Sex effects on short-term complications after hip fracture: a prospective cohort study

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Objectives: To evaluate potential sex differences and other factors associated with complications within 4 months after a hip fracture.

Methods: A total of 1,915 patients ≥65 years (480 men) with hip fracture were consecutively included in a prospective multicenter cohort study. A review of medical records and patient interviews according to a study protocol based on the Standardized Audit of Hip Fractures in Europe (SAHFE, RIKSHÖFT) was performed. Sex differences in comorbidity according to the American Society of Anesthesiologists score and complications 4 months after a hip fracture were registered. Multivariate logistic regression analysis was performed to identify factors related to complications.

Results: Male sex was associated with worse general health according to the American Society of Anesthesiologists classification (P=0.005) and with more comorbidities (P<0.001). Male sex emerged as a risk factor for developing pneumonia (P<0.001), and additionally, 18% of the men suffered from cardiac complications compared with 13% of the females (P=0.018). Female sex was predisposed for urinary tract infections, 30% vs 23% in males (P=0.001). Mortality was higher in the male vs female group, both within 30 days (15% vs 10%, P=0.001) and at 4 months (24% vs 14%, P=0.001). Conditions associated with pneumonia were male sex, pulmonary disease, and cognitive impairment. Cardiac complications were associated with delayed surgery and cardiovascular and pulmonary disease.

Conclusion: Before surgery, men with hip fracture already have a poorer health status and higher comorbidity rate than women, thus resulting in a twofold increased risk of pneumonia. Cognitive dysfunction and pulmonary disease contributed to pneumonia in men. Delayed surgery seems to increase the risk for cardiac complications. It is important to consider the sex perspective early on together with cardiopulmonary comorbidity and cognitive dysfunction to be able to counteract serious complications that may lead to death.

Keywords: hip fracture, male sex, complications, associated factors

Introduction

Patients with hip fracture are commonly encountered in orthopedic and geriatric wards.¹ These patients often suffer from several comorbidities² and therefore require considerable nursing and medical care, in addition to the specific care needed for the hip fracture. Presence of comorbidities increases the risk of complications and frequently causes increased suffering with prolonged hospital stay.³ ⁴ ⁵ ⁶ Few studies have been conducted with large samples to examine sex differences with focus on the effects of specific risk factors for short-term serious complications. It has been found that men more often suffer comorbidities at the time of hip fracture, that they are twice as likely to die after a hip fracture compared to women, and that the cause of death is dominated by infectious diseases such as pneumonia, influenza, and septicemia.⁷ Another study has confirmed that men are more likely to die from...
respiratory disease, malignant neoplasm, and circulatory disease compared to women. However, Endo et al. found that there was no difference across sex when considering the number of comorbidities prior to surgery, but men had a worse physical status when assessed according to the American Society of Anaesthesiologists (ASA) score. In the same study, men had a higher proportion of one or more postoperative complications, with particular focus on pneumonia, arrhythmia, delirium, and pulmonary embolism.

In 2009, we published a study analyzing sex differences in patients with a hip fracture and found that cognitive function in men was strongly associated with a higher risk of loss of walking ability and mortality. In another report from the same population, we analyzed associated factors for mortality in men and women with a hip fracture and presented a prognostic model including age, sex, ASA, and cognitive function.

Considering the serious complications that could occur after hip fracture surgery, especially in men, it would be of great value to better understand factors related to postoperative complications at admission in order to offer optimal care for patients at high risk.

The aim of the present study was to analyze sex differences and other possible factors associated with short-term complications. In contrast to our previous reports from this cohort, this report focuses on perioperative complications and possible associated factors within 4 months after surgery.

