). Increase in the number of patients undergoing revision arthroplasty, and an increase in the number needing more than one procedure is also raising the prevalence of intra- and postoperative complications, such as PF, in Finland. The use of a cementless primary hip prosthesis may increase the prevalence of PF. More than 40 % of THAs have been inserted without cement since the1980s (Puolakka et al. 2001).

The age-standardized incidence of low-trauma fractures is rising in elderly populations in western countries including Finland, but is not necessarily a global phenomenon (Kannus et al. 1996, Kannus et al. 1999, Kannus et al. 2000a, Kannus et al. 2002b). The incidence of hip fracture is also assumed to increase, the life-time risk being 6 % for men and 14 % for postmenopausal women (Laurinzen 1997). One reason is that the relative number of elderly people is growing in the Finnish population as large age cohorts born in the 1940s and 1950s are ageing. However, a greater difference in the incidence of hip fracture has been found between the European countries than between the sexes within the countries, and may be caused by genetic or environmental factors (Johnell et al. 1992). However, there are no studies showing a rise in the age-standardized incidence of PF.

The treatment of periprosthetic hip fracture is always expensive. Nurmi et al. (2003) calculated that in Finland the average cost of one proximal femoral fracture during the first year after the injury is 14,110 Euro. If the patient had to stay permanently in health a care unit the cost was 34,990 Euro per year. In a revision operation of periprosthetic fracture the average cost of operation and hospital stay is 10,000-15,000 euros in Pirkanmaa Hospital District. It has been suggested that the treatment of PF is significantly more expensive than the early revision of silent osteolysis (Lavernia 1998). Since the treatment of periprosthetic fractures is often expensive and subject to high complication rates, every possible effort should be directed to preventing these fractures (Tsiridis et al. 2003).

5.3.1 Incidence and prevalence

Fracture was the second leading cause of revision hip arthroplasty at the Mayo Clinic between 1989-1993, ranking after loosening of the implant and before dislocation and infection (Lewallen and Berry 1997). However, in the study of 75,000 primary or revision THAs in Finland, the most common reasons for revision were aseptic loosening, dislocation and infection the period 1980-1999 (Puolakka et al. 2001). The overall incidence of PF seems to vary between 0.1-20 % (Schwartz et al. 1989, Beals and Tower 1996, Lewallen and Berry 1997, Tower and Beals 1999). Löwenhielm et al. (1989) found the accumulated risk of PF

25.3 per 1000 during an observation period of 15 years and Tower and Beals (1999) calculated the incidence under 1% over the life of the implant in their study of 93 fractures.

The incidence is higher with cementless than with cemented primary hip arthroplasties, especially intraoperatively, and might also be higher than reported, because not all the simple, especially proximal fractures, can be seen in radiographs (Scott et al. 1975, Christensen et al. 1989, Löwenhielm et al. 1989, Schwartz et al. 1989, Stuchin 1990, Kavanagh 1992, Mont et al. 1992). After the primary operation using the cementless prosthesis the incidence of PF has varied between 3 and 20% (Schwartz et al. 1989, Fitzgerald et al. 1988, Stuchin 1990). The incidence of PF after cemented primary procedure has been near 1% (Beals and Tower 1996, Scott et al. 1975, Garcia-Cimbrero et al. 1992, Löwenhielm et al. 1989).

In revision procedure the incidence of periprosthetic fracture is higher than in primary operation also when cemented prostheses are used. Kavanagh (1992) estimated that the incidence of PF is under 1% in primary arthroplasties, but the rate increases to over 4 % in revision arthroplasties. The incidence has been about the same for revision hip surgery with impact allografting and other revision operations, ranging from 5 to 24 % (Masterson et al. 1997, Meding et al. 1997, Leopold and Rosenberg 2000). However, there are no reports that the incidence of PF is rising, although it has been suggested that the increasing number of patients undergoing revision arthroplasty, increased number of cementless prostheses and hip operations for older and heavier patients might have an influence on it (Garbuz et al. 1998).

Incidence of PF has been the same after revision surgery with impaction allografting and after other revision operations, ranging from 5 to 24 % (Masterson et al. 1997, Meding et al. 1997, Leopold et al. 2000). The incidence of PF after hemi-arthroplasty has not been extens ively studied. In the study by Tower and Beals (1999) 7 % of 94 PFs occurred around an Austin-Moore hemi-arthroplasty and in a study of 72 bipolar hemiarthroplasties with a minimum of four years of follow-up, one intraoperative PF was found (Sarvilinna et al. 2002).

The overall prevalence of PF has been between 0.1 and 1.1 per cent, when cemented and cementless primary or revision operation are included (McElfresh and Coventry 1974, Scott et al. 1975, Adolphson et al. 1987, Fredin et al. 1987, Löwenhielm et al. 1989).

5.3.2 Classification

There are many different kinds of classifications for periprosthetic fractures which makes comparison between follow-up studies and treatments difficult (Whittaker at al. 1974, Johansson et al. 1981, Bethea et al. 1982, Schwartz et al. 1989, Morrey and Kavanagh 1992, Mont and Maar 1994, Duncan and Masri 1995, Beals and Tower 1996). In these classifications fractures are separated into different groups by fracture location. Status of the implant (loose or stabile) and cementation are considered differently by various authors. In many classifications the fixation of the prosthesis is not considered (Table 1)(Johansson et al. 1981, Bethea et al. 1982). The Vancouver Classification (Table 2) is becoming the standard system in periprosthetic femoral fractures. It is based on fracture configuration, the quality of fixation of the stem as well as the quality of the bone and has been evaluated as reliable and valid among various researchers. (Duncan and Masri 1995, Brady et al. 2000).

Table 1. Johansson and Bethea classifications for PF

Johansson et al.	Bethea et al.
Type I: Proximal to tip of the prosthesis	Type C: comminuted fractures around the stem
Type II: At the tip of the prosthesis	Type B: Spiral fractures around the stem
Type III: Distal to the tip	Type A: below the tip of the prosthesis

Table 2. Vancouver Classification for periprosthetic fractures

Type	Location	Subtype
A	Trochanteric	A(G): Greater trochanter A(L): Lesser trochanter
B	About the stem tip	B(1): Prosthesis stable B(2): Prosthesis loose B(3): Bone stock inadequate
C	Well below the stem tip	-

Johansson et al. (1981) found the type II fracture (around the tip of the stem) and Myung-Sik et al. (2003) the dislocated (IIb) fracture around the tip of the stem the most common. A spiral fracture pattern was the most common pattern seen with the exception of implants with loose cemented interfaces in a study by Tower and Beals (1999). In cementless arthroplasty, type I fractures are the most common (Grigoris et al. 1993). With cementless prostheses the fracture is most often proximally to lesser trochanter (Schwartz et al. 1989, Mallory et al. 1989, Mont and Maar 1994). In the studies in which the Vancouver Classification is used, most of PFs are Vancouver type B (87%) fractures (Duncan and Masri 1995).

5.3.3 Risk factors of intra and postoperative periprosthetic fracture

The risk factors of PF in primary operation include cementless prosthesis, weakness of the bone (i.e. rheumatoid or osteoporotic bone), deformities and earlier operations in the hip area. The intraoperative fracture will manifest most often when the femoral canal is reamed or when the final prosthesis is inserted (Khan and O'Driscoll 1977, Schwartz et al. 1989, Fitzgerald et al. 1988, Mallory et al. 1989). It has been suggested that the conical shaped cementless prostheses could fracture weaker metaphysis during insertion in a similar manner to the way a wedge splits wood. The oversized component creates a stress in the bone and afterwards possibly a fracture (Kavanagh 1992). However, the outcome of fractures that are recognised and treated intraoperatively remains good (Mont et al. 1992). Mallory et al. (1989) found that if the fracture line remains proximal to the tip of the stem the outcome should be favorable.

Any kind of stress riser increases the risk of immediate postoperative PF (Scott et al. 1975). The femur may be weakened by overreaming the femoral canal. A stress riser is created at the tip of the stem by penetrating the anterior femoral cortex by reamers and a spiral fracture may propagate through the solidly fixed stem through the stress riser (Fredin et al. 1987, Scott et al. 1975, Missakian and Rand 1993). Larson et al. (1991) showed that anterolateral cortical defects on sheep femora decreased the torsional strength by 56 %.

The risk of PF has been estimated to be as much as double in revision compared to primary operations (Khan and O'Driscoll 1977). The fracture most often comes when the prosthesis is dislocated, when the cement is removed or when the final prosthesis is inserted. (Scott et al.1975, Taylor et al. 1978, Christensen et al. 1989, Kavanagh 1992). A trochanteric fracture may occur during cemented stem extraction if the cement remains bonded to the femoral component (Vaughn et al. 1995, Kavanagh et al. 1992). Perforation of the femoral cortex increases the risk of fracture propagation (Talab et al. 1979, Pazzagglia and Byers 1984, Fredin et al. 1987). The results with cemented revisions have mostly been disappointing, although the short-term complication rate is essentially the same for cemented and uncemented femoral revision implants (Amstutz et al. 1982, Callaghan et al. 1985, Kavanagh et al. 1985). By contrast Morrey and Kavanagh (1992) thought that there was little in the literature supporting the use of only cementless prostheses in revision operations. They also found a high incidence of fractures as a complication.

5.3.4 Risk factors for late postoperative periprosthetic fracture

The stress risers are somewhat different for late than for intraoperative or immediate postoperative PFs. The general risk factors for late PF include female gender, metabolic bone disease (osteopenia, osteomalacia, osteoporosis), rheumatoid arthritis, Paget's disease, osteogenesis imperfecta, preoperative femoral deformities and old proximal femoral fractures (McElfresh and Coventry 1974, Scott et al. 1975, Poss et al. 1976, Bethea et al. 1982, Christensen et al. 1989, Duncan and Masri 1995).

Other known risk factors include infection, proximal femoral bone loss, osteolysis, osteolysis associated with wear debris around the tip and component loosening (Pazzaglia and Byers 1984, Christensen et al. 1989, Kelley 1994, Astion et al. 1996, Moran 1996, Radl et al. 2000). An interposed cement on cortical defect may also lead to late stress fracture in the periprosthetic area (Eschenroeder and Krakcow 1988).

Preoperative diagnosis has been studied by Löwenhielm et al. (1989), but no effect on late PF was found.

Aseptic loosening of the prosthesis has been discussed over the past few years. Tower and Beals (1999) found 22 out of 87 patients to have periprosthetic fractures of pre-existing loose prostheses. Bethea et al. (1982) found as many as 75 % of patients with postoperative PF to have an underlying loosening of the implant. Recently Myung-Sik et al. (2003) found 32 % of prostheses loose before PF and suggested that one reason for the low rate of PF was the cementless stem. For cemented prostheses the fracture frequently developed just distal to the cement mantle through thinned expanded osteoporotic cortical bones.

