Master Thesis In Medicine

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Differences in mortality among hip fracture patients in the Swedish Fracture Register

Master Thesis in Medicine

Author: Lars Söderström

The Sahlgrenska Academy: Programme in Medicine

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Supervisors: Alicja Bojan, MD, PhD & Michael Möller, MD, PhD

Sahlgrenska University Hospital, Department of Orthopaedics

Sahlgrenska Academy, University of Gothenburg

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Abstract

Background

Sweden has one of the highest hip fracture incidence rates in the world. Even though surgical and medical treatment has been improved in the last decades the mortality rate among hip fracture patients still remains high, with a 1-year mortality rate of 25.7% in patients ≥50 years of age in Sweden. Different factors influencing mortality in hip fracture patients have been identified in the literature. This study was conducted in order to analyse a selection of these factors with data available from the Swedish Fracture Register.

Objective

To evaluate the overall mortality rate among hip fracture patients in the Swedish Fracture Register and subsequently analyse factors influencing mortality at 30, 90 and 365 days post-surgery. The factors in question were age, gender, fracture type, implant type and the influence of revision surgery on mortality. An additional 48 hours mortality rate analysis was made in patients treated with cemented hemiarthroplasty to study peri-operative mortality due to possible bone cement implantation syndrome.

Patients and methods

23 030 patients with primary hip fractures between 2012-04-01 – 2016-10-31 were derived from the Swedish Fracture Register. After exclusion 20 919 patients were included in the analysis, 14 289 women and 6 630 men. All statistical analyses were made with univariable logistic regression except the analyses of mortality rate in patients undergone revision surgery which was made with cox regression.

Results

The overall mortality within 30, 90 and 365-days from surgery was 8.1%, 14.7% and 26.2%, respectively. High age significantly increased the mortality rate in all follow-up analyses. Women had a significantly lower mortality rate in all follow-up analyses compared to men. No

significant difference in mortality could be seen between patients with intracapsular fractures compared to extracapsular fractures. Patients treated with cemented hemiarthroplasty, Excision arthroplasty (Girdlestone) and hook pins/screws had a significantly increased mortality rate when individually compared to all other treatments. Cemented hemiarthroplasty had an increased significantly ($p<0.0001$) mortality rate 48 hours after surgery compared to all other treatments OR 3.34. Patients undergone one or more reoperation had a significantly ($p<0.05$) lower mortality rate HR 0.87 compared to all other patients.

Discussion/Conclusion

As expected high age and male gender were factors highly associated with increased mortality. Surprisingly, reoperated patients had lower mortality rate than all other patients. However, this could be due to a selection bias and the results should be interpreted with caution. Patients treated with cemented hemiarthroplasty, Girdlestone and hook pins/screw had a significantly increased mortality compared to all other treatments. In the future, better recognition of patients at risk should be performed pre-operatively in order to lower the still high mortality rate in these patients.

Abbreviations

SUH – Sahlgrenska University Hospital, Gothenburg, Sweden

SFR – Swedish fracture register

THA – Total hip arthroplasty

HA – Hemiarthroplasty

SHS – Sliding hip screw

IMN – Intramedullary nail

BCIS – Bone cement implantation syndrome

RCT – Randomized controlled trial

OR – Odds ratio

HR – Hazard ratio

Background

Introduction

Sweden has one of the highest incidence rates of hip fractures in the world. It is suggested that the reason for this is environmental rather than genetic, but the cause of this variation is unknown (1). Hip fractures are associated with substantial morbidity, mortality and costs (2), with a 1-year mortality rate of 25.7% in Sweden among patients >50 years of age with a hip fracture estimated by the Swedish Association of Local Authorities and Regions (3). Hip fracture patients accounts for almost 25% of the total inpatient care in orthopaedic departments in Sweden where the cost for nursing time and rehabilitation sums up to approximately 1.5 billion SEK every year. Hence, the hip fracture patients are a major cause of inpatient care in the Swedish orthopaedic departments (4).

In the hip fracture patient group women are highly overrepresented in terms of incidence with reported ratios as high as 4:1 comparing women to men (5). The reason for this difference is explained by a higher presence of osteoporosis among women as well as a higher rate of falls in comparison to men. It should also be noted that women live longer and therefore have additional years to incur a hip-fracture (6).

The treatment of hip fractures was out of necessity non-surgical, consisting of bed rest and traction before the introduction of surgical fixation. Non-surgical treatment of hip fractures was abandoned due to high mortality rates, high complication rates and suboptimal fracture healing (7). As quoted by E.M. Evans in 1951 (8): “The evidence in support of the claim for a lowered mortality among patients treated by operation is overwhelming”. Evans reviewed the literature on differences in mortality between surgical and non-surgical treatment during the 1940s and reported mortality rates as high as 39% when treating hip fractures non-surgically.

The first nail implant was introduced by Smith Petersen in 1931. Sven Johansson, senior surgeon at Sahlgrenska University Hospital later modified Petersens idea by cannulating the nail. Johansson also invented a targeting device and used intraoperative radiographs in order to see the position of the guiding pins before inserting the nails. Johanssons surgical technique much resembles the one still used today. However, as later described in this study, this technique is now almost solely used for the non-dislocated intracapsular fractures whereas the dislocated fractures are treated with either hemiarthroplasty (HA), introduced by Charnley in the 1960's (7) or total hip arthroplasty (THA). The sliding hip screw (SHS) and plate was introduced by Ernst Pohl in the 1950s as a treatment for extracapsular fractures and has been the most widely used fracture implant. However, during the last decades the SHS has been challenged after the introduction of the intramedullary nail (IMN) in the mid 1980s (9).

Yet, the mortality rate in the hip fracture patient group remains high. The mortality in the hip fracture patient group is influenced by different factors such as gender, age, implant type and surgical complications. In this report, we were able to analyse the influence of certain factors due to the vast material of 23,030 patients from the Swedish Fracture Register (SFR). We were able to focus on differences in mortality regarding gender, age, implant-type, fracture-type, the use of bone cement in arthroplasties and the influence of revision surgery on mortality.

Epidemiology

According to The Swedish national board of health and welfare there are roughly 18,000 – 20,000 hip fractures annually in Sweden (4). The mean age of incurring a hip fracture has steadily increased in Sweden and was estimated to 83.8 years for women and 82.1 years for men (2009) among hip fracture patients >65 years. Studies have also shown that a trend break in hip fracture incidence has occurred in the mid 90's with a decreasing incidence, mainly among women and the young elderly (10). This decrease is also supported with studies from the United States that show declining incidence in hip fractures for both men and women between 1995-2005 (11). Although, more recent studies have shown that the decrease might have reached a plateau since 2012 in fracture incidence among women (12). Why this reduction has occurred is not entirely well-defined. Different reasons have been proposed: introduction of several new bisphosphonates, calcium and vitamin D supplementation, national fall-preventive arrangements, cohort effects (with a healthier elderly population) and increased awareness of osteoporosis among the public and physicians, among other preventive measures (4-11-12). Meanwhile as this reduction has been observed, Rosengren et al. have projected that the annual hip fracture in Sweden will double from 2002-2050, due to a higher number of elderly in the population in the year 2050 (13). Consequently, the healthcare in Sweden is facing major challenges in the near future.

Hip fractures and surgical treatment

Fracture classification

A hip fracture is defined as a proximal femur fracture, anywhere in-between the femoral head and 5 cm beneath the lesser trochanter (14). The fracture is further divided into intracapsular (femoral head and neck) or extracapsular (trochanteric and subtrochanteric) by whether the fracture is located inside or outside the joint capsule of the proximal femur. This distinction is critical due to the limited blood supply of the femoral head (15). The blood supply to the femoral head predominantly originates from the medial femoral circumflex artery (MFCA). There is also a limited supply from the lateral circumflex artery and the obturator artery (16). As a consequence, within intracapsular fractures the blood supply to the femoral head can easily be impaired, particularly in a dislocated fracture, when injuring the MFCA. These anatomical prerequisites must be taken into account when it comes to the choice of surgery and implant-type, due to the risk for complications of avascular necrosis (AVN) and non-union (17).

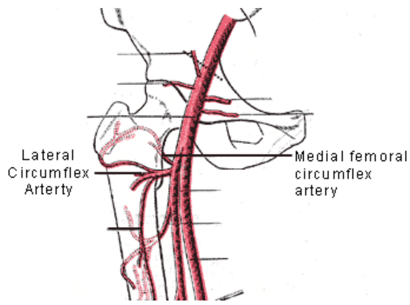


Figure 1. The femoral neck blood supply.

The classification of a hip fracture is generally made by plain radiographs. Based on certain characteristics, such as fracture location, dislocation and the number of fragments (i.e. comminution), the fractures are further subdivided (5).