**Materials and methods**

All patients admitted with a hip fracture to any of the four university hospitals in Stockholm were consecutively included in a prospective cohort study throughout 2003. The patients were enrolled for 1 year and then followed for 2 years. Patients with pathologic hip fractures, such as metastatic fractures, malign and benign bone cyst, and fracture due to Paget’s disease, and patients younger than 65 years were excluded. The overall aim of the initial study was to describe the population with hip fracture in a geographically defined urban area and to evaluate the effect of cognitive function and sex on functional outcome. This study aims to further evaluate the sex effect on complications within 4 months after surgery. Patients were treated according to the Swedish National Guidelines. The guidelines recommend surgery within 24 hours, and encouraged early mobilization, and restricted time for the routine use of perioperative urinary catheter. Data collection was performed by a trained research nurse at each hospital and was then confirmed by the senior orthopedic consultant responsible for the study. At inclusion, the research nurse made a review of the medical records and carried out a structured interview with each patient according to the study protocol based on the national register RIKSHÖFT-standardized audit of hip fractures in Europe (SAHFE). Data collection was performed at baseline and at 4 months. Proxy respondents were interviewed if the patients were unable to provide reliable answers.

Each patient’s physical and mental status on admission to the hospital were regarded as baseline. The index episode was defined as the patient status during the time period from admission to discharge from the hospital. Patient interviews were carried out during the index episode and at follow-up after 4 months.

The patient’s current residence status was defined as living in own home or in an institution, which would include nursing homes or other staffed facilities, for example. Activities of daily living (ADL) status was recorded according to the Katz ADL Index. The Katz ADL index status is based on an evaluation of the functional dependence or independence of patients in bathing, dressing, going to the toilet, transferring, continence, and feeding. ADL index A indicates independence in all six functions, index B independence in all but one of the six functions. Indexes C–G indicate dependence in bathing and at least one more function. Presence or absence of concomitant diseases (comorbidity) was based on the medical history obtained from the patient, a proxy, and the medical records. Comorbidities were classified as cardiovascular disease, stroke, pulmonary disease, renal disease, diabetes mellitus, rheumatoid arthritis, Parkinson disease, and malignancy. The patient’s smoking status was recorded as “current smoker” or “nonsmoker”. Experienced orthopedic surgeons classified the hip fractures according to the SAHFE protocol. The attending anesthesiologist assessed the patient’s health status using the ASA score.

Cognitive status was assessed during the index period using the Short Portable Mental Status Questionnaire (SPMSQ), which is a 10-item questionnaire. A range of 0–2 correct answers indicates severe cognitive dysfunction, 3–5 moderate dysfunction, 6–7 mild dysfunction, and 8–10 lucid. For the purpose of this study, we dichotomized the answers into two categories: cognitive dysfunction (ie, 0–7 correct answers) or no cognitive dysfunction (8–10 correct answers). In cases where the test was not conducted, patients were classified as having cognitive dysfunction if they had a diagnosis or known history of dementia; otherwise they were recorded as missing. Time to surgery was registered in days from admission to the hospital.
Pressure ulcers were classified as grades I–IV according to the European Ulcer Advisory Panel (EPUAP 1999). The following medical and general complications, as defined in the SAHFE protocol, were used for the purpose of this study: pneumonia, cardiac complications (cardiac failure, arrhythmia, angina), deep venous thrombosis, pulmonary embolism, wound infection (superficial and deep), urinary tract infection (UTI), acute renal failure, gastrointestinal bleeding, myocardial infarction, cerebrovascular lesion, and pressure ulcer.

Complications were identified by collecting information from medical records. Pressure ulcers were recorded on admission, during initial hospital stay, and at the time of discharge. Information on mortality was obtained from each hospital’s discharge register or from a proxy.

Statistical methods
Data were presented as mean ± SD (standard deviation) or as indicated. Categorical and nominal data were summarized as percentages (within sex group) and tested for sex differences with the $\chi^2$ test. The crude association between baseline variables and the most frequent complications is described and presented as odds ratios (ORs), with 95% confidence interval (CI), and $P$-values. Associated variables were entered into logistic regression models using the stepwise selection procedure, one model for each selected complication. All variables in the regression models were tested for interactions. All results are presented as ORs with their respective 95% CIs. All tests were two-sided, with the level of significance set at $P<0.05$. Analyses were performed with IBM SPSS Statistics 19 (IBM Corporation, Armonk, NY, USA).

The study was conducted according to the Helsinki Declaration, and the local ethics committee approved all protocols.