The subsidence of the prosthesis has been studied as a risk factor for aseptic loosening and PF. Kärrholm et al. (1994) found that the probability of revision operation is greater than 50 % if the subsidence of the prosthesis in RSA measurement was over 1.2 mm two years after the surgery.

It has also been shown that as the proximal fixation of the hydroxyapatite coated stem fails, stress is transferred to the distal third of the stem and proximal femoral bone loss can be the main reason for the high incidence of periprosthetic fractures (Radl et al. 2000). Cohen and Rushton (1995) used Dexa in bone mineral density (BMD) measurements in the proximal femoral area for 20 patients. One year after of the operation they found a 6.7 % reduction in BMD in the region of the calcar and a mean 5.3 % increase in BMD in the femoral shaft distal to the tip of the implant. These changes reflect both the pattern of reduced stress in the proximal femur and increased stress around the tip of the prosthesis. Dexa has also been used to predict periprosthetic bone loss. Rahmy et al. (2004) found that the patient's bone density measured at the spine, hip or forearm at the time of the operation was a major factor affecting bone loss around the stem. In a prospective study of 15 cemented THAs, after a phase of acute bone loss, further loss was minimal (Venesmaa et al. 2003).

Stem design as a risk factor of PF is discussed in few studies. It has been suggested that an axial loading effect of the stem produces a wedging effect of the stem and the surrounding cement, which produces hoop stresses to the surrounding bone (Harkess 1998). Löwenhielm et al. (1989) found that in a study of 1,442 total hip replacements and 22 PFs, Charnley-Müller, Christiansen and Brunswik prostheses were associated with proximal and Lubinus prosthesis with distal femoral fractures.

Trauma, especially falling is the most common reason for late PF (Montijo et al. 1989, Jensen et al. 1988, Stern et al. 1991, Incavo et al. 1998). Beals and Tower (1996) reported 84% of periprosthetic fractures resulting as a consequence of a fall, 8% after other kinds of injuries and 8% as spontaneous fractures. McLaughlan et al. (1997) in their study found that the average age of patients with Johansson type III fracture (under the tip of the prosthesis) was greater than of those with other injuries (Johansson et al. 1981). The authors suspected that the type III injury is likely to be a part of the natural incidence of femoral fracture rather than a prosthesis-related problem. Thus, according to the literature, it seems that elderly women or patients who have loose femoral components most commonly have periprosthetic fractures (Bethea et al. 1982, Tower and Beals 1999).

5.3.5 Risk factors of hip fracture and falls

There are numerous of studies on the risk factors of hip fracture and fewer on the risk factors of PF. As background for the risks of PF, the risks of hip fracture and falls are reviewed here first. Theories like increasing osteoporosis, increasing number of falls and fractures in certain population cohorts have been evinced as possible reasons for rising age-standardized incidence of hip fracture (Law et al. 1991, Greenspan et al.1994, Cummings et al.1995, Kannus et al. 1996, Cumming et al. 1997, Lips 1997, Greenspan et al. 1998 , Kannus et al.

1999, Kannus et al. 2000a, Kannus et al. 2002b). In an age-adjusted multivariate analysis Dargent-Molina et al. (1996) found four independent fall-related predictors for hip fracture: slower gait speed, difficulty in going tandem (heel to toe) walk, impaired visual acuity and small calf circumference. Low femoral BMD was also a significant and independent risk factor. Psychotropic drugs, two or more earlier fractures, falling during the last year and a residence that is not adequately equipped for safe daily living were found to increase the risk (Haentjens et al. 2002).

The risk of wrist fracture seems to increase after hip fracture but the risk of hip fracture is not increased after the wrist fracture. Family history of hip fracture (maternal, sister's or brother's) increased the risk of hip fracture in a study of 9,704 Caucasian women, aged 65 years or older (Fox et al. 1998).

A birth cohort effect means that one birth cohort would be more suspectible to fracture than others. Kannus et al. (1999) found no such effect behind the increasing age-standardized incidence of hip fracture in Finland during the years 1970-1997.

There is some evidence of an osteoporosis hypothesis and that age-spesific bone density and strength may have diminished over the last few centuries. In a study by Lees et al. (1993) pre- and post-menopausal femoral neck bone density was lost significantly faster in modern-day women than in Spitalfields women during years 1729-1852 . However, this is insufficient to explain the increase of fracture risk since 1970 and no clear evidence exists of increasing bone fragility during the last three decades (Kannus et al. 2002a). The fractures of osteoporotic patients may initially heal normally, but the lack of calcium may later lead to failure in mineralization of callus and remodelling of the bone (Einhorn et al. 1986). However, decreased bone mineral density is not a major risk factor for hip fracture (Alhava 1998, De Laet et al. 1997). De Laet et al. (1997) found that decrease in bone mineral density caused only 15 % of 13 times increased hip fracture risk for patients aged 60 to 80. Post-menopausal women in particular with an earlier non-hip fracture still seem to have a higher risk for hip fractures (Lauritzen 1997). This may be caused by accelerated bone loss after the menopause (Stevenson et al. 1988). Greenspan et al. (1994) concluded that fall characteristics and body habitus are important risk factors for hip fracture among elderly patients.

There is no clear evidence of the rising incidence of age-standardized or age-specific falls. However, the age-standardized incidence of severe fall-induced injuries other than bone fractures has risen in the Finnish population (Kannus et al. 2002a). There are several risk factors for falls among the elderly and these factors can easily be examined or questioned (Nevitt et al. 1989). The factors already identified as possible risks are: two or more falls for persons having difficulty in rising from a chair, difficulty in performing a tandem walk, arthritis, Parkinson's disease, three or more falls during the previous year, white race, use of sedatives, cognitive impairment, disability of lower extremities, palmomental reflex, abnormalities of balance and gait, foot problems, visual impairment, use of long acting barbiturates (Tinetti et al. 1988, Nevitt et al. 1989,Grisso et al. 1991). When factors like neuromuscular abnormalities increase the risk of falls in general, they may also determine whether any given fall will result in a hip fracture (Cummings et al. 1989, Cummings and Nevitt 1989).

5.3.6 Prevention of hip fractures

Falling is the immediate cause of hip fracture in most patients and thus the prevention of trauma is most important, even when there is a variety of medication to prevent osteoporosis (Parkkari et al. 1997, Heaney 1998, Dargent-Molina et al. 1996). The effective loading on the hip is 35 % of the body weight in unprotected falls on the hip. In a typical fall the peak stress comes to the greater trochanter and the energy is 10-20 times higher than needed for hip fracture. The soft tissue reduces it and decreases the risk of fracture. Thus an increase in bone mineral density in a population might not significantly decrease the risk of hip fracture. It has been demostrated that during a fall, peak stresses develop in the intertrochanteric region and that secondary peaks in the trabecular bone are in the subcapital region (Lotz and Hayes 1990). The use of hip protectors has been proven to prevent hip fractures, and in some studies the rate of fractures been reduced 50 % by using them (Laurinzen 1997, Kannus et al. 2000b, Parker et al 2000). However, not all trials have found hip protectors to be effective and there is always a problem of compliance with them (Van Schoor et al. 2003).

In elderly women genetic factors play a major role in determining the variations of the bone mineral density and the possibilities of reducing osteoporosis in the population are limited (Flicker et al. 1995). In addition, alendronate and risedronate have recently been found to decrease the risk of hip fractures by 40-50 % and are now considered primary medical treatment options for postmenopausal osteoporosis (Granney 2003). However, stronger evidence of efficacy has been found for women at high risk with osteoporosis and vertebral fractures (Ensrud et al. 1997). The Finnish Osteoporosis Group has also recommended vitamin D for all aged over 70 and with higher doses for all those elderly at institutional care to prevent osteoporosis (Pitkälä 2003).

Close et al. (1999) showed that a structured interdisciplinary approach is effective for elderly people in the prevention and management of falls and found a 50% reduction in the fracture rate with their method. Campbell et al. (1997) found that physical exercises lowered the risk of trauma by 39 per cent in a group consisting of people aged over 80. Tinetti et al. (1994) found multifactorial intervention, including adjustment of medication, behavioural instructions and exercise programme, to reduce significantly the risk of falling. High intencity strength training has a positive effect, expecially on postmenopausal women. The effect of physical exercises comes from increased muscle mass, strength and dynamic balance (Nelson et al. 1994, Gillespie et al. 2001).

Ray et al. (1987) found a significantly increased risk of hip fracture for patients using hypnotics-anxiolytics having long (> 24 hours) elimination half-lives. Patients treated with hypnotics-anxiolytics having short (< =24 hours) elimination half-lives had no increased risk of hip fracture. Thus it seems that changes in medication may reduce the risk of hip fracture.

5.3.7 Common risk factors for hip fracture and periprosthetic fracture

In many papers about the risks of PF only local prosthesis-related factors or stress risers are studied even though patient-related factors are also admitted (Berry 1999, Tsiridis et al. 2003). Falling or low-energy trauma is the immediate reason for both of these fractures in most cases (Jensen et al. 1988, Stern et al. 1991, Greenspan 1994). Other suggested risk factors common to both fractures are weakness of the bone, deformities, female gender and post-menopausal status (Law et al. 1991, Greenspan et al. 1994, Kannus et al. 1996, Tsiridis et al. 2003) It has been shown for hip fracture that there are several risk factors for falls among elderly and these can be easily examined and questioned (Nevitt et al.1989). Moreover, a structured interdisciplinary approach, physical exercises and hip protectors have been shown to prevent hip fractures (Campbell et al. 1997, Close et al. 1999,Gillespie et al. 2001). The same has not been shown for PF, even though both fractures have same risk factors (Jensen et al 1988, Berry 1999, Tsiridis et al. 2002) (Table 3).

Table 3. Suggested risk factors for PF. The factors that are also suggested risks for hip fracture are written in italics (Jensen et al. 1988, Law et al. 1991, Greenspan et al. 1994, Cummings et al.1995, Kannus et al. 1996, Cumming et al. 1997, Lips 1997, Greenspan et al. 1998 , Berry 1999, Kannus et al. 1999, Tsiridis 2002).