Müller AO/ASIF Classification

In the collected data from the SFR the AO-classification system is used. The AO/ASIF foundation (Arbeitsgemeinschaft für Osteosynthesefragen/Association for the Study of Internal Fixation) was founded by Swiss surgeons in 1958 and the AO-classification system was presented by Müller et al in 1987 and has been further developed and spread to the US and is currently called the AO/OTA- classification. OTA is the Orthopaedic Trauma Association in North America. To classify a fracture, the location has a corresponding number, whereas the femur has the number 3. Further location is based upon proximal [1], diaphysis [2], distal [3]. The morphology is further subdivided in type [A, B, C], group [1, 2, 3] and subgroup [.1 .2 .3]. In the proximal femur, the types are trochanteric 31-A, femoral neck 31-B and femoral head 31-C (18). Other classification systems than the generic AO/OTA-system is also currently used for the specific types of hip fractures and will also be used in the text.

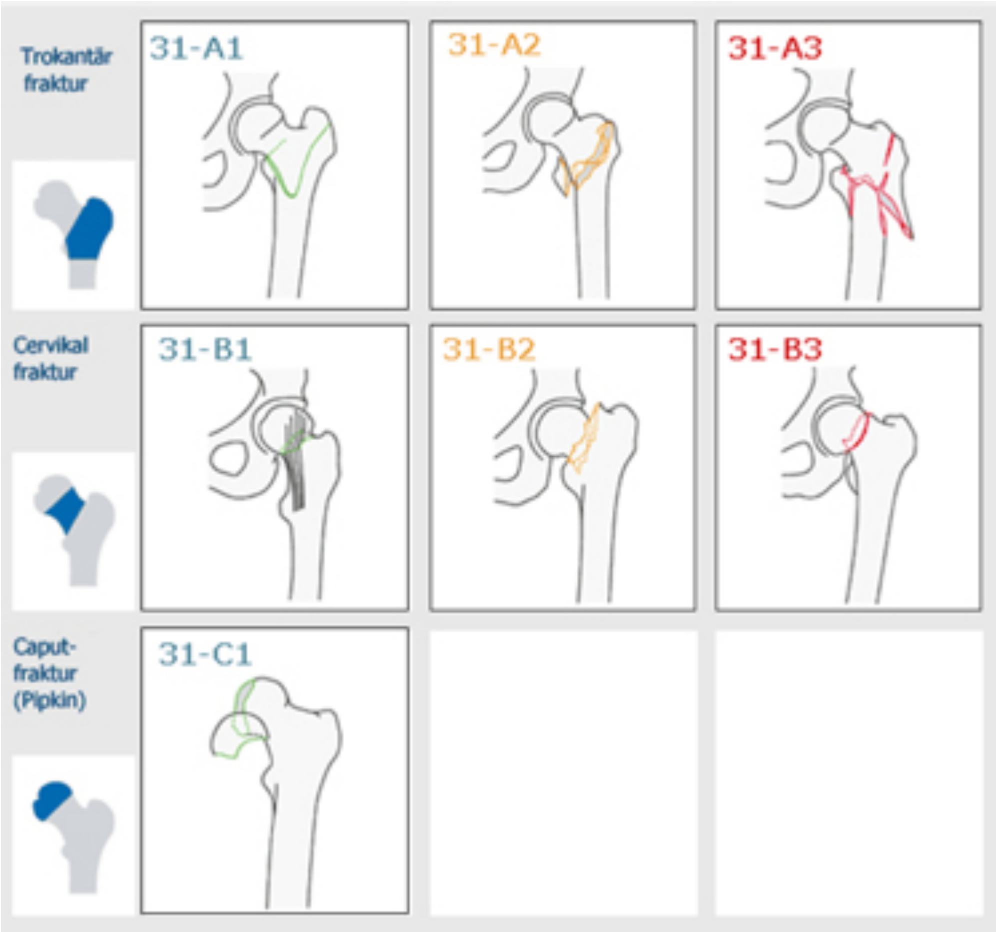


Figure 2. AO/OTA classification of proximal femoral fractures (18). 31-A group representing the trochanteric fractures. 31-A1: simple pertrochanteric fracture, 31-A2: comminute pertrochanteric fracture 31-A3: intertrochanteric fracture. 31-B group representing cervical fractures, 31-B1: Subcapital with slight displacement, 31-B2: transcervical, 31-B3: Subcapital fracture displaced. 31-C femoral head fractures, 31-C1: Pipkin-fracture.

Surgical treatment

The majority of hip fractures are treated surgically with either osteosynthesis, HA or THA (5). Patients that are treated non-surgically have a poor result due to long term immobilization, and is rarely used nowadays. However, avulsion fractures of the trochanter might be treated non-surgically because they are stable and the patient can be mobilised immediately (15). In regard of surgery the hip fracture patient group is relatively homogenous since almost 100% of the patients receive surgery as primary treatment (5).

Intracapsular fractures

Femoral neck classification

Femoral neck fractures can be further classified into subcapital, transcervical and basicervical. However, basicervical fractures (i.e. at the base of the femoral neck) are generally treated as an extracapsular fracture since they rarely impair the blood supply to the femoral head (19) and will therefore not be treated as a separate entity.

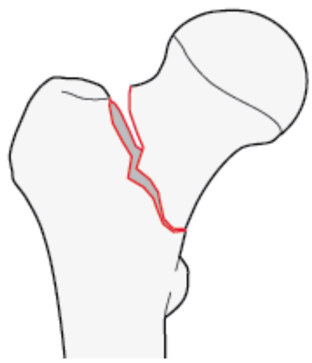


Figure 3. Basicervical femoral neck fracture. AO/OTA 31-B2.1. (18)

As depicted earlier there is no universal classification system of the femoral neck fractures. However, some have reached a more prominent position. R.S. Garden proposed a classification system in 1961, which include four stages. Stage I: Incomplete fracture, Stage II: complete fracture without dislocation, Stage III: complete fracture with limited dislocation, Stage IV: complete fracture with complete dislocation (20). Nonetheless, the Garden system does have some difficulties with inter-observer variation as highlighted by Frandsen et al (21) who described that out of a 100 cases, only 22% were classified identically by eight independent reviewers. Therefore, in clinical practice, only a distinction between dislocated and non-dislocated fractures is generally made in order to decide appropriate treatment (22) .

Femoral neck fracture treatment

Besides the fracture appearance, pre-fracture physical/mental functioning, co-morbidities and age must be taken into account upon the decision of treatment (22). Non-dislocated fractures are generally treated with osteosynthesis: either with two or three cannulated screws or hook pins (14). Dislocated fractures can be treated with either osteosynthesis, HA or THA. Although, in the elderly HA/THA is in favour due to lower failure rate. Rogmark et al. (23) randomized 409 patients >70 years to either osteosynthesis or arthroplasty. Patients treated with osteosynthesis had a 43% failure rate whereas the patients treated with arthroplasty had a 6%

failure rate during the two-year follow up period. Tidermark et al. (24) presented similar results in 2003 after randomising 102 patients (mean age 80 years) with a displaced femoral neck fracture to either osteosynthesis or THA. Where the patients treated with THA had a significantly lower failure rate of 4% compared to 36% in the patients treated with osteosynthesis at the two-year follow-up. The study also showed that the revision surgery rate in THA was significantly lower, 4% versus 44%. Additionally, results considering pain, walking ability and movement were all significantly better in favour for the THA.

The choice between HA or THA is based upon the patient´s health status. Frail, elderly patients with low functional demands and/or mental impairment and a shorter life expectancy are generally treated with HA. The advantages with this treatment include less haemorrhage and shorter operative time. The HA surgery can also be done by a less experienced surgeon (25). Upon deciding on HA as the appropriate implant, two additional issues must be taken under consideration: the use of bone cement and uni- or bipolar hemiarthroplasty. A unipolar HA replaces the femoral head and neck i.e. a single articulation between the HA and the acetabulum. In addition, the bipolar HA has a second articulation between a smaller inner head inside a larger outer head. The theoretical benefits from the bipolar implant is to reduce acetabular erosion since the bearing surface of the pelvis is additionally protected by the outer head (22). The differences in mortality between unipolar and bipolar HA will not be analysed in this study. The use of bone cement in hemiarthroplasty is a matter of controversy. Clear orthopaedic and functional benefits such as less pain, lower reoperation rates and increased mobility has been reported on cemented arthroplasties (26). On the contrary, the use of bone cement is associated with other adverse systemic effects. Bone cement implantation syndrome (BCIS) is a critical complication, characterized by both pulmonary and cardiac effects as systemic drop in blood pressure, hypoxia, pulmonary hypertension, cardiac arrhythmias, potential cardiac death or any combination of these complications (27). The etiology is not entirely clear. Pulmonary fat embolisms due to increased pressure in the femoral canal inserting the cemented stem, seems to be the general explanation for BCIS (28). However, other proposed causes as complement activation, histamine release and anaphylaxis should not be excluded discussing this matter (27).

Girdlestone

The Girdlestone surgical procedure, where the femoral head and neck are resected, is generally seen as a last resort. The treatment is used in patients when arthroplasty has failed or when the arthroplasty is infected and resistant to antibiotics and very seldom as the primary treatment. Other factors including poor quality of soft tissues and bone, multiple comorbidities and poor health are important upon deciding if Girdlestone is an appropriate treatment or not. The aim is to gain pain relief and infection control (29).