Results
Of the initial 2,134 patients with a history of hip fracture, 179 patients were younger than 65 years and hence excluded from the study. The study sample consisted of 1,955 elderly patients. Of them, 12 patients died before surgery. Interview data were missing at baseline for an additional 28 patients, leaving just 1,915 patients (1,435 women and 480 men) in the final analysis. Baseline demographics, fracture type, and medical conditions are presented by sex in Table 1.

Comorbidity – sex differences at baseline
Mean age was higher in the female population, at 84±6.8 vs 82±7.4 years in men ($P<0.001$). Male sex was associated with a higher percentage ASA 3–4, 69% vs 61% in female ($P=0.002$). Men also had more comorbidities, mean, 1.6 (SD, 1.08) compared to 1.4 (SD, 0.96) in women ($P<0.001$). Cardiovascular disease was found to be 66% among men and 67% among women ($P=0.824$). Significantly more men had a history of stroke (22% men vs 14% women, $P<0.001$), pulmonary disease (20% men vs 15% women, $P=0.002$), Parkinson disease (5% men vs 3% women, $P=0.017$), renal disease (6% men vs 4% women, $P=0.038$), and malignancy (21% men vs 14% women, $P<0.001$). In the male group 14% were suffering from diabetes mellitus vs 11% in the female group ($P=0.097$). Rheumatoid arthritis was found to be 5% among men and 7% among women ($P=0.169$). Fifty-nine percent of males and 58% of females had a cognitive dysfunction, according to the SPMSQ ($P=0.594$) (Table 1).

Complications – sex differences
The overall complication rate was 59% in the male group vs 56% in the female group ($P=0.119$). About 14% of male patients suffered from pneumonia compared to 6% women ($P<0.001$), and 18% of the men had a cardiac complication compared to 13% of the women ($P=0.018$). Female sex predisposed to UTI, 30% vs 23% in males ($P=0.001$). Mortality was higher in the male group when compared with women, both within 30 days (15% vs 10%, respectively, $P=0.001$) and at 4 month follow-up (24% vs 14%, respectively, $P=0.001$) (Table 2).

Associations between baseline variables and complications
Sex, age, ASA, time-to-surgery, cardiovascular or pulmonary disease, and cognitive function emerged as significantly associated with complications. In the crude analysis, cognitive dysfunction had a negative association with pressure ulcer, cardiac complication, and pneumonia (Table 3). A history of stroke did not correlate with any of the complications. A similar lack of correlation was found for a history of diabetes mellitus.

Patients with pneumonia had 2.6 times higher odds (OR: 2.6, 95% CI: 1.7–3.9, $P<0.001$) and patients with cardiac complications 3.9 higher odds (OR: 3.9, 95% CI: 2.9–5.4, $P<0.001$) of increased 30-day mortality. At 4 months, the mortality was still 2.2 times more likely in patients with pneumonia (OR: 2.2, 95% CI: 1.5–3.2, $P<0.001$) and 2.5 times more likely in patients with cardiac complication (OR: 2.5, 95% CI: 1.8–3.3, $P<0.001$) (Table 3).

The effect of the status at baseline on the four most common complications was analyzed in a stepwise logistic regression
analysis (Table 4). Female sex posed a higher risk for UTI, whereas male sex was associated with a higher risk of pneumonia. Cardiac complications did not associate with sex. Cognitive dysfunction, present pulmonary disease, and male sex were the strongest factors related to the development of pneumonia. Surgical delay was associated with cardiac complications and increased incidence of developing pressure ulcer.

### Discussion

In this study, we confirm that before surgery, men with hip fracture already have a poorer health status and higher comorbidity rates than do women, resulting in a twofold increased risk of pneumonia and also an increased risk of cardiac complications.

Cognitive dysfunction increased the risk of any kind of complication and was, together with present pulmonary disease, a dominating factor related to pneumonia in men. Delayed surgery seems to increase the risk for cardiac complications and should be avoided if possible. It is important to consider the sex perspective early on together with cardiopulmonary comorbidity and cognitive dysfunction to be able to counteract serious complications that may lead to death.