	Intraoperative fractures	Late fractures
Patient related factors	*Osteoporosis* *Osteomalacia* *Female* *Post-menopausal status*	*Osteoporosis* *Osteomalacia* Paget's disease Rheumatoid arthritis *Osteogenesis imperfecta* *Female* *Post-menopausal status*
Other factors	Cementless prosthesiss Earlier operation Stress raisers Revision operation	Stress risers Osteolysis Loosening of component *Trauma: falling* Infection Proximal femoral bone loss

5.3.8 Prevention of periprosthetic fracture

There are many recommendations for the intraoperative prevention of periprosthetic fractures. Avoiding the creation of cracks, defects, or windows in the bone intraoperatively and, if these stress raisers are present, bypassing them with a stem of sufficient length, a stem ending two or three cortical diameters distal to the defect are all well-accepted methods for prevention (Eschenroeder et Krackow 1988, Fredin et al. 1987, Larson et al. 1991, Morrey et Kavanagh 1992, Incavo et al. 1998). An intraoperatively detected cortical defect in hip fracture operation is an indication for a long-stemmed prosthesis (Scott et al. 1975). Extravasation of cement from bone defects shoud be avoided because this may predispose subsequent fracture through the unhealed stress-raiser (Lewallen and Berry 1997). When necessary, a trochanteric osteotomy should be performed to ensure adequate surgical exposure (Charnley 1960, Younger et al.1995). A prophylactic strengthening of the femur with a bone clamp or cerclage wires may also be useful in some cases (Wagner et al. 1996, Garbuz et al. 1998).

Only the simplest intraoperative, mostly metaphyseal fractures can heal without fixation, others should be fixated during the operation using wires, auto- or allografts or metal plates to prevent any further fractures (Lewallen and Berry 1997, Berry 2002). Incavo (1991) found that cerclage wire can prevent a fracture when an intraoperatively detected fissure is fixed. A careful plan using the prosthesis models before the operation might also prevent fractures (Kavanagh et al. 1992).

In any revision operation preservation of the bone stock whenever possible and achievement of stable fixation of the stem into intact host bone is necessary. Classification of the fracture, with assessment not only of its location but also of the fixation of the stem and the quality of the bone, allows a rational choice of reconstructive options for the management of these patients (Lewallen and Berry 1997). Careful exposure of the ingrowth surface during removal of a cementless stem using the techniques described by Glassman and Eng (1992) is suggested. A trochanteric fracture may occur during cemented stem extraction if cement remains bonded to the femoral component (Kavanagh et al. 1992, Vaughn 1995). Extended trochanteric osteotomy will allow access to the femur to remove cement or for cementless prostheses will access the ingrowth surface (Younger et al. 1995). Removal of cement can be done safely by splitting it radially at several levels or by using ultrasound (Tsiridis et al. 2003).

The postoperative follow-up using radiographs has been suggested. Lewallen and Berry (1997) found regular follow-up 1, 2, 5, 7 and 10 years after surgery and thereafter every 2-3 years to be useful. The RSA measurements during the first two years after the surgery have also been found to predict the subsequent clinical failure, such as revision operation (Kärrholm et al. 1994, Ryd et al. 1995). Particularly patients with recurrent dislocation, loosening, subsidence and osteolysis should be identified after total hip arthroplasty in follow-up controls, because these patients are at greatest risk of developing periprosthetic fractures (Pazzaglia and Buyers 1984, Reich and Jaffe 1994).

Venesmaa et al. (2001) found that alendronate reduces periprosthetic bone loss after uncemented total hip arthroplasty in six-months follow-up, but concluded that follow-up was too short to permit any long-term conclusions. To our knowledge, there are no studies of on physical exercises and hip protectors as preventive treatment for PF.

5.3.9 Non-operative treatment

Intraoperative PF is more common than postoperative PF and the treatment is often much less complicated. Identification and management of the fracture are important at the time of surgery (Sharkey et al. 1992, Weiss et al. 2003).

Casts and external braces have earlier been used. Scott et al. (1975) thought that because of the options of conservative treatment the risks of a surgical procedure may not be tenable. However, later high rate of complications was found to be associated with traction (Adophson et al. 1987). It is only rarely used as a treatment of PF as it is also difficult to maintain reduction (Johansson et al. 1981, Mont and Maar 1994). Kligman et al. (1999) found that in Johansson I-II fractures the Mennen plate internal fixation was better than conservative treatment leading to faster fracture healing and shorter time to full weight-bearing.

The non-operative treatment of PF has been found to give poor long-term results. Prolonged bed rest and difficulties in maintaining reduction are common problems with non-operative treatment (Johnson et al. 1984). The rate of revision because of femoral loosening has been between 19 and 100 %, nonunion rates have been between 25 and 42 % and malunion rate 45 % for non-operatively treated patients (Johansson et al. 1981, Bethea et al. 1982 and Beals and Tower 1996). Thus, nowadays it is recommended to treat only proximal fractures with stable implant non-operatively (Tower and Beals 1996).

5.3.10 Operative treatment

There are many ways to treat postoperative PF including closed reduction, traction and immobilisation of the limb by the use of external casts or braces, open reduction and internal fixation by cerclage wires, bands, cables and screws with or without additional plates or cortical onlay strut allograts, percutaneus plate osteosynthesis, revision surgery of the femoral component, external fixation, or partial proximal or distal femoral replacement by the use of composite consisting of an allograft and a standard or special femoral replacement prosthesis. Cancellous bone grafting can be combined with all of these methods (Weiss et al. 2003).

In the surgical treatment of PF, early union of fracture, anatomical alignment and length, a stable prosthesis, early mobilization, a return to pre-fracture function and maintenance of bone stock are the main goals (Tsiridis et al. 2003). The surgical treatment of PF is supported by recent studies (Mont and Maar 1994, Beals and Tower 1996).

Stable fixation after open reduction has been found to be associated with good outcome (Stern et al. 1991, Zenni et al. 1988). If the fracture is well above the tip of the stem, a standard-length prosthesis with additional cerclage wire or cable fixation is recommended, but if the fracture is around or under the tip of the stem, the use of the long-stemmed femoral component with or without additional fixation using cerclage wires or cables is recommended. In all cases the most important factors to be considered are location of the fracture, stability of the implant, and bone quality (Duncan and Masri 1995).

Studies of implants and combinations of implants to ascertain which serves best to achieve rigid fixation. Cerclage wires alone are not suitable (Garcia-Gibrelo and Gil-Garay 1992). Several studies report good results with different plates (Johansson et al. 1981, Bethea et al. 1982, Sisto et al. 1985, Culp et al. 1987, Scott 1988, Mont and Maar 1994) but in some studies the results using compression plates have been poor (Merkel and Johnson 1986, Cain et al. 1986, DiGioia and Rubash 1991).

Thus, in cases when the prosthesis stem is stable, when its removal would entail great risks and, when the biomechanical conditions are optimal, the optimal treatment would be plate fixation. In cases where the stem is loose and where there is a choise, stem revision is preferable to plate fixation (Jukkala-Partio et al. 1998). The advantage of revising a femoral component associated with a femur fracture to a long-stem prothesis is that the stem acts as an intramedullary rod in maintaining alignment and affording stability (Mont and Maar 1994).

In a review article of Mont and Maar (1994) PFs were divided into six groups and guidelines for treatment were given. However, this study was based on old classifications and studies from 1964 to 1991. Moreover, as there are many ways to treat postoperative PF, the following treatment algorithm based on the Vancouver Classification has been presented by Berry (2002):

1. *Pertrochanteric fracture* with a stable prosthesis, acceptable fracture displacement and minimal osteolysis can be treated with closed management. Displaced fractures or fractures that have occurred because of osteolysis usually require surgery.

2. *Fractures remote from the stem* should be treated like any other femoral fractures, mostly using open reduction and internal fixation.

3. *Fractures around the stem or around the tip of the stem* are the most common and are divided into three groups; A: stem is well fixed and functioning well, B: stem is loose, C: stem is loose with poor nonsupportive proximal bone.

In group A the stem can be retained and the fracture fixed with plate, cerclage wires, bicortical screws or strut grafts or with a combination of these fixation methods. Femoral revision almost always is needed in group B. Each revision is different and demands initiative ingenuity on the part of the surgeon. However, certain key treatment principles should be followed: the failed implant is removed using the fracture to help gain acces to the implant, the fracture is usually bypassed with a long-stem implant, stable fracture fixation is achieved and the blood supply of the femur is damaged as little as possible to promote subsequent healing. If cement is used, the fracture should be reduced anatomically before cementation to prevent cement from entering the fracture line and potentially causing a nonunion. In group C proximal femoral substitution is often needed and either tumor prostheses or allograft prosthetic composites can be used. The prosthesis must be stable both axially and rotationally in the distal femur because the proximal bone is not supportive (Berry 2002).

A pathologic periprosthetic fracture is possible in large osteolytic lesions caused by wear debris. Berry (2003) has proposed that such fractures in the greater trochanter with minimal displacements should be treated conservatively for three months and then the particle generator should be removed and the greater trochanter grafted. For metaphyseal or diaphyseal fracture early revision is recommended.

5.3.11 Prosthesis options in re-operation

The prosthesis options for the treatment of PF are cemented stem, a long stem with proximal or extensive porous coating (inserted without cement), a composite consisting of an allograft and a prosthesis, a proximal femoral replacement stem and a custom implant, stem sleeve and extension.

A cementless prosthesis is commonly used in femoral replacement of PF, but the cementation in revision procedure of an aseptic loose component has been discussed in the literature (Morrey and Kavanagh 1989). Extensively porous-coated femoral implants have been used successfully in revision total hip arthroplasty (Lawrence et al. 1994, Moreland and Bernstein 1995, Krisnamurthy et al. 1997) and the same implants can be used successfully in the revision arthroplasty of a PF (MacDonald et al. 2001). In as study of 123 PFs, the use of an uncemented, extensively coated cylindrical stem restored function and allowed the healing of the fracture (Parvizi et al. 2004).

Long-stemmed revision is biomechanically favorable for the treatment of femoral fractures as long as the prosthesis has adequate length to bypass distally the fracture and any other cortical stress raisers (Korkala et al. 1992, Tower and Beals 1999). Cemented long-stem femoral prostheses could be reserved for older patients with simple fractures and good bone stock in whom the risk of the extrusion of cement leading to delayed or nonunion can be minimised and for whom early mobilisation and recovery are crucial for the outcome (Duncan and Masri 1995, Berry 2002).

The use of strut allografts in revisions enhances the mechanical stability and graft uniting with the host bone. Thus, the long term bone mass and stability are improved (Wong and Gross 1999, Head et al. 1999 and Haddad et al. 2000).

5.4 COMPLICATIONS AFTER HIP ARTHROPLASTY

The main reason for reoperation in the first two years after arthroplasty of hip fracture in a meta-analysis of 106 published reports was recurrent luxation and after two years the primary reasons were acetabular erosion and loosening of the femoral part of the prosthesis. Deep infection, deep-vein thrombosis and pulmonary embolism are possible postoperative complications (Lu-Yao et al. 1994). Dislocation is the most common complication after THA (Soong et al. 2004).