Femoral head fracture classification and treatment

These fractures are quite rare and are related to posterior hip dislocation and high energy trauma. They very seldom occur in elderly patients. The Pipkin classification system from 1957 is generally used in clinical practice (30). The classification is divided into four categories. Type I and II are related to fracture location above or below the fovea in the femoral head, where fractures above the fovea do not impair the weight bearing part of the femur. Type III and IV refers to any femoral head fracture with an additional fracture on the femoral neck or the acetabulum. Most femoral head fractures are treated with osteosynthesis, but in certain cases non-surgical treatment or excision of fragments may be an option (31).

Extracapsular fractures

Classification

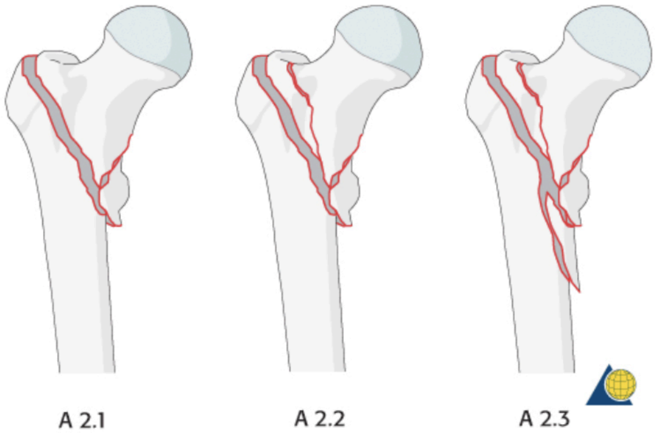


Figure 4. AO/OTA classification of trochanteric fractures. (18)

31-A2: Comminute pertrochanteric fractures

- A2.1: With avulsion of the lesser trochanter
- A2.2 With 1 intermediate fragment
- A2.3. With 2 or more fragments

The extracapsular fractures include trochanteric and subtrochanteric fractures. Among the trochanteric fractures there are many proposed classification systems. The Evans classification (32), later modified by Jensen (30) is one among many. At SUH, the AO/OTA classification is most commonly used. Trochanteric fractures are classified as 31-A. The A1 and A2 groups are described as pertrochanteric fractures, beginning anywhere on the greater trochanter and ending superior or inferior of the lesser trochanter. The A1 group is considered as a simple two-part fracture and the A2 group are multi-fragmented. The A2-group is further subdivided into 2.1, 2.2 and 2.3 indicating the magnitude of the fracture fragmentation with loss of medial support. The A3 group are considered intertrochanteric (i.e. fracture in-between the greater and lesser trochanter) running either proximal-medial to distal-lateral (e.g. reverse oblique) or transverse (18). The A1 group and A2.1 are generally considered as stable while the other trochanteric fractures are categorised as unstable (33).

The definition of the subtrochanteric fracture is determined by the fracture location, from the lesser trochanter and 5 cm distally. These fractures are all unstable due to the strong muscle forces acting on both the proximal and distal fragments which can dislocate the fracture. The subtrochanteric fractures can be challenging to treat (30). Further classification of the subtrochanteric fractures will not be covered in this thesis since these fractures are generally all treated with IMN (34).

Treatment

Trochanteric fractures are generally treated with either SHS or IMN. The A1 and A2.1 fracture types are considered stable and are generally treated with the SHS. The SHS is advantageous in these fractures due to lower costs and good clinical outcomes (33). For the unstable fractures the treatment is still a matter of discussion. Furthermore, the transverse and reverse oblique (AO 31-A3) and subtrochanteric fractures the IMN seems to be the most appropriate treatment. Matre et al. (35) investigated outcomes after treatment with either SHS or IMN in these fractures and found a significantly lower reoperation rate in favour for the IMN. Additionally, minor advantages regarding pain, mobility and quality of life were also associated with the IMN. Although, it should be noted that in 63% of all fractures treated with the SHS an additional trochanteric stabilizing plate was used for further stabilisation, which might have affected the results. For the unstable trochanteric fractures AO 31-A2.2 and A2.3 the treatment still is controversial. In a recent (2017) meta-analysis by Zhu et al. (36) comparing 8 RCTs with 909 patients treated with the SHS or IMN, the authors found some evidence: increased mobility, lower infection rate, shorter hospital stay, less haemorrhage and leg shortening suggesting that the IMN might be superior in these fractures.

Surgical complications

Due to inadequate inclusion of the cognitively impaired patient group and absence of proper follow-up in these patients, the exact incidence of complications following surgical management of a hip fracture is challenging to estimate (37). However, Tsang et al. (38) followed 795 patients for 4 years postoperatively in the United Kingdom and estimated an overall reoperation rate of 6.9% for patients with surgical complications following a hip fracture.

Among the intracapsular fractures treated with osteosynthesis non-union (i.e. failure of union between two bone fragments) and AVN (i.e. necrosis of the femoral head due to insufficient blood supply) are the two dominant complications (39). Acetabular erosion is a painful complication associated with HA since the implants metal head articulates straight with the native cartilage of the acetabulum. This is mainly seen in more physical active patients with a longer life expectancy. Hip dislocation is more frequently occurring in THA compared with HA (40). To estimate the true incidence of BCIS in cemented arthroplasties is a complex task, since there has been no clear definition in the literature. However, Donaldson et al. (41) proposed a grading system in 2009, see table 1. The classification system was later applied by Olsen et al. (27) in 2014, in a retrospective study including 1016 patients with a femoral neck fracture and treated with cemented hemiarthroplasties at SUH. Olsen et al. found a total BCIS incidence of 28%. Whereas the corresponding grades 1, 2, and 3 had an incidence of 21%, 5.1% and 1.7%.

Severity classification of BCIS
▪ Grade 1: moderate hypoxia (SpO2,94%) or hypotension [fall in systolic blood pressure (SBP) >20%].
▪ Grade 2: severe hypoxia (SpO2,88%) or hypotension (fall in SBP >40%) or unexpected loss of consciousness.
▪ Grade 3: cardiovascular collapse requiring CPR

Table 1. Proposed BCIS classification system By Donaldsson et al. (37)

Among the extracapsular fractures, screw cut-out (i.e. the lag screw perforates through the femoral head) is the most common mechanical complication (39). This complication is occurring within both the SHS and the IMN treatments (37) and is seen in 1.1% to 6.3% of the patients treated for extracapsular fractures (39). As depicted by Bojan et al. (42) unstable and complex fracture patterns, positioning of the lag screw and fracture reduction are all factors influencing the likelihood of the cut-out complication. Whereas the positioning of the lag screw and optimizing the fracture reduction is based upon the surgeons performance. Implant breakage, peri-implant fracture, implant detachment and infection (37) are other known surgical complications which will not be further described in this thesis.

Mortality

Numerous studies have described an excess mortality among patients with a hip fracture in comparison to the general population (43–48). The mortality peaks during the first months post-fracture, and then slowly declines (48). However, the excess mortality does persist for several years post-fracture (45-47-49-50). Von Friesendorff et al. (45) have seen an excess mortality for as long as 10 years in women and 20 years in men post-fracture.

Increasing age is positively correlated with excess mortality in hip fracture patients, i.e. the absolute mortality rate rises with increased age. However, in comparison with the general population, the relative risk of death is higher among the younger aged hip fracture patients (43).

Although women are more likely to sustain a hip fracture, male gender can be seen as a major risk factor associated with higher mortality rates compared to women (43–46-48-49-51–53).This difference is poorly understood. Multiple studies has been made but no consensus has been reached (43). Kannegaard et al. (46) stated that male gender is a standalone risk factor for excess mortality when adjusting for fracture type, age and comorbidities.

A slightly higher mortality rate has been seen in extracapsular fractures compared to intracapsular fractures. Although, the results are conflicting. Fox et al. (54) found a marginally higher mortality in trochanteric fractures during hospital stay and at 2 and 6 months' follow-up compared with femoral neck fracture. No difference was seen in the 1-year follow-up. Although, the patients with trochanteric fracture were slightly older (mean value of 1.8 years), there were also more patients with 4 or more comorbidities in the trochanteric fracture group. Karagiannis et al. (55) found no difference in mortality up to 2 years post-fracture, however at the 10-year follow-up trochanteric fractures showed an independently increased mortality rate compared to femoral neck fractures. It should be noted that these two studies had relatively few participants, n=923 respectively n=499. Sund et al. (56) found no difference in mortality regarding hip fracture type during the 1-year follow up in 15.544 patients matched for gender, age, comorbidities and length of in-patient care.

As earlier described, the extracapsular fractures are generally treated with either SHS or IMN. A meta-analysis by Zhang et al. (57) from 2018 comparing 10 RCTs (n=1277) treating unstable trochanteric fractures with either SHS or IMN, found no difference in mortality rates between these two treatments. Also supported in the meta-analysis by Zhu et al. (36) comparing the AO/OTA 31-A2 fractures, no differences in mortality was found between SHS and IMN during the 1 year follow-up.