The relatively high complication rate compared to other similar studies may be explained by our approach of including all patients admitted for a hip fracture; in other words, that we also included patients with cognitive dysfunction. Cognitive dysfunction is known to be associated with a negative outcome after a hip fracture. The SPMSQ 10-item questionnaire has been reported to provide relevant information about the cognitive status of patients with hip fractures. We have previously reported the negative impact of severe cognitive dysfunction on mortality. Patients with mild to
Table 2 Complications 0–4 months after a hip fracture in 1,915 patients aged ≥65 years

|                      | Women |      | Men |      | P*   |
|----------------------|-------|------|-----|------|------|
|                      | N     | %    | N   | %    |
| Number of complications |      |      |     |      |      |
| None                 | 613   | 44   | 194 | 42   | 0.119|
| One                  | 500   | 33   | 156 | 33   | 0.7  |
| Two or more          | 290   | 21   | 118 | 25   |      |
| Type of complication  |      |      |     |      |      |
| Pressure ulcer       | 248   | 18   | 96  | 20   | 0.2  |
| Urinary tract infection | 435   | 30   | 109 | 23   | 0.001|
| Cardiac complication | 191   | 13   | 85  | 18   | 0.018|
| Pneumonia            | 79    | 6    | 65  | 14   | <0.001|
| Wound infection, superficial | 69    | 5    | 16  | 3    | 0.174|
| Wound infection, deep | 24    | 2    | 9   | 2    | 0.768|
| Acute renal failure  | 32    | 2    | 10  | 2    | 0.416|
| Gastrointestinal bleeding | 27    | 2    | 9   | 2    | 0.993|
| Myocardial infarction | 49    | 3    | 18  | 4    | 0.729|
| Cerebrovascular lesion | 27    | 2    | 11  | 2    | 0.577|
| Pulmonary embolism   | 14    | 1    | 5   | 1    | 0.899|
| Deep venous thrombosis | 17    | 1    | 4   | 1    | 0.899|
| Mortality            |       |      |     |      |      |
| Mortality, 30 days   | 136   | 10   | 74  | 15   | <0.001|
| Mortality, 0–4 months | 207   | 14   | 116 | 24   | <0.001|

Notes: *All P-values chi-square tests. Women vs men. *Pressure ulcers grade I–IV developed during hospital stay.

Table 3 Crude effect of preoperative variables on pressure ulcer, cardiac complication, and pneumonia