Mortality after surgical treatment of proximal fracture of hip is high. Lu-Yao et al. (1994) found 6-13 % mortality within month of surgery and 10-28 % mortality within 2-3 months after surgery. Mortality was higher after arthroplasty than after internal fixation within thirty days after the operation, but the mortality rates were subsequently similar in the groups. In a Finnish series of 562 femoral neck fractures the mortality during the first month was 5 % for the hemiarthroplasty group and 1.7 % for the patients treated by osteosynthesis (Kuokkanen et al. 1990). Death rate after THA is not higher than after hemiarthroplasty (Skinner et al. 1989). Factors associated with increased risk of mortality within thirty days after total hip arthroplasty include age over 70, male gender and history of cardiorespiratory disease (Parvizi et al. 2001). Huuskonen et al. (1999) found 40 % mortality 1.5 years after surgery in a population of 233 Finnish male hip fracture patients. It was over three times higher than the mortality in age matched Finnish male population. In a study by Lu-Yao et al. (1994) there was a clear trendency for arthroplasty, particularly bipolar and total, to be associated with fewer secondary major operations than internal fixation for hip fracture patients. For THA patients managed by surgeons operating on fewer than two hip replacements annually the mortality and revision operation rate is higher. In addition, they have more infections and more serious complications during the hospitalization (Kreder et al. 1997). This has not been shown for hemiarthroplasty patients, which are often treated by residents in most Finnish hospitals (Sarvilinna et al. 2002).

Jain et al. (2003) studied retrospectively 50,235 hip fracture patients, 89 % treated operatively. Thirty-day mortality rate in the nonoperatively treated group was higher than in the surgically treated group. Mortality was higher in non-surgically treated group for bed rest patients than than for early mobilized patients. However, mortality was statistically the same for early mobilized nonoperatively treated patients and surgically treated patients. Ions and Stevens (1987) reported a mortality rate of as much as 60,8 % at 6 months in nonsurgically treated patients with hip fractures and severe medical comorbidity.

Morrey and Kavanagh (1992) compared the complication rate after cemented and cementless revision of the femoral component. They found the overall complication rates 41 % and 34 %, respectively. The reoperation rates were 15 % and 12 %, respectively. The patients in the cemented group 3 % and the patients in cementless group 18 % sustained PF at the time of revision.

Cancer as a complication of THA has been studied by Puolakka et al. (2001) in a large register-based study using the Finnish Arthroplasty Register and the Finnish Cancer Register. The risk of cancer of the respiratory system and digestive tract in THA patients has not increased in the Finnish registers. No increase was found in the risk of lymphohematopoietic cancers or sarcomas. Similar results have been reported in earlier register-based studies in Finland (Visuri et al. 1996) and in other Nordic countries (Mathiesen et al. 1995, Nyren et al. 1995, Olsen et al. 1999).

5.4.1 Complications after the treatment of periprosthetic fracture

There are often complications after the treatment of periprosthetic fracture. The mortality after periprosthetic fracture is high, varying from 3 to 20 %. (McLauchlan et al. 1997, Jensen et al. 1988). Tower and Beals (1999) found high incidence of significant complications to be related to either arthroplasty or the fracture and greater than 50% poor outcome and explained it by many surgeons treating relatively few cases with varied interventions. In a study of 1,049 PFs reported in a Swedish register between 1979 and 2000, the results after treatment were poor with a high frequency of complications and low long-term survivorship (Lindahl et al. 2004).

The nonunion of periprosthetic fracture is an infrequent problem but it is extremely difficult to treat. A high level of complications and relatively poor functional outcomes have been found. The prevention of non-union by optimum treatment of the initial fracture is most important (Crockarell et al. 1999). A loose prosthesis after PF must be primarily treated. Jensen et al. (1988) found low rate of nonunion in treatment of PF by osteosynthesis or femoral revisions. However, if a loosening of the prosthesis was not primarily treated, it resulted in a large number of secondary revision arthroplasties and a poor clinical outcome.

Short term complication rate has been about the same for cemented or cementless revision prostheses. However, the incidence of PF and the subsidence of the prosthesis have been found to increase in the cementless group (Morrey and Kavanagh 1992).

5.5 TESTING NEW PROSTHESIS MODELS BY RADIOSTEREOMETRIC ANALYSIS

In the studies of hip prostheses a large number of patients is needed to ascertain the possible difference between the old and the new models. A long follow-up (at least 10 years) is often needed. In recent years it has been suggested that a new surgical procedure should be tested in extensive pre-clinical test and in a randomized controlled trial before general use (Huiskes 1993 and Gross 1993). In a radiostereometric analysis (RSA) it is possible to measure implant migration in three dimensions. RSA measurements during the first two years after surgery have been found to predict subsequent clinical failure, such as revision operation (Kärrholm et al. 1994, Ryd et al. 1995). Kärrholm et al. (1994) found that the probability of revision was greater than 50 % if the subsidence in RSA was over 1.2 mm two years after the surgery. It has even been proposed that all new implants should be studied by RSA before being released on the market (Alforo-Adrian et al. 1999). Even though Kärrholm et al. (1997) considered RSA a gold standard in *in vivo* measurements of implant fixation, the method contains several possible error sources (Mäkinen et al. 2004). Standardized radiographic technique, accurate patient positioning and stadardization and calibration using phantom models are essential before RSA is used (Mäkinen et al. 2004).

6 AIMS OF THE PRESENT STUDY

The present research was designed to study the incidence, risk factors and follow-up results of periprosthetic fracture. The study hypothesis was that there still are unknown risk factors for periprosthetic fracture.

The specific aims were:

1. To study risk factors of periprosthetic hip fractures.

2. To study the risk factors for periprosthetic fracture for patients primarily operated on after hip fracture.

3. To study the clinical follow-up results of revision hip arthroplasty after periprosthetic fracture and aseptic loosening of the prosthesis

4. To study the incidence of periprosthetic hip fracture after total hip arthroplasty in Finland.

7 PATIENTS AND METHODS

7.1 CASE-CONTROL STUDY OF RISK FACTORS OF PERIPROSTHETIC FRACTURE (STUDY I)

The Finnish Arthroplasty Register was used to calculate the absolute number of periprosthetic fractures in Finland and in the Pirkanmaa Hospital District during the years 1990-2000. In addition, we had permission to conduct a more specific areal case-control study for patients operated on in the Pirkanmaa Hospital District during years 1990-1999. A specific personal identification number allowed us to examine the patient files at the hospitals where the operations were performed. An unmatched case-control study was conducted to find any possible predisposing factors for periprosthetic fracture. Patients for the case group were selected from the Finnish Arthroplasty Register.

The patients in the case group had been re-operated on because of a periprosthetic fracture using a new femoral prosthesis during the years 1990-1999. Data was collected from all four units of the Pirkanmaa Hospital district. Eight patients incorrectly reported as PF to the Arthroplasty Register were excluded. No other selection criteria were used leaving 31 patients with 31 fractures in the case group. According to this information, the previous operation date was collected from the patient files. There were 27 (87%) primary and 4 (13%) re-operations. Of re-operations 2 were done after aceptic loosening of a prosthesis and 2 after secondary arthrosis caused by complications to internal fixation. The median time from primary operation to PF was 5.8 years (Q_1-Q_3 =1.3-10.5) and from re-operation to PF 5.6 years (Q_1-Q_3 =1.4-11.0).

The control group was selected from the University Hospital Register. The date of patients' index operation in the case group was used to select the control group patients. A control group patient was defined as the next patient operatedon in the same hospital district. Of these 24 (77 %) were primary and 7 (23 %) were re-operations. 2 re-operations were done after aseptic loosening of the prosthesis, 5 after secondary arthrosis caused by complications to internal fixation. No other selection criteria or matching criteria for control group patients were used. The index and the revision operations were done at the Pirkanmaa Hospital District on all patients in both groups. All data on both groups was collected from patient files, and the date of surgery was also re-checked.

The median age at the time of index operation was 71 years (range 53-89, Q_1-Q_3 = 62-76) in the case group and 65 years (range 37-93, Q_1-Q_3 = 59-75) in the control group. There were 22 (71 %) females in the case group and 20 (65 %) females in the control group. Age was over 70 years in 17 patients (55 %) in the case group and in 12 patients (39 %) in the control group. Age was over 80 years in 5 patients (16 %) in the case group and 2 patients (7 %) in the control group. Age was categorised into three groups (<70, >-70 and >-80) and logistic regression analysis was performed to analyse the impact of BMI on PF. Based on BMI values, patients were divided into four groups (BMI= <22.6, 22.6-25.9, 26.0-28.7 and >28.7).

7.2 CASE-CONTROL STUDY FOR HIP FRACTURE PATIENTS REVISION OPERATED ON AFTER PERIPROSTHETIC FRACTURE (STUDY II)

Patients for the case group were selected from the Tampere University Hospital Register. Data was collected from all four units of the Pirkanmaa Hospital District. The patients in the case group had been operated on using a revision femoral prosthesis during the years 1992-1999 because of a periprosthetic fracture. All revision prostheses were long stemmed, two of the stems were cemented. Patients' primary diagnosis for the first hip operation was hip fracture. No other selection criteria were used leaving 16 patients with 16 fractures into the case group. According to this information, previous operation date was collected from the patient files. Previous operation (index operation) in this group was primary for 11 patients and re-operation for 5 patients. Four of the patients re-operated on were primarily treated by internal fixation and one by unipolar prosthesis (Table 4). Median time from index operation to re-operation was 2.8 years (Q_1- Q_3 =1 – 8). There were 12 females and 4 males with a median age of 74 years (Q_1- Q_3= 69-78). One patient in the case group had a loose prosthesis and was waiting for re-operation at the time of PF. The closing time of our study was 1 December 2002. Thus in both groups the follow-up for possible periprosthetic fracture varied from index operation to closing time, re-operation or decease.