Regarding the intracapsular fractures, Rogmark et al. (58) found no significant difference in their meta-analysis in 30 days and 1-year mortality rate between arthroplasty (HA and THA) and osteosynthesis. Another meta-analysis by Zi-Sheng et al. (59) comparing HA and THA in dislocated intracapsular fractures, found no significant difference in mortality rate between the treatment groups. Although, it should be noted that no subgroup analysis was performed, the use of cement or uni-/bipolar hemiarthroplasty was not examined in this analysis. In a more recent study (2017) Hansson et al. (40) studied differences in mortality and reoperation rate between THA and HA matching for age, gender, ASA-class and BMI. They still found a significantly higher mortality rate among the patients treated with HA. Hansson et al. suggested that there might be several other confounding factors that explains this difference, for example comorbidities and the wider term known as frailty.

Costain et al. (28) retrospectively studied 25000 patients with either cemented or uncemented HA, where the uncemented HA had a significantly lower 1-day mortality rate, hazard ratio (HR) 0.59. Yet, the cemented HA had a significantly lower mortality rate at the 1-week, 1-month and 1-year follow-up. However, it should be noted that this study was not a RCT and therefore the surgeons' choice of implant might have affected the results. In 1999 Parvizi et al. (60) published their study reviewing 38,488 arthroplasties whereas 23 (0.05%)

intraoperative deaths were found among 23,077 patients treated with cemented arthroplasties. The incidence of intraoperative death was slightly higher in patients treated with cemented HA 0.17% compared to cemented THR 0.05% (no p-values available). Furthermore, the intraoperative death rate was significantly higher ($p<0.05$) among patients with hip fractures 0.18% than those treated for other reasons 0.03%. There were no intraoperative deaths among patients treated with uncemented arthroplasties in this study. However, the studied patient group is small n=23 and therefore the results should be interpreted with caution. As earlier described by Olsen et al. (27), whom found a 28% BCIS incidence in their study, noted an overall perioperative (48 hours post-surgery) mortality of 2.0%. The 30-day mortality rate for patients with no BCIS was 5.2%. Grade 1,2 and 3 had correspondingly 9.3%, 35% and 88% 30-days mortality rate. However, the difference in results between patients with no BCIS and grade 1 BCIS was not significant.

A reoperation of a hip fracture is generally due to a surgical complication, as earlier described. An early report made by Söreide et al. (61) in 1980, found no significant excess mortality in patients undergoing one or more reoperations. The study group was small (n=31) and therefore the statistical power is highly questionable. However, interesting issues with the hypothesis were discussed. Söreide et al. argued that the most ill patients die during or early after the primary surgery. Hence, the patients surviving the primary surgery represent a selection bias. Also, upon deciding if a patient should be admitted for reoperation or not, the surgeon is at risk for another selection bias, only admitting the healthy and fit patients for reoperation. Sipilä et al. (62) found no statistical significant excess mortality in patients primarily treated with hemiarthroplasty or osteosynthesis at 4 months and 1-year post-fracture among re-operated patients. Contradicting results have been proposed by Thakar et al. (63) who found a significant excess mortality among re-operated patients (n=144) in comparison with matched controls, presenting a mean survival of 209 days in the re-operated patient group and

496 days for the matched controls. Hence, it still remains unclear whether patients undergoing one or more reoperations are at risk for excess mortality or if the selection bias favour this patient group, leading to increased survival rate.

Known contributors to excess mortality in hip fracture include high ASA-class (65). ASA-class is a system developed by the American Society of Anaesthesiologists in order to quantify the patients biological reserves at the time for surgery. The classification system is based on 6 different classes, where a high number indicate a lower biological reserve (64). Other known contributors to excess mortality in hip fractures are cognitive impairment (65), two or more comorbidities or independent comorbidities: cardiovascular disease, renal failure and malignancy (66).

Research aims

- Map the 30, 90 and 365 days mortality rate after surgery in patients ≥65 years of age with primary hip fractures in the SFR.
- Analyse the influence on mortality in the following factors: age, gender, fracture-type, implant-type and revision surgery.
- Analyse the perioperative (48 hours) mortality rate in cemented hemiprosthesis in comparison to all other treatments.

Hypothesis

We propose that age, gender, fracture-type, implant-type, revision surgery and the use of bone cement in hemiarthroplasty has an influence on mortality.

Material and methods

Swedish Fracture Register

The SFR is a national quality register which collects information about the patient, cause of fracture, fracture classification, treatment, reoperations and date of death as well as patient reported outcomes. Approximately 75% (2018) of all orthopaedic departments in Sweden are currently using the SFR. Since 2012 hip fractures are registered in the SFR. In Rikshöft (4), a national fracture registry for hip fracture treatment and in the SHAR (67) (Swedish Hip Arthroplasty Register) hip fractures might also be registered and evaluated. However, in this study the SFR has solely been used.

Validation of the SFR

Since this is a part of a larger project, the study includes validating a part of the SFR. The larger project aims to validate all trochanteric fractures treated at SUH in order to estimate reoperation frequency, cause of reoperation and completeness of registration (i.e. are all the reoperations registered in the SFR?). See figure 5 for flowchart of validation process. In SFR there was found a reoperation rate of 4.3% (86 patients). Preliminary data after the validation study was calculated to 6.2% (125 patients). The completeness of SFR registrations of reoperations compared to the registrations in the hospitals surgery planning program was 69.4%.

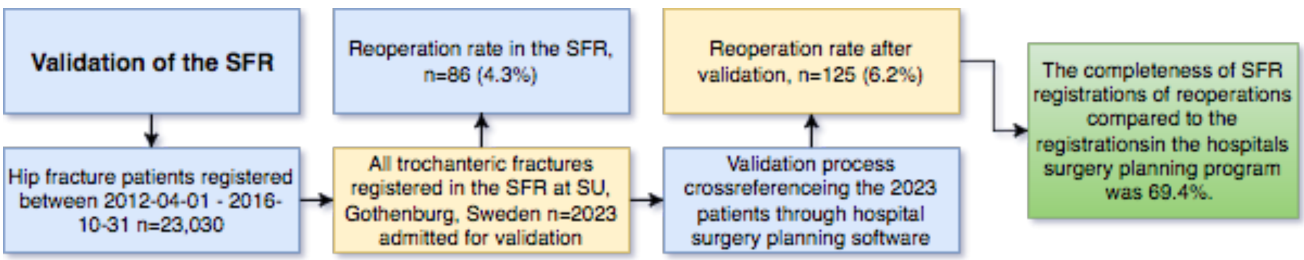


Figure 5. Flowchart for the validation process of the SFR and completeness in reoperation registration.

Ethics

This thesis is part of a larger scientific study in epidemiology, reoperation frequency, patient reported outcome measures and mortality in hip fractures. The data includes personal code numbers and other sensitive variables which have been treated confidentially. The study has been approved by the regional Ethical Review Board in Gothenburg, Sweden. DNR 1111-16.

Data collection procedures

After ethical approval data were extracted from the SFR based on the following selection criteria

- All patients with ICD-10 codes: S72.00;72.01 S72.10;72.11; S72.20;72.21.
- Registered between 2012-04-01 and 2016-10-31.

The data was extracted and delivered 2018-01-19 as Microsoft Excel files. Censoring date was set to 2017-12-19 (i.e. last date of register update on date of death).

Further inclusion criterias:

- Patients ≥ 65 years of age
- Primary hip fracture
- Hip fracture due to trauma

Exclusion criterias:

- Pathological fractures
- >30 days between injury and treatment

ICD10 – DIAGNOSTIC CODES	
S72.00	Femoral neck fracture, closed.
S72.01	Femoral neck fracture, open.
S72.10	Trochanteric fracture, closed.
S72.11	Trochanteric fracture, open.
S72.20	Subtrochanteric fracture, closed.
S72.21	Subtrochanteric fracture, open.

Table 2. ICD 10 – diagnostic codes for hip fractures.

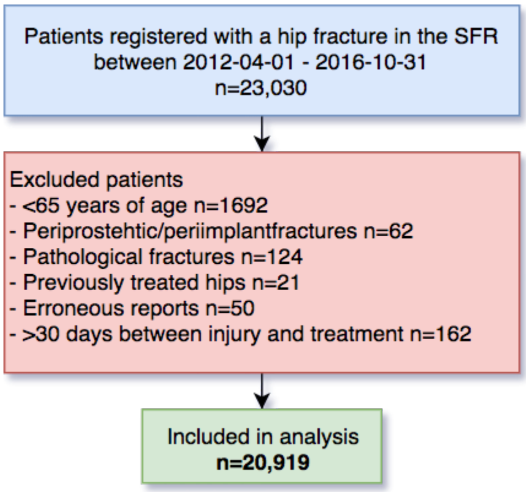


Figure 6. Process of patient data collection and patient exclusion

Variables in The SFR

The variables used in this analysis includes: age at injury, date of injury, date of death, treatment date, ICD-code for injury classification and treatment codes, AO/OTA-classification, cause of injury, fractured side and gender.