| Binary variable                                      | Pressure ulcer | Cardiac complication | Pneumonia |
|------------------------------------------------------|---------------|----------------------|-----------|
|                                                      | OR (95% CI)   | OR (95% CI)          | OR (95% CI) |
| Baseline                                             | P             | P                    | P         |
| Sex, male vs female                                 | 1.2 (0.9–1.6) | 1.4 (1.1–1.9)        | 2.7 (1.9–3.8) |
|                                                | 0.2           | 0.016                | <0.001    |
| Age, 85–103 vs 65–84                                 | 1.4 (1.1–1.8) | 1.3 (1.0–1.6)        | 1.2 (0.8–1.7) |
|                                                | 0.003*        | 0.06                 | 0.3       |
| Residence, institutional vs own home                 | 1.4 (1.1–1.8) | 0.8 (0.6–1.6)        | 1.2 (0.8–1.8) |
|                                                | 0.012         | 0.3                  | 0.3       |
| ADL, assisted vs independent                          | 1.6 (1.2–2.0) | 0.9 (0.7–1.2)        | 1.4 (0.9–2.0) |
| (Katz A–B vs C–G)                                    | 0.001*        | 0.5                  | 0.09      |
| Fracture type, extracapsular vs intracapsular        | 1.2 (1.0–1.5) | 0.9 (0.7–1.1)        | 1.1 (0.8–1.5) |
|                                                | 0.1           | 0.3                  | 0.7       |
| ASA classification, 3–4 vs 1–2                        | 1.4 (1.1–1.8) | 2.2 (1.6–3.0)        | <0.001    |
|                                                | 0.013         | 0.001                | <0.001    |
| Time to surgery, 0–1 day                             | 1.6 (1.3–2.1) | 1.7 (1.3–2.3)        | 1.5 (1.0–2.1) |
| vs 2 or more days                                   | <0.001*       | <0.001               | 0.045     |
| Presence vs absence of specific concomitant disease |               |                      |           |
| Cardiovascular disease                               | 1.1 (0.9–1.4) | 2.6 (1.9–3.5)        | <0.001*   |
|                                                | 0.42          | 0.001                | 1.1 (0.8–1.6) |
| Stroke                                              | 1.0 (0.8–1.4) | 1.1 (0.8–1.5)        | 1.1 (0.7–1.7) |
|                                                | 0.9           | 0.7                  | 0.7       |
| Pulmonary disease                                    | 1.5 (1.1–2.0) | 2.1 (1.5–2.8)        | 2.7 (1.9–3.9) |
|                                                | 0.006*        | <0.001               | <0.001    |
| Renal disease                                       | 1.2 (0.7–2.0) | 1.5 (0.9–2.6)        | 1.2 (0.5–2.7) |
|                                                | 0.6           | 0.6                  | 0.6       |
| Diabetes                                            | 0.8 (0.6–1.2) | 1.2 (0.8–1.8)        | 1.1 (0.6–1.7) |
|                                                | 0.4           | 0.3                  | 0.9       |
| Rheumatoid arthritis                                | 0.8 (0.5–1.3) | 1.2 (0.7–2.0)        | 1.1 (0.6–2.1) |
|                                                | 0.3           | 0.4                  | 0.8       |
| Parkinson’s disease                                 | 1.4 (0.8–2.6) | 0.8 (0.4–1.7)        | 1.9 (0.9–4.2) |
|                                                | 0.3           | 0.5                  | 0.08      |
| Malignancy                                          | 1.3 (1.0–1.8) | 1.3 (1.0–1.9)        | 1.3 (0.8–2.0) |
|                                                | 0.065         | 0.08                 | 0.3       |
| Cognitive function, mild vs normal*                 | 1.5 (1.2–2.0) | 1.6 (1.2–2.1)        | 2.4 (1.6–3–6) |
|                                                | 0.001         | 0.002*               | <0.001*   |
| Presence of additional complications and mortality  |               |                      |           |
| Number of complications, 2 or more vs 1               | 1.6 (1.2–2.0) | 2.6 (1.8–3.1)        | 3.1 (2.0–4.7) |
|                                                | <0.001        | <0.001               | <0.001    |
| Mortality within 30 days, yes vs no                  | 2.0 (1.5–2.8) | 3.9 (2.9–5.4)        | 2.6 (1.7–3.9) |
|                                                | <0.001        | <0.001               | <0.001    |
| Mortality 0–4 months, yes vs no                      | 1.6 (1.2–2.2) | 2.5 (1.8–3.3)        | 2.2 (1.5–3.2) |
|                                                | <0.001        | <0.001               | <0.001    |

Notes: *All P-values chi-square tests. **Variables still significant after adjusting for associated baseline variables. *According to the Short Portable Mental Status Questionnaire (0–7 vs 8–10). Reference group.

Abbreviations: ASA, American Society of Anesthesiologists; ADL, activities of daily living; CI, confidence interval; OR, odds ratio.
aspect when assessing the patients’ risk for serious complications such as pneumonia or cardiac complications. Despite this knowledge, it seems that the care of these patients needs to be improved, for example, by taking into account male sex as a strong risk factor, considering a more active pre- and postoperative physiotherapeutic treatment, and starting antibiotic treatment sooner. Patients with cardiac disease need to be identified early to be able to consider a more active pre- and postoperative treatment. Under optimum conditions, there is a clear treatment algorithm that includes cardiac evaluation such as adjustment of fluid balance, hemoglobin, and saturation. Assessment by a cardiologist already at the emergency ward should be considered, also including a plan for follow-up during the hospital stay. In certain orthopedic clinics in Sweden, there is now a staff geriatrician, and this has been a valuable contribution to optimize the medical treatment of hip fracture patients.