Table 4. Previous and index operations for PF patients in Study II

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Primary operation	Internal fixation1975	Internal fixation 1994	Thompson prosthesis 1993	Internal fixation 1988	Internal fixation 1978
Second operation	Austin Moore 1976				
Reason for index operation	Loosening of prosthesis	Broken screws, failed ossification	Loosening of prosthesis	Postraumatic arthrosis	Failed ossification
Index operation	Cemented Lubinus 1982	Exeter bipolar 1995	Cementless Bi-metric 1994	Cementless Bi-metric 1991	Thompson 1979

The date of index operation was used to find three control group patients for each case. Control patients were operated on at the same hospital district and were the next hip fracture patients operated on after the index operation. No other selection criteria were used leaving 48 patients with 48 hip fractures and no periprosthetic fractures in the control group of the present study. 45 (94 %) patients were operated on due to hip fracture using hip arthroplasty. Three patients were undergoing revision operations of earlier hip fracture, two because of failed ossification of internal fixation and one because of loosening of Thompson prosthesis. There were 42 females and 6 males with median age of 80 years (Q_1- Q_3= 74-86). The median time from index operation to closing time (12 patients), re-operation (3 patients) or decease (33 patients) was 3.8 years (Q_1- Q_3 = 2-8)

Postoperative and late complications after index operation were compared. The information for this was taken from patient files and normal follow-up controls. All complications needing hospital care or follow-up control are recorded in patient files in Pirkanmaa hospital district. Age (under or over 70 and under or over 80), sex, number of drugs (0, one, two or more), any medication affecting the central nervous system (0, one or more), patients' diseases mentioned in patient files at the time of index operation one by one, number of earlier fractures in other bones (0, one or more), ASA-group (Table 5), prosthesis type and BMI (< 25 or > 25) at the time of index operation were compared between the two groups. Patients diseases mentioned in patient files at the time of index operation were compared between the groups one by one and in categorised groups (<2 or >= 2 and < 3 or > = 3 diseases) (Table 5). The index operation type (primary or re-operation) was compared between the groups. The study groups included 7 different types of endoprostheses (Table 6). Endoprostheses were divided into two groups: Exeter and other type of endoprostheses. The possible specific association between the polished and wedge design of the prosthesis and the incidence of PF was studied. Surgeons were divided into three groups based on their experience at the time of the index operation: orthopedic trainees, general surgeons and orthopedic surgeons. A multivariate analysis was done for age, BMI and sex and to evaluate the possible risk of PF for elderly (>70 or >80 years) light (BMI <25) women.

Table 5. ASA-classification and patients diseases at the time of index operation

	Case group (N = 16) N	Control group (N = 46) N
ASA = 1	1	0
ASA = 2	5	10
ASA = 3	9	28
ASA = 4	1	8
Dementia	3	4
Depression	3	4
Diabetes	2	8
Dizziness	4	5
Hemiparesis or TIA	1	7
Rheumatoid arthritis	2	2
Elevated blood pressure	6	24
Cardiac insufficiency	3	14
Lung disease	1	2
2 or more of symptoms mentioned above	5	17
3 or more of symptoms mentioned above	5	6

Table 6. Prosthesis types before periprosthetic fracture

Prosthesis type	Case group N = 16	Control group N = 48
Austin-Moore	0	1
Bi-metric bipolar	2	0
Biomet total	1	3
Euro	0	1
Exeter	6	6
Lubinus	1	3
Thompson	6	34

7.3 PERIPROSTHETIC FRACTURE VERSUS ASEPTIC LOOSENING AS ETIOLOGY FOR REVISION OPERATION (STUDY III)

We compared two patient groups in this study, both operated on in revision operations, some because of periprosthetic fracture (PF), others because of aseptic loosening (AL) of the prosthesis. Patients in the PF group (39 patients with 39 prostheses) were operated on in Tampere University Hospital during the years 1992-1999 because of periprosthetic fracture with a new femoral, or both femoral and acetabular part of prosthesis. The etiology for fracture was trauma for all patients. Patients in the AL group (83 patients with 83 prostheses) were re-operated on during the years 1992-1999 with a new prostheses because of aseptic loosening. At least 9 AL patients were randomly selected for each year. The end-point was 31 December 2002.

There were 24 (61.5 %) females and 15 (38.5 %) males in the PF group and 57 (68.7 %) females and 26 (31.3 %) males in the AL group. Median age at the time of re-operation was 76 years (Q_3-Q_1 = 68-80) in the PF group and 73 years (Q_3-Q_1 = 67-79) in the AL group. Patients' diseases, BMI and ASA classification at the time of revision surgery were found in the patient files (Table 7).

Table 7. ASA classification, BMI and patients' diseases at the time of revision operation

	PF group N= 39 %	AL group N= 83 %
ASA = 1	2.6	8.4
ASA = 2	28.2	38.6
ASA = 3	56.4	45.8
ASA = 4	10.3	3.6
BMI < 25	48.7	34.9
BMI = 25-30	41.	47
BMI = 30-35	5.1	9.6
BMI > 35	2.6	3.6
Congenital heart failure	25.6	8.4
Ischemic heart disease	17.9	16.9
Arrhythmia	20.5	10.8
Elevated blood pressure	48.7	32.5
Lung disease	12.8	3.6
Rheumatoid arthritis	15.4	10.8
Depression	17.9	3.6
2 or more of these diseases	48.7	3.6

The median follow-up time from the revision operation to the latest clinical follow-up examination was 1 year (Q_1-Q_3 =0.5-2.3) in the PF group and 3 years (Q_1-Q_3=1-5) in the AL group. Cementation varied between the groups: 4 (10.3 %) cemented and 35 (89.7 %) cementless revision prostheses in the PF group and 6 (7.2 %) cemented and 76 (91.6 %) cementless revision prostheses in the AL group.

The power analysis showed that the groups were too small to allow univariate analysis for all variants. We were able to study only the patients operated on after 1990 and so it was not possible to enlarge the PF group. Patients operated on by plate or other fixation mechanisms after periprosthetic fracture were not included in this study to make groups and operations more similar.

The information on complications, clinical follow-up status and postoperative functional capability were retrospectively collected from the patient files. A clinical follow-up for patients was done by a senior consultant and a hysiotherapist. In this examination the information was collected on a form of the Finnish Arthroplasty Society including functional capability and clinical status. The parameters were the same as those needed in the calculation of Harris hips score. These forms and patient files were used to estimate the postoperative functional status. HHS was calculated for 14 patients in the PF group and for 38 patients in the AL group. Johansson's classification was used for periprosthetic fractures (Johansson et al. 1981) (Table 8).

Table 8. Johansson's classification of periprosthetic fractures

Fracture type	Johansson's classification	Patients (N= 34) %
Proximal to tip of the prosthesis	I	56
At the tip of prosthesis	II	21
Distal to the tip of prosthesis	III	9
Fracture in many fragments from trochanter to distal femur, below the tip	-	15

7.4 INCIDENCE OF PERIPROSTHETIC FRACTURE (STUDY IV)

The Finnish Arthroplasty Register was used to collect all 33,154 primary hip arthroplasty operations done in Finland during the years 1990-1999. The cutoff point for our study was 31 October 2002, which was the last date when deaths and revision operations were updated in the register.

We selected from the register all the patients operated on due to hip arthrosis. From this population, other parameters including sex, side of the prosthesis, cementation, date of the surgery, reason for the revision operation, date of the revision operation and date of death were collected using the personal identity number. All the information was collected from the register and thus patients were not personally contacted, nor were the patient files studied.

There were 19,886 (60%) females and 13,267 (40%) males. 63% (20,887) of prostheses were cemented and 37% (12,114) cementless. The whole population included 199 different kind of combinations of proximal and femoral parts of various endoprosthesis types.

The Kaplan-Meier method was used for the analysis of the survival of prostheses. Revision operation of femoral or both components for periprosthetic fracture was recorded as revision. Death of a patient, the cuoff point for our study, or revision for other causes than periprosthetic fracture were recorded as withdrawals. The observation time for each prosthesis was the period from the date of surgery to revision or withdrawal. The survival analysis concerning revision operated PF was calculated for the six most used total hip arthroplasties: ABG cemented (558), ABG cementless (2,001), Biomet cemented (1,151), Biomet cementless (5,556), Elite Plus (1,050), Exeter (4,798), Lubinus SP I or SP II (7,588) and Müller (3,025) (Table 1). The classification of prostheses was based on type of the femoral part. The rest of prostheses were in cemented (2,717) and cementless (4,557) group. The survival analysis was also calculated for both sexes and age cohorts. Cox's regression model was used including the studied risk factors age, sex, and prosthesis type.

The incidence for periprosthetic fracture was calculated for the whole period and separately for patients primarily operated during the years 1990-1994 and 1995-1999.

7.5 STATISTICAL ANALYSIS

The statistical analyses were performed using SPSS versions 9.0 and 10.1 for Windows (SPSS Inc, Chicago, Illinois, USA) and STATA software version 7.0 (Stata Corporation, Texas, USA).

7.5.1 Follow-up study

Pearson chi-square and Fisher`s exact tests were performed to investigate whether any differences between subgroups were statistically significant. A univariate analysis was performed comparing each variable in the two groups. P-value under 0.05 was considered significant.

7.5.2 Case-control studies

An unmatched case-control design was used in Study I and matched design in Study II. It was estimated that the date of surgery was a factor without any bias which could motivate an matched design in the study I. When PF after hip fracture was studied (II), the groups were matched by date of operation to make sure that the patients in both groups had the same treatment options at the time of hip fracture operation.

A power analysis in Study I showed that BMI difference >3.6 with SD of 5 would result in a statistically significant difference (80% power) with our sample size. Concerning age (SD=11, difference over 8 years), primary diagnosis and cementation the sample size was large enough to show statistically significant differences (80% power) but for the 10 different types of prostheses it was too small. A power analysis in Study II showed that the sample size was large enough to show statistically significant differences (>80% power) between the groups when the percentual difference in prevalence of studied factor between the case (n = 16) and control (n = 48) group was over 45 % units (ko) ($p < 0.05$). Patients were matched using the date of index operation.

Odds ratios with 95 % confidence intervals (CI) were calculated for category variables in Study I using 2x2 tables and using conditional logistic regression analysis in Study II. Median and quartiles (Q_1-Q_3) were calculated for time variables. P-value under 0.05 was considered significant. Median and quartiles (Q_1-Q_3) were calculated of time variables.

7.5.3 Survival analysis and incidence of PF.

Both Kaplan-Meier survival and Cox regression analysis were used when the incidence of PF between the prosthesis types was compared .

8 RESULTS

8.1 RISK FACTORS OF PERIPROSTHETIC FRACTURE

Risk factors of PF were studied in case (n =31)-control (n = 31) Study I. Female gender (OR= 1.3, CI = 0.5-3.9), age over 70 vs. below 70 (OR = 1.9, CI = 0.7-5.3), or 80 vs. below (OR = 2.8, CI = 0.5-15.6) were not significantly associated with increased risk for PF. The prosthesis was cemented in 24 (77 %) and cementless in 7 (23 %) patients in the case group and cemented or cementless in 21 (67 %) and 10 (33 %) patients in the control group. For patients operated on with a cementless prosthesis the risk for PF was not higher than for patients operated on with a cemented prosthesis (OR = 0.6, CI = 0.2-1.9). High BMI (> 28.7) had no association to the incidence of PF (p = 0.74)

There were no intraoperative or immediate postoperative PFs in the case group. The median time from the index operation to the revision operation due to fracture was 70 months (range 1-174, Q_1-Q_3 = 15-128).The etiology to PF was trauma in all 31 cases. 29 cases (94 %) had had a fall and two cases (6 %) reported some kind of distortion.