Statistical methods

Statistical analysis on 30, 90 and 365 day mortality rate after surgery was made by univariable logistic regression. Additional 48 hours mortality rates after surgery between cemented hemiarthroplasty and all other treatments was made by univariable logistic regression. Adjustment for age at surgery was made by logistic regression. Statistical analysis on differences in mortality between reoperated and non-reoperated patients was made with cox regression. All tests were two-tailed and conducted at 5% significance level. All analyses were performed using SAS® v9.4 (Cary, NC).

Results

20 919 patients were included in the analyses, 14 289 women and 6 630 men. The mean age for sustaining a hip fracture was 82.6 in men and 84.2 in women. The overall mortality within 30, 90 and 365-days from surgery was 8.1%, 14.7% and 26.2% respectively.

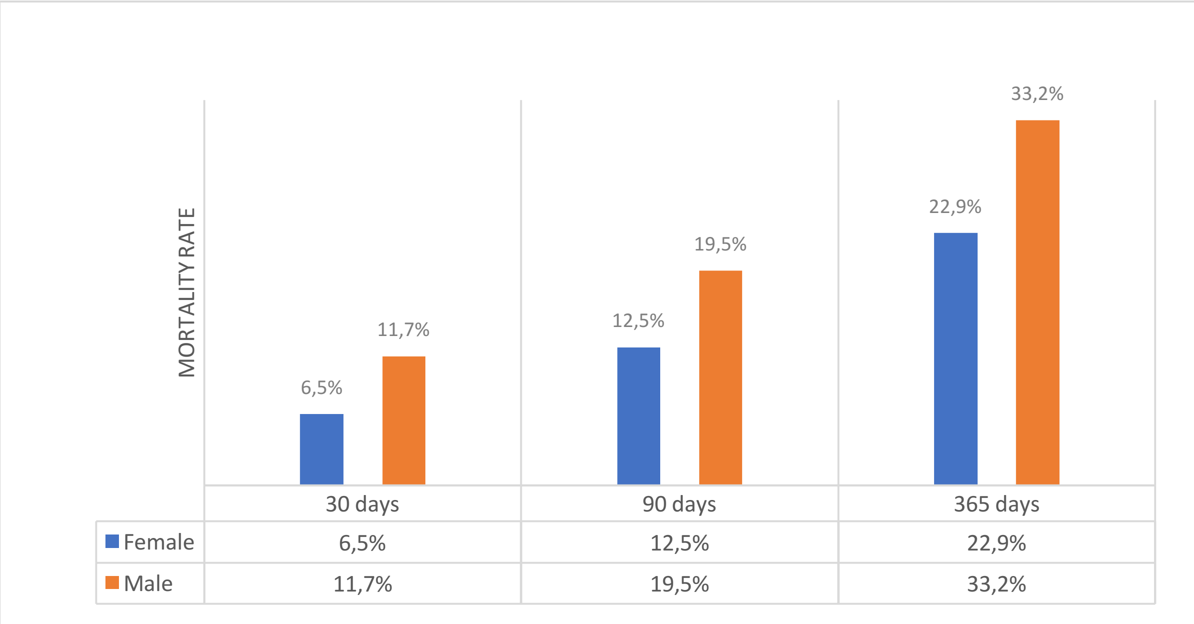


Figure 7.1 Descriptive statistics of 30, 90, 365 days mortality (%) after surgery by gender.

Gender

The women had a significantly lower mortality rate compared to men, see figure 7.1, within 30, 90 and 365 days from surgery ($p<0.0001$) when age was not taken in consideration (unadjusted). Adjusted for age as a contributing factor the women still had a significantly lower mortality rate within 30 days OR 0.44;(95%CI 0.40-0.49 $p<0.0001$), 90 days OR 0.50;(95%CI 0.46-0.50 $p<0.0001$) and 365 days OR 0.51;(95%CI 0.47-0.54 $p<0.0001$) postoperatively when compared with men. Within 365 days from surgery 3 276 (22.9%) women and 2 200 (33.2%) men diseased.

Impact of fracture type on mortality

The patients with extracapsular fractures had a significantly higher mortality rate compared to those with intracapsular ones unadjusted for age within 30 days from surgery OR 1.11;(95%CI 1.00-1.23 $p<0.05$), within 90 days OR 1.18;(95%CI 1.09-1.28 $p<0.0001$) and within 365 days OR 1.14;(95%CI 1.07-1.22 $p<0.0001$), see figure 7.2. When age was taken into account, no significant difference in mortality rates could be seen between extracapsular (mean age at surgery 84,7) and intracapsular fractures (mean age at surgery 83,0).

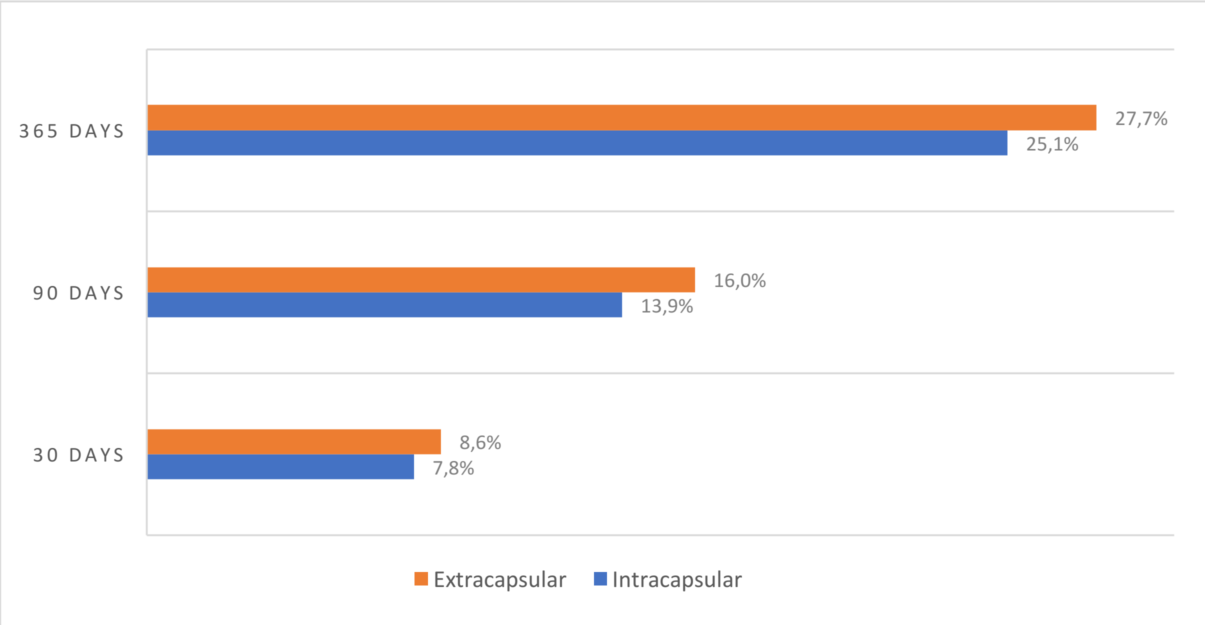
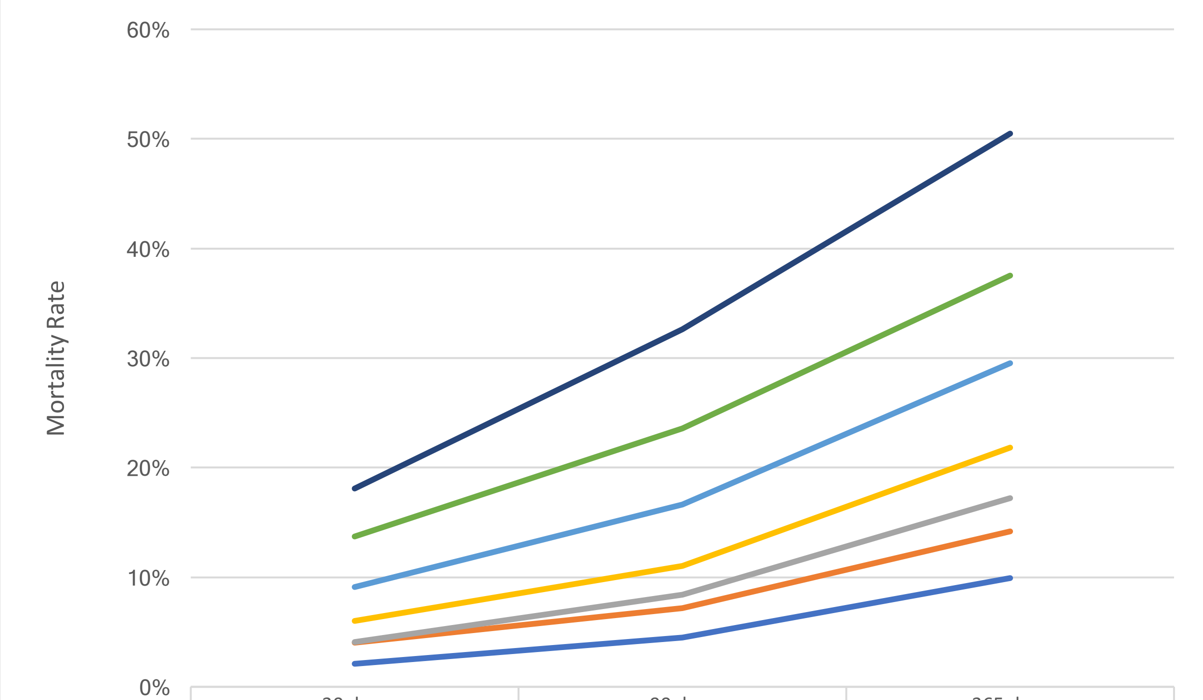


Figure 7.2. Descriptive statistics of mortality (%) within 30, 90 and 365 after surgery by hip fracture classification



	30 days	90 days	365 days
65-<70	2,1%	4,5%	9,9%
70-<75	4,0%	7,2%	14,2%
75-<80	4,1%	8,4%	17,2%
80-<85	6,0%	11,0%	21,8%
85-<90	9,1%	16,6%	29,5%
90-<95	13,7%	23,6%	37,5%
95+	18,1%	32,6%	50,5%

Figure 7.3. Descriptive statistics 30, 90 and 365 days mortality (%) after surgery by age in 5-year intervals.