Somewhat surprising, a previous history of stroke did not correlate with any complication, but identical results have also been reported previously. In the current study, UTI was identified if antibiotics were provided for this condition. UTI was found to be the most common complication, which is in line with several other studies. Still, the present incidence was even higher than reported by others. This may be explained by the fact that we followed all patients up to 4 months after the fracture. Time to surgery was associated with an increased incidence of pressure ulcers, which is consistent with prior findings. Furthermore, cardiac complications were associated with delayed time to surgery. Previous studies have shown the importance of reduced waiting time to surgery to increase the patients possibility to return to independent living, to reduce hospital stay, and possibly decrease complication rate and mortality. The Swedish Board has placed a major focus on this issue and demands an annual account of the number of patients with hip fracture who have had surgery within 24 hours. This time limit is also linked to economic compensation, and this could be one way to raise the awareness of the importance of providing a fast track to surgery for patients with hip fracture.

Table 4 Logistic regression models of baseline variables associated with the most frequent complications

|                          | Urinary tract infection | Pressure ulcer | Cardiac complication | Pneumonia |
|--------------------------|-------------------------|----------------|----------------------|-----------|
| **Sex**                  |                         |                |                      |           |
| Female[^a]               |                         |                |                      |           |
| Male                     | 0.7 (0.5–0.9)           | 2.4 (1.7–3.6)  | <0.001               |           |
| **Age**                  |                         |                |                      |           |
| 65–84[^b]                |                         |                |                      |           |
| >85                      | 1.2 (0.0–1.5)           | 1.4 (1.1–1.8)  | 0.008                |           |
| **ADL**                  |                         |                |                      |           |
| Independent[^c] (Katz A–B) |                        |                |                      |           |
| Dependent (Katz C–G)     |                         |                |                      |           |
| **Time-to-surgery**      |                         |                |                      |           |
| 0–1 day[^b]              |                         |                |                      |           |
| 1 days                   | 1.6 (1.2–2.1)           | 1.6 (1.2–2.2)  | 0.001                |           |
| **Cardiovascular disease** |                         |                |                      |           |
| No[^b]                   |                         |                |                      |           |
| Yes                      | 2.2 (1.5–3.0)           | <0.001         |                      |           |
| **Pulmonary disease**    |                         |                |                      |           |
| No[^b]                   |                         |                |                      |           |
| Yes                      | 1.6 (1.2–2.2)           | 2.0 (1.4–2.8)  | <0.001               | 2.8 (1.8–4.2) | <0.001 |
| **Cognitive function**   |                         |                |                      |           |
| Normal (SPMSQ[^c] 8–10) |                         |                |                      |           |
| Dysfunction (SPMSQ 0–7)  | 1.5 (1.1–2.0)           | 2.5 (1.6–3.8)  | <0.001               |           |

Notes: *The SPMSQ[^c]:Reference variable.

Abbreviations: ADL, activities of daily living; CI, confidence interval; OR, odds ratio; SPMSQ, Short Portable Mental Status Questionnaire.
manageable instrument. In a study evaluating the impact of surgical timing on surgical outcomes, the orthopedic Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity (POSSUM) was used. The study showed a small improvement of the physiological score from admittance to before surgery and that the POSSUM may be used to identify patients with a higher risk for morbidity if surgery was delayed over 24 hours.32

The strengths of this study are the large number of patients as well as the inclusion of patients with cognitive dysfunction. Cognitive dysfunction is often an exclusion criterion in prospective studies of hip fracture patients. The other strengths of the study are the use of validated instruments and protocols, for example, as in our use of the SAFHE, as well as the thorough review of all the charts. These were performed by specially trained research nurses who also interviewed all the patients. There are several limitations of the study. The study did not include current medications, laboratory parameters, or secondary causes of osteoporosis that could have further contributed to the assessment of the patients’ risk of mortality. A possible limitation was the missing data which, however, only comprised 1.4% of the patients and therefore is unlikely to affect the outcome.

Conclusion
Before surgery, men with hip fracture already have a poorer health status and higher comorbidity rate than women, resulting in a twofold increased risk of pneumonia and also an increased risk of cardiac complications. Cognitive dysfunction and present pulmonary disease were related to pneumonia in men. Delayed surgery seems to increase the risk for cardiac complications. It is important to consider the sex perspective early on together with cardiopulmonary comorbidity and cognitive dysfunction to be able to counteract serious complications that may lead to death.

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