The prevalence of reoperated patients was higher in the control group (23 %) than in the case group (13 %) but the risk for PF was not higher for reoperated patients; OR= 0.51 (0.1-2.0).

There were 10 different types of prostheses in these two groups. The small number of cases in each group did not permit a reliable statistical evaluation (Table 9).

Table 9. Odds ratios for prostheses

	Case group N = 31 %	Control group N = 31 %	Odds ratio	95 % Confidence interval
Exeter	26	16	1.809	0.52 - 6.32
Thompson	16	3	5.769	0.63 - 52.61
Lubinus	29	29	1.0	0.33 - 2.99
Biomet	13	32	0.31	0.09 - 1.13
Lord	6.5	10	-	-
ABG	6.5	0	-	-
Omnifit	3	0	-	-
S-ROM	0	3	-	-
Euro	0	3	-	-
Link RS	0	3	-	-

Four (13%) patients in the case group were waiting for revision operations at the time of periprosthetic fracture, all because of aseptic loosening, detected at routine clinical follow-up and radiographic examinations (Table 10). There were more late complications after index operation in the case group than in the control group, although this was not statistically significant; RR=1.62 (0.4-6.4).

Table 10. Complications after the index operation

	Case group n = 31 %	Control group n = 31 %
Aseptic loosening	12.9	3.2
Luxation	0	6.5
Wound infection	0	3.2
Myositis ossificans	3.2	0
Debilitating pain	3.2	0
Postoperative thrombosis	0	6.5

The prevalence of fracture as the indication for the primary operation was higher in the case (52%) than in the control group (19%) (p= 0.016). The prevalence of arthrosis as a primary diagnosis was lower in the case (35.5%) than in control (61%) group (p= 0.074) (Table 11).

Table 11. Primary Diagnoses

	Case group N = 31 %	Control group N = 31 %	Odds ratio	95 % confidence interval
Fracture	52	19	4.4	1.4 - 13.8
Primary arthrosis	35.5	61	0.35	0.12 - 0.97
Rheumatoid arthrosis	6.5	3	2.1	0.18 – 24.1
Congenital dysplasia	0	13	-	
Caput necrosis	3	0	-	
Congenital hip luxation	3	0	-	
Legg perthes	0	3	-	

8.2 PERIPROSTHETIC FRACTURES AFTER HIP FRACTURE

Risk factors for PF after hip fracture were studied in case (n = 16)-control (n = 48) Study II. The reason for index operation was falling on level ground for 15 patients, and car-accident for 1 patient in the case group. The reason was falling on level ground for 44 (91.7 %), slipping for 3 (6.3 %), a blow for 1 (1.6 %) patients in the control group. Thus, 93.8 % of injuries in the case group and 100 % of injuries in the control group were low-energy traumas. In the case group 2 of fractures and in the control group 16 of fractures occurred at home.

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In conditional logistic regression analysis the ASA group, number of medications, number of medication affecting the central nervous system, BMI, weight, experience of surgeon, complications at the time of index operation, patient's diseases one by one (heart failure, neurological diseases, lung diseases, rheumatoid arthritis, blood pressure, diabetes, depression, dementia) and sex had no statistically significant association with PF. There was no statistically significant difference in postoperative or late complication rate between the groups after the index operation (Table 12).

Table 12. Postoperative and late complications for patients in Study II

	Postoperative complications		Late complications	
	Case group N= 16	Control group N= 48	Case group N= 16	Control group N= 48
Myositis ossificans	0	0	1	
Loosening of prosthesis	0	0	1	0
Luxation of prosthesis	1	1	1	3
Luxation and loosening of prosthesis	0	0	0	1
Dizziness		1		
Pulmonary embolism		1		
Paralysis of peroneal nerve		1		

Re-operation as indication for index operation was a risk factor for PF (OR = 13.1 , CI = 1.5 – 114.1). BMI and age together were not found to have a statistically significant effect on PF in multivariate analysis. Age under 70 years (OR = 4.9, CI = 1.2 - 20) alone increased the risk of PF in conditional regression analysis.

8.3 PROSTHESIS TYPE AS A RISK FACTOR FOR PERIPROSTHETIC FRACTURE

The polished, wedge-shaped (Exeter) prosthesis type compared to all other prostheses (OR = 11, CI = 1.2 – 97) increased the risk of PF in conditional regression analysis in Study II (Table 13). One of these prostheses was operated on after non-union of internal fixation, the rest were primary operations. In Study IV the survival analysis of 33, 154 hip arthrosis patients and prostheses showed no difference between the prosthesis types (p = 0.99). In Study I there were 10 different types of prostheses in the two groups and the small number of patients in each group made a reliable statistical evaluation impossible.

Table 13. Prosthesis types in Study II

Prosthesis type	Case group n = 16	Control group n = 48
Austin-Moore	0	1
Bi-metric	2	0
Biomet total	1	3
Euro	0	1
Exeter	6	6
Lubinus	1	3
Thompson	6	34

8.4 INCIDENCE OF PERIPROSTHETIC FRACTURE

In Finland (population 5.1 million) the total number of periprosthetic fractures treated by revision rose from 18 per year in 1990 to 45 per year in 2000. In the Pirkanmaa Hospital District (population 450 000) the total number also rose from 0 in 1990 to 9 in 2000 (Table 10). These numbers include periprosthetic fractures treated by revision operation and registered in the Finnish Arthroplasty Register.

Table 14. Revision operated periprosthetic fractures in Finland and in Pirkanmaa Hospital District

	Area	
Year	Finland total=339	Pirkanmaa Hospital district total=48
1990	18	0
1991	18	2
1992	18	3
1993	23	1
1994	46	4
1995	38	6
1996	24	4
1997	34	3
1998	34	6
1999	41	10
2000	45	9

Median age at the time of primary operation was 69 years (Q_1-Q_3 = 62-74). Median age for female patients was 70 years (Q_1-Q_3= 64-75) and the median age for male patients was 66 years (Q_1-Q_3= 60-72). Survival analysis between the sexes showed that male patients had more revisions after PF (p= 0.08). In the Cox regression model the age-standardized male sex showed a tendency for higher risk of PF (p = 0.053, RR = 1.86, CI = 0.99-3.5).

We found 40 revision-operated periprosthetic fractures in a group of 33,154 patients, the previous operation being due to hip arthrosis (Table 15). 1515 patients were revised for other reasons than periprosthetic fracture. The most common reasons for revision were femoral loosening (558 patients), acetabular loosening (252 patients), loosening of both components (226 patients), luxation (146 patients) and infection (112 patients).The overall incidence for fractures was 18.36 (CI = 13.47 – 25.03) per 100,000 person years. For patients operated primarily during years 1990-1994 the incidence was 20.45 (CI = 13.93 - 30.04) per 100,000 person years and for patients operated on primarily during the years 1995 - 1999 it was 15.43 (CI = 9.14 - 26.05) per 100,000 person years.

Table 15. Types of prostheses and causes of revisions

Prosthesis (N)	Reason for revision								
	loosening both	loosening acetabulum	loosening femur	infection	luxation	prosthesis in wrong position	fracture of bone	other reason	total
ABG cemented (558)	2	3	7	1	6	1	1	0	21
ABG cementless (2,001)	1	5	1	3	6	1	1	9	27
Biomet cemented (1,151)	11	8	39	5	4	2	2	5	76
Biomet cementless (5,556)	10	61	20	12	47	13	7	79	249
Elite Plus (1,050)	12	3	40	6	1	3	0	0	65
Exeter (4,798)	8	16	15	18	22	6	5	0	90
Lubinus (SP I and SP II) (7,588)	91	46	153	23	23	6	9	11	362
Müller (3,025)	14	9	55	15	2	4	4	6	109
Other cemented (2,717)	25	17	81	14	14	2	4	9	166
Other cementless (4,557)	52	84	157	16	21	12	7	41	390

8.5 PERIPROSTHETIC FRACTURE VERSUS ASEPTIC LOOSENING

Mortality was 5.2 % in the PF group and 1.2 % in the AL group one year after the revision surgery. The total mortality at the end point of the study (31 November 2002) was 33.3 % in the PF group and 27.7 % in the AL group. For these patients median time to decease was 2 years (Q_1-Q_3 =1.3 - 4) in the PF group and 5 years (Q_1-Q_3 = 2.7-6.5) in the AL group.

Of the patients in the PF group 33 % and of those in the AL group 19 % had serious postoperative or late complications (p = 0.09) (Table 16). There were significantly more reoperations in the PF group (p = 0.02): 8 patients were re-re-operated on in the PF group, and one of these was operated on once more. Of reoperations in the PF group five were done after a new PF, one because of a loose cup, one after luxation and one to remove fixation material. Correspondingly, 2 patients were reoperated in the AL group.

Table 16. Postoperative and late complications for revision hip arthroplasty

	Postoperative complications		Late complications	
	AL N = 83 N	PF N = 39 N	AL N = 83 N	PF N = 39 N
Wound infection	4	2	0	0
Peroneal paresis		1	0	0
DVT	1	1	0	0
Luxation of prosthesis	0	1	2	2
New PF		1	2	4
Deep infection	1	0	0	1
Cup loosening	-	-	2	0
Femoral loosening	-	-	1	0
Liner wear	-	-	1	0
Stem migration	-	-	1	0
Stem fracture	-	-	1	0

The median university hospital treatment period was 8 days (Q_1-Q_3 = 7–8) for the AL group and 7 days (Q_1-Q_3 =5–8.25) for the PF group. 26 % of patients in the PF group and 6 % of patients in the AL group were discharged from the sixth postoperative day ($p = 0.05$). 49 % of patients in the PF group group needed hospital care in other hospitals and 36 % in a health care centre after leaving the university hospital, the rest were able to go straight to home. In the AL group the shares were 23 % and 24 % respectively ($p = 0.02$).