Age at surgery

When analysing age at surgery in 5-year interval groups, see figure 7.3, mortality significantly increases by OR 1.08;(95%CI 1.07-1.09 $p<0.0001$) for every 5-year interval patient group at 30 days after surgery. Similar results are presented for 90 days OR 1.08;(95%CI 1.08-1.09 $p<0.0001$) and 365 days OR 1.08;(95%CI 1.07-1.08 $p<0.0001$) after surgery. See figure 7.4. for age distribution and frequency of sustained hip fractures for the analysed patient group.

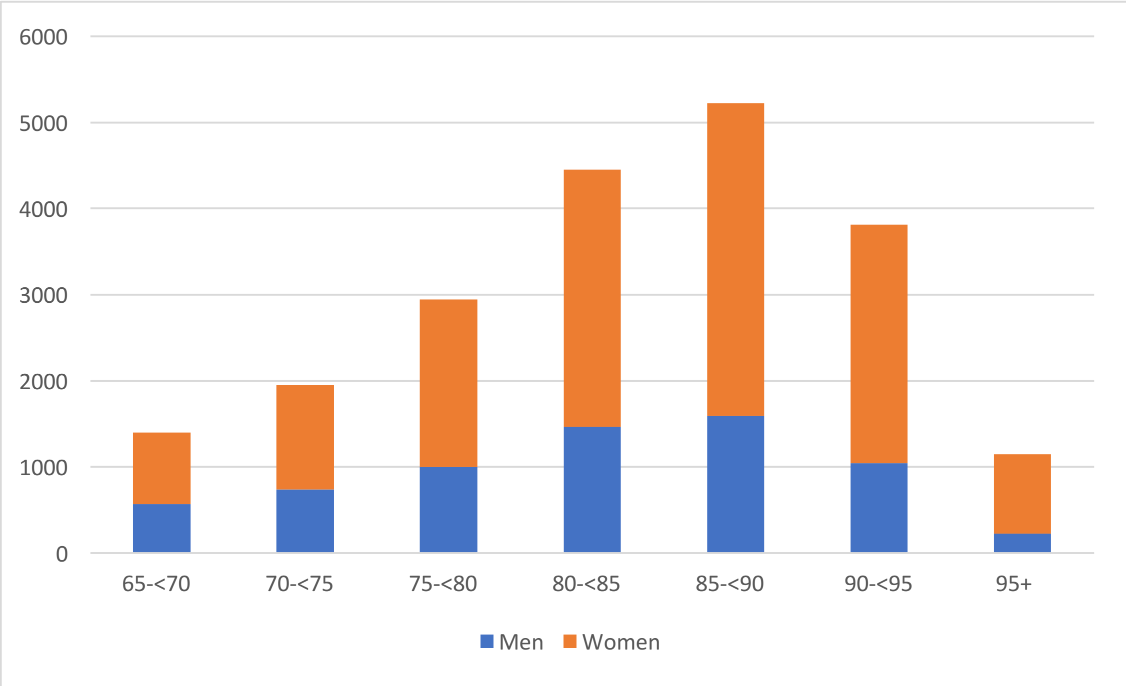


Figure 7.4. Frequency of sustained hip fractures in men and women by age in 5-year intervals.

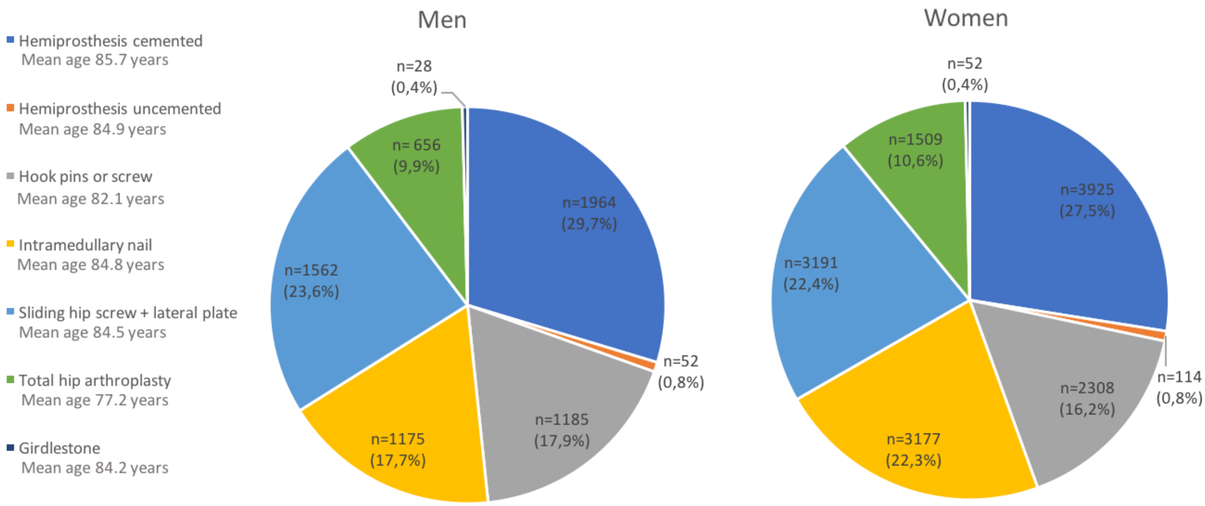
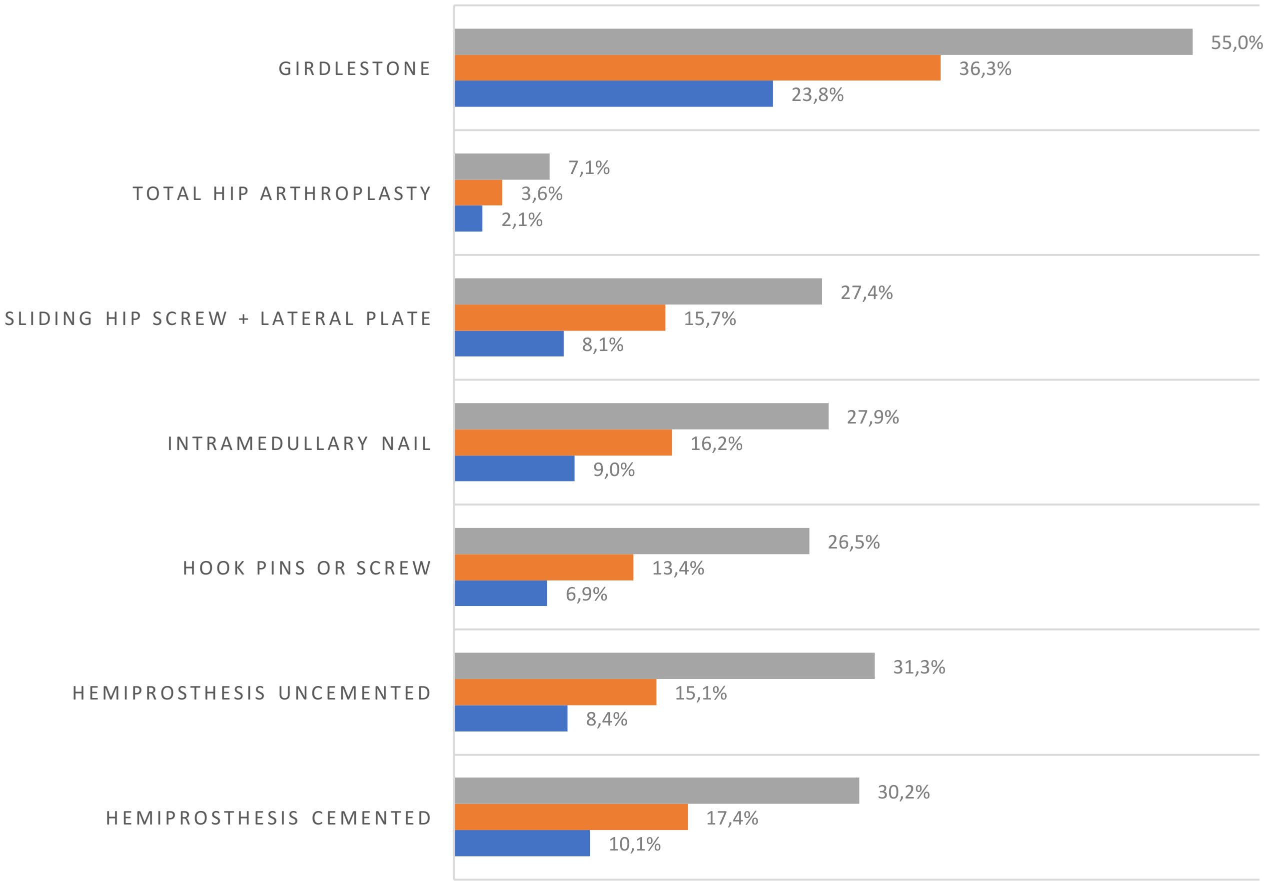


Figure 7.5. Frequency (n) and percentage (%) of implant-type in men and women. Mean age in all treatment groups presented in years.