The median Harris hip score was 87 (Q_1-Q_3 = 80-89) in the PF group and 85 (77-93) in the AL group at the time of last follow-up control. At the time of the last follow-up control more patients in the AL group were living at home ($p = 0.01$) and there were more patients in the AL group using no walking stick or any kind of support ($p = 0.01$). More patients in the AL group were able to walk over 500 metres and outside, but the difference was not statistically significant ($p = 0.53$). There was no difference in pain between the groups ($p = 0.78$, Table 17)

Table 17. Daily activities at the time of follow-up control

	Reason for revision operation	
	AL %	PF %
Walking outside or at least >500m	77	69
No pain	78	81
No support	53	33
Living at home	76	51

9 DISCUSSION

Hip fracture risk factors and prevention methods have been extensively studied **(**Law et al. 1991, Greenspan et al. 1994, Cummings et al. 1995, Kannus et al. 1996, Cumming et al. 1997, Lips 1997, Greenspan et al. 1998 , Kannus et al. 1999, Kannus et al. 2000a, Kannus et al. 2002a). Nevertheless, the periprosthetic fracture of the operated hip is a less well known entity. Intraoperative and immediate postoperative factors affecting the PF are easy to understand. However, it remains unsolved if the risk factors for late PF are the same as for hip fracture or if there are special risk factors for both of these fractures.

9.1 METHODOLOGICAL CONSIDERATIONS

9.1.1 The Finnish Arthroplasty Register

The Finnish Arthroplasty Register was used to locate patients in two of our studies. In that way the patients were easily found but it excluded the PFs treated by osteosynthesis from our study. In Finland the THA:s are recorded in the Finnish Arthroplasty Register. However, hemiarthroplasties after hip fracture are not recorded. The coverage of the Finnish Arthroplasty Register has varied from almost 90 % in 1995 to over 95 % in 1999, and thus some patients are allways excluded from the register (Puolakka et al. 1997, Puolakka et al. 1999). In some studies it has been difficult to perform detailed analyses of the data in the register, mainly because acetabular and femoral components as well as the material and size of the femoral heads have been recorded separately only since 1996. These limitations must also be kept in mind when the results of our study are estimated. However, the factors needed in our study were easily found in the register. All registers are subject to a certain frequency of errors and incompleteness. Incorrect classification of diagnosis in the register may have reduced the number of patients in the Studies I and IV. On the other hand, data was more homogenic in these studies as it was taken from the same database.

9.1.2 Statistical analysis

Three different kinds of statistical methods were used: clinical follow-up study, register-based study and case-control (unmatched and matched) studies (Table 18). The clinical follow-up study is widely used when operations and prosthesis types are compared. In our follow-up study the results of the rearthroplasty because of aseptic loosening of the prosthesis or periprosthetic fracture were compared (IV).

Table 18. Methods and study types

	Study I	Study II	Study III	Study IV
Type	Case-control	Matched case-control	Follow-up	Register-based
Number of patients	31 + 31	16 + 48	39 + 83	33,154
Factors studied	Risk of PF	Risk of PF for hip fracture patients	Daily activities, complications after revision	Incidence of PF, risk of PF
Analysis	Odds ratio Cox regression	Odds ratio Cox regression	Harris hip score Crosstabbs	Survival Cox regression

A register-based study (IV) for a very large patient population was the only possible way to calculate the incidence of revision operated PF. Dobbs introduced Kaplan-Meier univariate analysis for hip prostheses in 1980 and it has been used ever since to evaluate the survival of endoprostheses (Kaplan 1958, Dobbs 1980). It has been regarded as a valid technique for long-term evaluation of joint prostheses, although many patients are lost to follow-up, assumptions of lost patients are made and the interpretations are increasingly uncertain at the tail-end of curves (Dorey and Amstutz 1989). In addition, Johnsson et al. (1994) found that the true risk factors for revision operations can be identified accurately by a combination of univariate survival and multivariate statistical analyses. Still most authors prefer to use only survival analysis in their studies. We used both Kaplan-Meier analysis and Cox's regression model. In our study, patients with a single primary diagnosis and revisions only for PF patients must increase the accuracy of the findings in survival analysis, although patients were lost to follow-up.

A pure case-control study, however, is not so often reported in orthopaedic literature. For a rare complication like periprosthetic fracture treated with revision hip arthroplasty, the patient material is difficult to find. In a case-control study the number of patients in the case group may be much smaller than in a follow-up study and statistically significant results can still be achieved (Altman 1991). In this kind of study the case group patients have the complication that control group patients do not have, which is the most significant difference between the groups. Groups can still be matched for some factor like the date of operation as we did in our study II. We used case-control method in two studies (I and II), when risk factors of PF were studied. A power analysis was used to count the number of control patients needed. We used conditional logistic regression analysis. The groups in our studies were small, but the case-control method proved to be a good method, since we found statistically significant differences between the groups.

9.2 INCIDENCE OF PERIPROSTHETIC FRACTURE

Periprosthetic fracture, especially revision operated PF, is quite a rare complication of hip arthroplasty. In the light of the literature it has not been clear if the incidence of PF as a complication of hip arthroplasty is increasing. The overall incidence of PF seems to vary somewhere between 0.1 and 18 % (Beals and Tower 1996, McLauchlan et al. 1997, Tower and Beals 1999). Fracture was the second leading cause of revision hip arthroplasty at the Mayo Clinic 1989-1993, ranking after loosening of the implant and before dislocation and infection (Lewallen and Berry 1997). However, in the study of 75,000 primary or revision THAs, the most common reasons in Finland for revision were aseptic loosening, dislocation and infection during years 1980-1999 (Puolakka et al. 2001). In our Study IV aseptic loosening was the commonest reason for revision.

We found that in Finland (population 5.1 million) the total number of periprosthetic fractures treated by rearthroplasty rose from 18 per year in 1990 to 45 per year in 2000. In the Pirkanmaa Hospital District (population 450,000) the total number also rose from 0 in 1990 to 9 in 2000. These numbers include only the periprosthetic fractures which have been treated by rearthroplasty and registered to Finnish Arthroplasty Register. There are many options for the treatment of PF, rearthroplasty being only one, and thus the incidence of PF treated by rearthroplasty must be somewhat lower than the total incidence. The incidence of revision operated PF after THA revealed by our register- based study was very low, only 18.36 per 100,000 person years.

There are no large studies on PF after hemiarthroplasty, but in a study on 94 PFs by Tower and Beals (1999) 7 % of fractures were found around an Austin-Moore hemi-arthroplasty. In a study on 128 Austin Moore hemiarthroplasties two peroperative and three late PFs were found (Vajanto et al. 1998). Sarvilinna et al. (2002) found one (1.4 %) intraoperative, later dislocated and revision operated periprosthetic fracture and one postoperative fracture of trochanter major in a group of 72 bipolar hemiarthroplasty patients with a minimum follow-up time of four years.

Our special interest was in periprosthetic fractures treated with rearthroplasty and it seemed that the survival of the eight most used cemented or cementless prostheses was the same with no significant difference. We found only 40 periprosthetic fractures, needing a femoral revision operation in a population of 33,154 patients with hip osteoarthritis. The incidence of most serious, revision operated PF was lower for patients primarily operated on during the years 1990-1994 than for patients operated on during the years 1995-1999. Thus, revision operated periprosthetic fracture seems to be a very rare complication for patients with primary osteoarthritis. However, periprosthetic fractures treated in other ways were excluded from our study. Additionally, hemiarthroplasties are not included in the Finnish Arthroplasty Register. The follow-up in our study varied from three to twelve years and a longer follow-up is needed to see the incidence of PF as a late complication. The differences in the prevailing practices of PF treatment between countries and the variety of registers thorough out the world makes it difficult to compare these results with those of other studies. A study using, for example, a Swedish register, including both hemiarthroplasties and hip fracture operations would be more informative.

9.3 RISK FACTORS OF PERIPROSTHETIC FRACTURE

9.3.1 Revision arthroplasty

The risk of peroperative PF has been estimated to be as much as two times higher in revision than in primary arthroplasties (Khan 1977). The results of cemented revisions have been inferior to those of cementless revisions, even though the short-term complication rate is essentially the same (Amstutz et al. 1982, Callaghan et al. 1985, Kavanagh et al. 1985). Nevertheless, Morrey and Kavanagh (1992) thought that there was little in the literature supporting the exclusive use of only cementless prostheses in revision operations. Our results from Study II is in concordance with those of earlier studies. We found that re-operation as an indication for index operation was a risk factor for PF (OR = 13.1 , CI = 1.5 –114.1).

9.3.2 Aseptic loosening and osteolysis

When the risk factors for PF in the early postoperative period include pre-existing stress risers like cortical windows or perforations (Scott et al. 1975, Missakian et al. 1993), the known risk factors for late postoperative PF are component loosening, osteolysis and proximal femoral bone loss (Johansson et al. 1981, Christensen et al. 1989, Kelley 1994, Astion et al. 1996, Moran 1996, Radl et al. 2000).

According to the literature, it seems that elderly women or patients with loose femoral components most commonly have periprosthetic fractures (Bethea et al. 1982, Tower and Beals 1999). Tower and Beals (1999) found that 22 out of 87 patients and 93 fractures were cases of pre-existing loose prosthesis. Bethea et al. (1982) found as many as 75 % of patients with loose prostheses before PF. In our Studies I and III 13 % of patients were waiting for revision operation because of aseptic loosening of femoral or both components at the time of the PF and in Study II one out of 16 patients had had a loose prosthesis before PF. Thus, at least for these patients the waiting time to revision operation because of aseptic loosening was too long.

It has been shown that when the proximal fixation of the hydroxyapatite coated stem fails, stress is transferred to the distal third of the stem and thus the proximal femoral bone loss can be the main reason for the high incidence of periprosthetic fractures (Radl et al. 2000). As osteolysis can sometimes be almost asymptomatic, it is possible that the changes in the bone progress so that the PF is the first real symptom. Regular postoperative follow-up using radiographs has therefore been recommended and would be the only way to find the patients with osteolysis in time. Lewallen and Berry (1997) found regular follow-up 1, 2, 5, 7 and 10 years after surgery and thereafter every 2-3 years to be useful.

9.3.3 Falling

Low-energy trauma, especially falling - sometimes spontaneous fracture during daily activities - is the most common etiology for late PF. Beals and Tower (1996) reported 84% of periprosthetic fractures resulting as a consequence of a fall, 8% after other kinds of injuries and 8% as spontaneous fractures. In our Study I all the periprosthetic fractures were a consequences of injuries (94% because of a fall) a long period after surgery, all of them being low-energy injuries. In Study II 15 of 16 PFs were low-energy injuries. It has been suggested that Johansson type III injury (beyond the tip of the prosthesis) could be part of the natural incidence of femoral fracture rather than a prosthesis-related problem (Johansson et al. 1981, McLaughlan et al. 1997). Thus, according to our Studies I and II, the prevention of a fall would be most necessary in the prevention of PFs. This finding is substantiated in the literature.

9.3.4 Gender and medication

Schwartz et al. (1989) found that female patients had a higher incidence of intraoperative PFs than male patients. We found no correlation in Studies I or II with patients' sex and the incidence of PFs, but in a register-based Study IV of hip osteoarthritis patients, male gender was associated with increased risk of PF, although the result was not statistically significant (P = 0.053).). In a Finnish study of Visuri et al. (2002) young age, male sex, uncemented prosthesis and first 10-year period (1980-1989 vs 1990-1999) of surgery were found to be statistically significant risk factors for loosening of the prosthesis. Loosening of the prosthesis may explain why the male gender was found to be a risk factor in our study. However, we do not know how many of these patients had an underlying loosening of the implant.

Changes in psychiatric medication also have a positive effect on risk of falls and the use of hip protectors has been proven to prevent hip fractures, although there are also opposite results (Parkkari et al. 1997, Kannus et al. 2000b, Gillespie 2002). To our knowledge, the same has not been shown for PF. However, we found no evidence of medication affecting the central nervous system or of any medication increasing the risk of PF.

9.3.5 Prosthesis type

The Exeter type of prosthesis compared to other prosthesis designs increased the risk of PF. To our knowledge this is a new finding, although prosthesis type and osteolysis associated with prosthesis type have earlier been discussed as a possible risk factors (Löwenhielm et al. 1989, Radl et al. 2000). The number of Exeter and Charnley prostheses in the PF group in Swedish Arthroplasty Register has been higher than the numbers of other prostheses (Lindahl et al. 2004). However, many other factors like osteoporosis and patients' daily activities were not included in our study and thus further studies are needed to explain these findings.

Hip fracture patients under the age of 70 years had a 4.9 times higher risk for PF than older patients, even though the median time from index operation to next operation, closing-time or exitus was longer in the control group (Study II). This is a somewhat obscure finding since old age has been thought to be a risk for PF. We think that since the patients in the case group were younger and since a statistically significant difference between the prostheses was still found, it makes our results regarding the differences between the prostheses even more important. Thus, the increased risk of PF for younger patients may be explained by more strenuous daily activities, but the shorter time to PF in the Exeter group supports the theory of prosthesis type as a risk factor of PF.

Middleton et al. (1998) compared primary Exeter stems and found that polished stems behaved differently than the matte-surfaced stems. The average subsidence of polished stem was 1 mm at two years after the operation, but without subsequent loosening of stems at as long as 12 years after implantation. Matte surface of the stem even seemed to increase loosening of the stem. The results were the same in a study by Rockborn and Olsson (1993). On the contrary, Kärrholm et al. (1994) found that the subsidence of femoral Lubinus stem over 1.2 mm at two years after the operation predicted subsequent revision. One theory is that the axial loading effect produces a wedging effect of the stem and the surrounding cement, which produces hoop stresses on the surrounding bone (Harkess 1998).

In a fall there is often a peak stress on the greater trochanter. In our study it remained unsolved how the prosthesis acts in that situation. One theory is that the subsidence of the femoral part is a reason for a rised stress in the hip area and a fracture with lower energy. It has been shown that the incidence of PF and the subsidence of the prosthesis are increased in cementless prostheses (Morrey and Kavanagh 1992). It can also be deduced that the wedge design of the stem might predispose to fall-related subsidence and subsequent fracture.

9.3.6 Primary diagnosis

The absolute number and relative incidence of hip fracture are increasing and have been predicted to increase significantly in the very near future (Lüthje 1983, Kannus et al. 1999). Consequently, the number of surgical treatments will also rise. The likelihood of increasing osteoporosis, of increasing amounts of falls and fractures in certain birth cohorts has been discussed (Lees et al. 1993, Kannus et al. 1999, Kannus et al. 2002a). A previous hip fracture is a possible risk factor for PF. 52 % of patients in the case group of Study I had had previous arthroplasty due to fracture and consequently a previous fracture seems to have an influence on subsequent PFs. However, no such correlation was found in a study by Löwenhielm et al. (1989).

Both hip fracture and PF often result as a consequence of a fall (Beals and Tower 1996). In our study most of the late PFs occurred after a fall and previous hip fracture was a risk factor for PF. Other risk factors that are similar for both of these fractures are weakness of the bone, deformities, female gender and post-menopausal status. Some of the theories describing the risk factors of hip fracture of the elderly might also therefore describe the risks of the periprosthetic fracture and when the prevention of PF is considered, these factors should also be remembered in addition to prosthesis-related factors and surgical protocol.

It has been shown for hip fracture that there are several risk factors for falls among the elderly and these can easily be examined and questioned (Nevitt 1989). Moreover, a structured interdisciplinary approach, physical exercises and hip protectors have been shown to predict hip fractures (Campbell et al. 1997, Close et al. 1999, Gillespie et al. 2001). Patients recovering from a hip operation could have higher risk for falls and PFs because of altered walking abilities and proprioseptics. Finally, if the patient has a loose or painfull prosthesis, walking distances and abilities will be poor and the risk for a fall and fracture may be higher. Not only is it therefore important to monitor the patient and the prosthesis clinically and radiologically; patients' daily activities should be monitored and all possible methods used to prevent falls, treat osteoporosis and to recommend appropriate physical exercises for all patients with hip prostheses to prevent PFs.

9.4 COMPLICATIONS AFTER REARTHROPLASTY OF PERIPROSTHETIC FRACTURE

Periprosthetic fracture and aseptic loosening of the prosthesis are totally different indications of revision operation. However, we wanted to see if there are differences in postoperative recovery. It has been thought that the recovery is poorer for PF patients.

9.4.1 Mortality

Mortality after periprosthetic fracture has varied from 3 to 20 %. (McLauchlan et al. 1997, Jensen et al. 1988). In our study mortality one year after the revision was higher in the PF group (5.2 %), than in the AL group (1.2 %), but at the endpoint of our study it was only slightly higher in the PF group. The median time to decease wasshorter for these patients in the PF group and may partly be explained by the lower age of patients. Thus mortality after PF in our study was almost as high as mortality reported after hip fracture (Lu-Yao 1994).

9.4.2 Other complications

A high incidence of significant complications related to either revision arthroplasty or the periprosthetic fracture has been reported. Tower and Beals (1999) suspected that it might be explained by many surgeons treating relatively few cases with various interventions. In the Tampere University hospital a team of only two orthopaedic surgeons was performing the revision operations at the time of our study and thus complications cannot be explained in that way. As expected, there were more serious complications in the PF group than in the AL group in our study.

A cementless prosthesis is commonly selected for femoral reconstruction in PF to prevent cement interdigitation into the fracture line. Extensively porous-coated cementless femoral implants have been used successfully in revision total hip arthroplasty (Lawrence et al. 1994, Moreland et al. 1995 and Krisnamurthy et al. 1997) and the same implants can be used successfully in the revision arthroplasty of a PF (MacDonald et al. 2001). In our study most of the patients were treated with cementless prostheses.

The nonunion of a periprosthetic fracture is an infrequent problem and extremely difficult to treat (Crockarell et al. 1999). A loose prosthesis after PF obviously necessitates a new revision. Jensen et al. (1988) found a low rate of nonunion in the treatment of PF by osteosynthesis or femoral revisions. However, if a loosening of the prosthesis was not primarily treated, it resulted in a large number of secondary revision arthroplasties and poor clinical outcome. We found as many as 8 reoperated patients, 5 with a new periprothetic fracture in a group of 39 revision operated patients.

As expected, patients after revision of PF recovered less easily and had higher mortality. Even the surviving patients at follow-up controls had poorer parameters. This may be explained by older age, longer hospital stay, longer time in nursing homes or health care centres.

It is also commonly recognised that aseptic loosening predisposes to periprosthetic fracture (Bethea et al. 1982, Myung-Sik et al. 2003). In our studies I and III 13 % of the patients in the PF group had had a loosened stem. In addition to decreasing mortality, the economic impact of this finding points out the importance of performing revision of an aseptically loosened femoral component without a delay.

10 CONCLUSIONS

In the present study the clinical factors having influence on periprosthetic fracture and on the incidence of periprosthetic fracture in Finland were evaluated.

The most important conclusions to be drawn are:

1. Hip fracture as a primary diagnosis was found to increase the risk for subsequent periprosthetic fracture

2. Both age under 70 years and wedge-shaped prosthesis type increased the risk of late PF among hip fracture patients.

3. The mortality and the complication rate were found to be higher after rearthroplasty of PF than after rearthroplasty of aseptic loose hip prosthesis

4. There was no association between the incidence of PF and the type of prosthesis used for hip osteoarthritis patients. Male gender showed a tendency towards increased risk of periprosthetic fracture.

11 SUMMARY

Quite a lot is known today about the risk factors for hip fracture. Hip protectors and the medical treatment of osteoporosis are discussed as current prevention methods. It has been estimated that the total number of hip fractures will rise to 19,000 per year in Finland by 2030 while in 2003 it was 7,411 for over 50-year-old population. A large part of hip fractures is treated by arthroplasty. At the same time the number of primary and revision-operated total hip arthroplasties is growing. Thus, the number of complications including periprosthetic hip fractures is increasing.

Periprosthetic fracture can be treated conservatively or by many kinds of fixation methods or in rearthroplasty surgery. We aimed to study the risk factors of serious periprosthetic fractures treated by revision hip arthroplasty. As periprosthetic fracture is a rare complication and the patient population was heterogeneous, the study methods had to be carefully considered. We used three kinds of methods: follow-up , register-based and case-control studies. The studies were conducted during years 1995-2004 for patients operated during the years 1990-2003. The register-based study included all primary arthroplasties for hip osteoarthritis patients in Finland operated on during the years 1990-1999. Other studies concerned patients operated on in Pirkanmaa Hospital District.

Our findings suggest that hip fracture as a primary diagnosis before hip arthroplasty is a risk factor for subsequent periprosthetic fracture. This is a new finding. The wedge shape of the femoral component of the Exeter prosthesis seemed to carry an extra risk. Age under 70 years was also found to be a risk factor for hip fracture patients. However, for hip osteoarthritis patients, the prosthesis type seemed to have no effect on the risk of periprosthetic fracture.

The mortality and the complication rate were found to be higher after rearthroplasty of PF than after rearthroplasty of aseptic loose hip prosthesis. The results also confirm that a swift revision can prevent periprosthetic fractures.

The incidence of revision hip arthroplasty of PF was found to decline during the years 1990-1999 although the indications for total hip arthroplasty changed at that time.

Based on these findings it is highly recommended that in addition to total hip prostheses, hemiarthroplasties after hip fracture are also included in a hip arthroplasty register. It would ensure that the complications, such as periprosthetic fracture, could be reliably followed up and reported.

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