The cemented HA was the most common treatment in both women and men followed by SHS, see figure 7.5. Due to insufficient treatment data 21 patients were excluded in the implant-type analysis.



	Hemiprosthesis cemented	Hemiprosthesis uncemented	Hook pins or screw	Intramedullary nail	Sliding hip screw + lateral plate	Total hip arthroplasty	Girdlestone
365 days	30,2%	31,3%	26,5%	27,9%	27,4%	7,1%	55,0%
90 days	17,4%	15,1%	13,4%	16,2%	15,7%	3,6%	36,3%
30 days	10,1%	8,4%	6,9%	9,0%	8,1%	2,1%	23,8%

Figure 7.6. Descriptive statistics of 30, 90 and 365 days mortality (%) after surgery by treatment type.

Implant-type

When analysing mortality in relation to implant-type, each implant mortality rate was compared to all other implants mortality rate. The patients who received the cemented HA treatment had a significantly ($p<0.0001$) higher mortality rate, unadjusted for age, across all follow-up analyses, 30 days OR 1.43;(95%CI 1.29-1.59), 90 days OR 1.33;(95%CI 1.22-1.44) and 365 days OR 1.33;(95%CI 1.23-1.42). These patients also had a significantly ($p<0.0005$) higher mortality rate, when adjusting for age across all follow-up analyses, 30 days OR 1.23;(95%CI 1.11-1.37), 90 days OR 1.14;(95%CI 1.04-1.24) and 365 days OR 1.13;(95%CI 1.06-1.21). On the other hand, patients treated with the uncemented HA had no significant increase or decrease in mortality rate at any follow-up analyses. Mortality rate 365 days after surgery adjusted for age was OR1.21;(95%CI 0.86-1.70 p=0.27).

Patients treated with hook pins and/or cannulated screws had a significantly ($p<0.005$) lower mortality rate at 30 and 90 days but not at 365-days from surgery unadjusted for age. However, adjusted for age the hook pins/cannulated screws had a significantly ($p<0.0005$) increased 365 days mortality rate in comparison to all other treatments OR 1.17;(95%CI 1.08-1.28). The 30 and 90 day mortality was not significant.

The patients treated with an IMN had a significantly higher ($p<0.05$) mortality rate unadjusted for age across all follow-up analyses, 30 days OR 1.15;(95%CI 1.02-1.30), 90 days OR 1.16;(95%CI 1.06-1.27) and 365 days OR 1.12;(95%CI 1.04-1.20) within surgery. Although, when adjusting for age no significant difference in mortality could be seen between IMN and all other treatments. Patients treated with SHS had a significantly ($p<0.05$) increased mortality rate when compared to all other treatments and age was not taken into account at 90 days OR 1.11;(95%CI 1.01-1.21) and 365 days OR 1.09;(95%CI 1.01-1.17) from surgery. When adjusted for age no significant difference in mortality could be seen.

The patients in the THA treatment group had the ($p<0.0001$) lowest mortality rate across all follow-up analyses unadjusted for age, 30 days OR 0.22;(95%CI 0.17-0.30), 90 days OR 0.20;(95%CI 0.16-0.25) and 365 days OR 0.19;(95%CI 0.16-0.23) within surgery. Adjusted for age the THA treatment group still had a significantly ($p<0.0001$) lower mortality rate, 30 days OR 0.38;(95%CI 0.28-0.52), 90 days OR 0.33;(95%CI 0.26-0.42) and 365 days OR 0.30;(95%CI 0.26-0.36).

The Girdlestone treatment group had the ($P<0.0001$) highest mortality rate across all follow-up analyses, 30 days OR 3.56;(95%CI 2.12-5.96), 90 days OR 3.32;(95%CI 2.10-5.24) and 365 days OR 3.47;(95%CI 2.23-5.40) within surgery unadjusted for age. When adjusting for age the Girdlestone still had the highest significant ($p<0.0001$) mortality rate, 30 days OR 3.52;(95%CI 2.05-6.03), 90 days (95%CI 2.10-5.52) and 365 days (95%CI 2.33-5.91) within surgery compared to all other treatments.

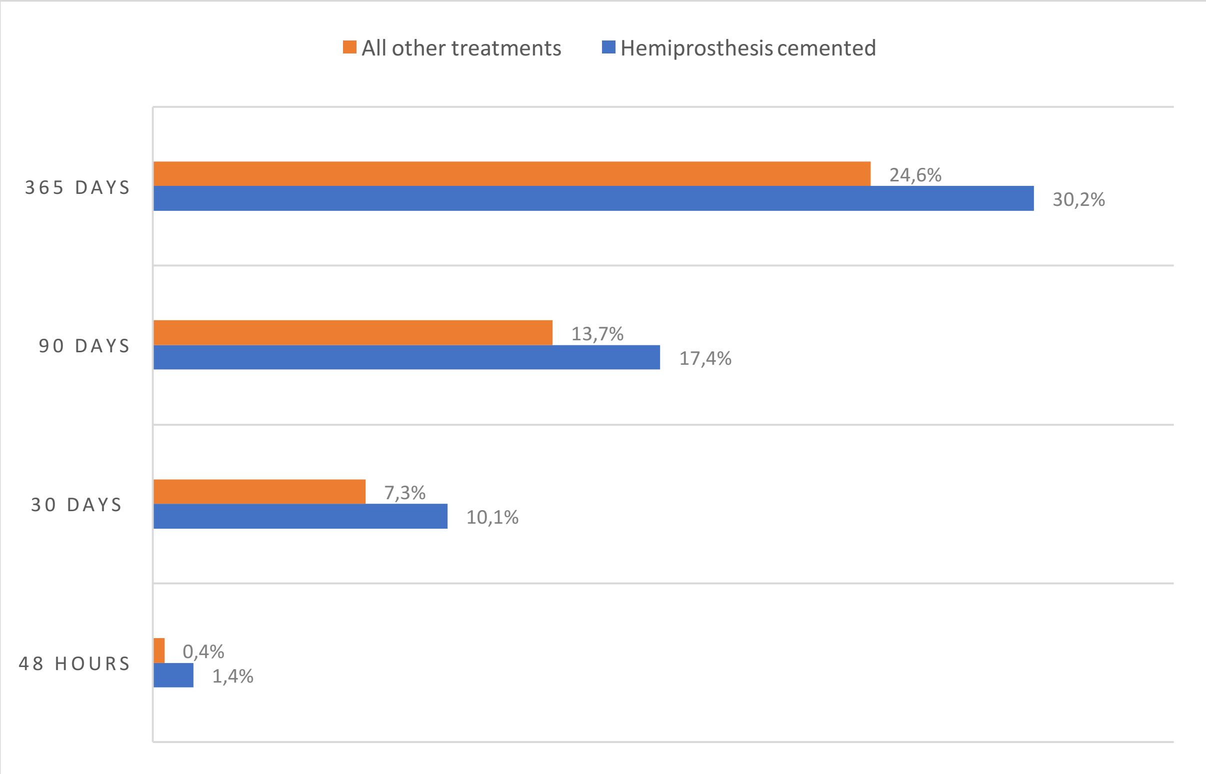


Figure 7.7. Descriptive statistics of 48 hours, 30, 90 and 365 days mortality (%) after surgery for patients treated with cemented hemiprosthesis compared to all other treatments.

As depicted earlier the patients treated with cemented HA had a significantly higher mortality rate within 30, 90 and 365 days after surgery. Additionally, when analysing the 48-hour mortality after surgery, see figure 7.7, the cemented HA had a significantly higher mortality OR3.34;(95%CI 2.41-4.63 $p<0.0001$). When age was taken into account the cemented HA still had a higher mortality rate OR2.88;(95%CI 2.07-4.00 $p<0.0001$) when compared to all other treatments.

Reoperations

627 patients underwent one or more reoperation. The reoperated patients had a significantly ($p<0.005$) lower mortality rate HR 0.80;(95% CI 0.70 – 0.92) when compared to patients with

no reoperation. Adjusted for age reoperated patients still had a significantly ($p<0.05$) lower mortality rate HR 0.87;(95% CI 0.76 – 1.00).

Discussion

This study was made possible due to the vast amount of data from the SFR, analysing differences in mortality after hip fracture surgery in 20 919 patients, in the Swedish population. However, a limitation in this study was that there was no possibility to adjust for other variables influencing mortality as ASA-class, comorbidities and dementia in the collected data.

The overall mortality within 30, 90 and 365 days after surgery was 8.1%, 14.7% and 26.2% respectively. The 365-days mortality, as earlier described, for patients >50 years of age with a hip fracture was estimated to 25.7% by the Swedish Association of Local Authorities and Regions (3). Our findings suggest a somewhat higher mortality rate but one should take into account that this study exclude patients <65 years of age.

Our findings show that women have significantly lower mortality rate compared to men in 30, 90 and 365 days follow-up analyses in patients with a primary hip fracture. These findings are in accordance with earlier studies (43–46-48-49-51–53). As previously described women have a higher incidence of sustaining a hip fracture, although not as high as a 4:1 ratio as reported by Parker et al (5) our data show a ratio of 2.16:1 when comparing women and men in Sweden ≥65 years of age.

When analysing the mortality by fracture-type no significant difference could be seen when age was taken into account. Our findings are in accordance with Sund et al. (56) who found no significant differences in mortality during the 1-year follow up comparing intracapsular and extracapsular fractures. However, Sund et al. matched their patient group for a variety of possible confounding factors as earlier described.

Patients treated with cemented HA do have a significantly higher mortality rate when compared to all other treatments. In these patients, we also analysed the mortality 48 hours after surgery as made by Olsen et al (27), and found a significantly higher mortality rate among patients treated with cemented HA. This difference in mortality might possibly be explained by the occurrence of BCIS in these patients. However, only limited conclusions can be drawn from these results since the data does not tell whether a patient has been affected with BCIS or not. Yet, we intend to analyse which groups who are at risk for developing BCIS in cemented HA treatment in future studies.

Neither the IMN nor the SHS had any significant difference in mortality when age was taken into account and compared to all other treatments. These findings are in accordance with the meta-analysis by Zhang et al. (57) and Zhu et al. (36).

Patients treated with hook pins and/or cannulated screws had a lower mortality rate at 30 and 90 days postoperatively unadjusted for age, these results were not significant when adjusting for age. However, at 365 days postoperatively these patients had a significantly higher mortality rate when age was taken into account, implying that regardless of age these patients has a higher mortality rate when compared to all other treatments 1 year after surgery.

The patients treated with THA had the lowest mortality rate in all the follow-up analysis when compared to all other treatments. However, this is not a randomized controlled trial and therefore there are a lot of confounding variables regarding the treatment groups. First of all, patients treated with THA are healthier, more active and has a longer life expectancy than patients treated with HA. Furthermore, the meta-analysis made by Rogmark et al. (58) and Zi-Sheng et al. (59) found no significant difference in mortality between patients treated with THA and HA. Hansson et al. (40) also suggested that there might be several confounding variables besides age, gender, ASA-class and BMI that influences the mortality rate in these treatment groups. Further research needs to be done on this matter in order to determine if THA really is the superior treatment.

The patients treated with the Girdlestone resection arthroplasty had the highest mortality rate of all the treatments investigated, which is not surprising because the treatment is only given to a patient that is at a very high surgical risk.

Our analyses show that patients that have undergone one or more reoperation has a significantly lower mortality rate, both unadjusted and adjusted for age, when compared to non-reoperated patients. In this study, we chose to analyse the mortality on the reoperated patients from the date from the last reoperation instead of comparing both the reoperated and the non-reoperated groups from the date of the primary surgery in order to eliminate immortality bias (i.e. the reoperated group would be considered immortal during a mean of 215.5 days between surgery and last reoperation). Even so, these results are startling and should be interpreted with caution. First of all, the completeness in registration in the SFR as earlier shown was calculated to 69.4% (ongoing validation study). Yet, our study included 627 (3%) reoperated patients and according to the ongoing validation study the true number of reoperated patients should have been 903 (4.3%). The explanation, as earlier discussed by Söreide et al. (61) could be that the most ill patients die before developing any complications in need for a reoperation and that the surviving patient group represents a selection bias. The reason might also be that only patients fit enough for a reoperation will be reoperated, yet again responsible for another selection bias.

Conclusions

This study is primarily a survey of mortality among hip fracture patients in the SFR. Male gender and high age are contributing factors for increased mortality in the hip fracture patient group. Reoperated patients has a lower mortality rate when compared to non-reoperated patients, although these results should be interpreted with caution. No difference in mortality could be seen between patients with intracapsular and extracapsular fractures when age was taken into account. Patients treated with cemented hemiarthroplasty, and Hook pins/screws had a significantly higher mortality rate when compared to all other treatments. In the future, recognition of the patients at risk, men with high age, should be performed pre-operatively in order to lower the still high mortality rate in the hip fracture patient group.

Populärvetenskaplig sammanfattning

Sverige är ett av de länder i världen med högst incidens av höftfrakturer i sin befolkning. Många olika faktorer som påverkar dödligheten vid en höftfraktur har beskrivits i den vetenskapliga litteraturen. I den här studien undersöker vi ett antal av dessa faktorer i svenska patienter som ådragit sig en höftfraktur. I studien har vi undersökt om ålder, kön, implantattyp, frakturtyp och om patienten har reopererats till följd av någon komplikation har någon betydelse för dödligheten.

I stort sett 100% av alla höftfrakturpatienter opereras med någon typ av implantat. Valet av implantat baseras på särskilda behandlingsalgoritmer som innefattar frakturtyp, patientens biologiska ålder och generella hälsa. De implantat vi valt att inkludera i studien är LIH-spik/skruv, cementerad och ocementerad halvprotes, helprotes, glidskruv, intramedullär spik och slutligen slinkledsplastik (en ovanlig behandling för de allra sjukaste).

Det finns många olika sätt att klassificera höftfrakturer, i denna studie har vi jämfört intrakapsulära mot extrakapsulära frakturer. Kort sagt är indelningen baserad på var på lårbenet frakturen sitter, där de intrakapsulära sitter närmre ledhuvudet och de extrakapsulära längre ned.

Vid en lårbenshalsfraktur som behandlas med en cementerad halvprotes kan det uppstå en allvarlig komplikation, Bone cement implantation syndrome (BCIS). Man tror att denna komplikation uppstår då halvprotesen förs in i märghålan, vilket gör att trycket ökar och fettembolier bildas som kan sprida sig till lungorna. Denna komplikation kan leda till dödlig utgång.

Utgångspunkten för studien är data från det Svenska Frakturregistret (SFR), ett nationellt kvalitetsregister som samlar in information om frakturtyp, skadeorsak och behandling. Vi samlade in alla patienter med höftfraktur mellan 2012-04-01-2016-10-31, vi inkluderade alla patienter som var ≥65 år, med primär höftfraktur, totalt 20 919 patienter. Med statistiska analyser har vi undersökt dödligheten 30, 90 och 365 dagar efter operation med hänsyn till ovan nämnda faktorer som påverkar dödligheten. För att undersöka om patienter som behandlats med cementerad halvprotes dör i högre utsträckning på grund av ett möjligt BCIS undersökte vi dödligheten 48 timmar efter operation jämfört mot alla andra behandlingar.

Analyserna visade att 30, 90 och 365 dagars dödlighet efter operation för alla inkluderade patienter med höftfraktur var 8,1%, 14,7% respektive 26,2%. Som förväntat visade analyserna att män dör i större utsträckning än kvinnor samt att med ökad ålder ökar dödligheten i höftfraktur, i enlighet med tidigare studier. Patienter som behandlats med LIH-spikar/skruvar, cementerad halvprotes samt slinkledsplastik hade alla högre dödlighet när varje implantat-typ testades individuellt mot alla andra behandlingar. Patienter som behandlats med cementerad halvprotes hade högre dödlighet 48 timmar efter operation jämfört mot alla andra behandlingar, 1,4% respektive 0,4% vilket kan bero på förekomsten av BCIS. Vi kan dock inte dra några definitiva slutsatser om detta då analysen inte kan visa att dessa patienter drabbats av BCIS utan endast att de har en högre dödlighet. De som behandlats med helprotes hade lägst dödlighet av alla behandlingar, man bör dock beakta att dessa patienter har en bättre generell hälsa och är mer fysiskt aktiva än de ”sköra” patienter som behandlas med halvprotes. För att välja mellan helprotes eller halvprotes används ovan nämnda behandlingsalgoritmer. Vi kunde inte se någon skillnad i dödlighet mellan patienter med intrakapsulär och extrakapsulär fraktur. Förvånande nog hade de patienter som reopererats till följd av en komplikation lägre mortalitet jämfört med alla andra patienter, detta kan dock bero på urvalsskevhet där de sjukaste patienterna dör innan de utvecklar några komplikationer .

I framtiden rekommenderar vi att man identifierar patienter i riskzonen, dvs äldre, män och patienter som skall få cementerad halvprotes innan operation för att erbjuda dessa patienter extra medicinsk optimering och uppmärksamhet innan operationer.

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Fig 1.

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