Early mortality and morbidity after total hip arthroplasty in patients with femoral neck fracture

A nationwide study of 24,699 cases and 118,518 matched controls

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Submitted 2016-03-10. Accepted 2016-07-13.

Background and purpose — Early postoperative mortality is relatively high after total hip arthroplasty (THA) that has been performed due to femoral neck fracture. However, this has rarely been investigated after adjustment for medical comorbidity and comparison with the mortality in an age-matched population. We therefore assessed early mortality in hip fracture patients treated with a THA, in the setting of a nationwide matched cohort study.

Patients and methods — 24,699 patients who underwent THA due to a femoral neck fracture between 1992 and 2012 were matched with 118,518 controls. Kaplan-Meier survival analysis was used to calculate cumulative unadjusted survival, and Cox regression models were fitted to compute hazard ratios (HRs) and 95% confidence intervals (CIs), with adjustment for age, sex, comorbidity, and socioeconomic background.

Results — 90-day survival was 96.3% (95% CI: 96.0–96.5) for THA cases and 98.7% (95% CI: 98.6–98.8) for control individuals, giving an adjusted HR of 2.2 (95% CI: 2.0–2.4) for THA cases compared to control individuals. Comorbidity burden increased in THA cases over time, but the adjusted risk of death within 90 days did not differ statistically significantly between the time periods investigated (1992–1998, 1999–2005, and 2006–2012). A Charlson comorbidity index of 3 or more, an American Society of Anesthesiologists (ASA) grade of 3 and above, male sex, an age of 80 years and above, an income below the first quartile, and a lower level of education were all associated with an increased risk of 90-day mortality.

Interpretation — The adjusted early mortality in femoral neck fracture patients who underwent THA was about double that in a matched control population. Patients with femoral neck fracture but with no substantial comorbidity and an age of less than 80 years appear to have a low risk of early death. Patients older than 80 years and those with a Charlson comorbidity index of more than 2 have a high risk of early death, and such patients would perhaps benefit from treatment strategies other than THA, but this should be investigated further.

Mortality after hip fractures in the elderly is relatively high. Within the first 48 hours after a surgical procedure for this injury, mortality is around 1%—including patients who have had internal fixation (Hossain and Andrew 2012). 1-year mortality after treatment of femoral neck fractures with internal fixation or hip arthroplasty has been estimated to be approximately 20%, with no obvious change over the last 3 decades (Mundi et al. 2014). Early mortality after THA performed in patients with femoral neck fracture appears to be lower than with hemiarthroplasty or internal fixation, presumably due to selection of more frail patients for the latter 2 procedures. After THA, the 30-day mortality has been estimated to be 1.4% and the 90-day mortality to be 3.2% (Jameson et al. 2012, Stafford et al. 2012). The early mortality after THA is thus considerably lower than after hemiarthroplasty, where an in-hospital mortality of 5.7% has been described (Ginsel et al. 2014).

Most studies on mortality after hip arthroplasty for femoral neck fracture have lacked information on medical comorbidities and have not taken into account the background mortality in an age-matched population. The mortality rate in patients with femoral neck fracture is usually compared to an average mortality rate (SMR). Moreover, socioeconomic background variables that are known to have an impact on mortality (Zoller et al. 2012, Dzayee et al. 2013) are usually not considered. A

control group that is comparable to THA patients regarding age, sex, comorbidity, and socioeconomic background is desirable for correct interpretation of mortality data, but such a control group has seldom been used in previous studies (Hunt et al. 2013). Thus, the actual increase in mortality associated with femoral neck fracture treated with THA remains nebulous.

We investigated early mortality and morbidity after THA performed in elderly patients with femoral neck fractures, with adjustment for medical comorbidities and socioeconomic background and using an age-matched population not exposed to THA surgery for comparison. We designed a matched cohort study such that each patient operated with THA for femoral neck fracture was compared with 5 controls from the general population, with matching for age, sex, and place of residence. We stratified the study population into age groups in order to enable comparisons with early mortality in unoperated controls of similar age. The primary endpoint of our analyses was 90-day mortality. Secondary endpoints included 90-day mortality for cardiovascular reasons and the risk of admission to hospital care within 90 days of the index date.

Patients and methods

Study design and sources of data

The study was designed as a nationwide matched cohort study during the period 1992–2012. The cohort of patients with a femoral neck fracture who were treated with THA as a primary or secondary treatment was obtained from the Swedish Hip Arthroplasty Register (SHAR), which has been repeatedly validated (Soderman 2000). Only traumatic non-pathological femoral neck fractures were included.

Each of the cases identified was matched by age (defined as the same year of birth as the corresponding case), sex, and place of residence, with 5 control individuals obtained from Statistics Sweden. Information on medical comorbidities (classified according to the International Classification of Diseases (ICD)-9 and ICD-10) was obtained for both cases and controls from the Swedish National Patient Register, together with admission and discharge dates (Ludvigsson et al. 2011). Diagnoses concerning all individuals were collected for 1 year preceding the index date (the basis for calculating the modified Charlson comorbidity index (CCI; Charlson et al. 1987) and for 90 days after the index date. The ASA classification has been reported in the Swedish Hip Arthroplasty Register (SHAR) since 2008. Causes of death for all individuals were obtained from the Cause of Death Register.

Definitions

Patients who underwent THA for a femoral neck fracture as a primary or secondary treatment were defined as being exposed, whereas controls were not exposed. In patients with bilateral THA, the date of insertion of the first THA was chosen as the index date. The index date for the control individuals was defined as the date of surgery for each corresponding case. Some controls had died or emigrated prior to the index date, since the controls were age-matched by year but not by exact date of birth. These controls were excluded. In the final study cohort, the ratio of cases to controls was therefore 1 to 4.8.

Cardiovascular disease was defined as myocardial infarction, chronic heart failure, peripheral vascular disease, and/or cerebrovascular disease.

Statistics

Expression of continuous data was done using means, medians, and ranges. 95% confidence intervals (CIs) were used to describe estimation uncertainty. Categorical data were cross-tabulated and investigated by chi-square test. Although 90-day mortality was the primary outcome and the number of censored individuals within this time period was very small, survival analyses were used in order to facilitate comparisons with other studies on mortality after THA. Kaplan-Meier survival analysis was used to calculate cumulative unadjusted survival, with death or admission to hospital as the endpoints. Cox regression models were fitted in order to calculate crude and adjusted hazard ratios (HRs) with CI. In order to decide what covariates to include in the multivariable models, directed acyclic graphs of possible causal relationships were used (Shrier and Platt 2008). Model assumptions were investigated by calculating and plotting the correlation coefficient between transformed survival time and the scaled Schoenfeld residuals. The fitted models did not deviate from the assumption of proportional hazards. In addition to unadjusted and adjusted survival analyses, we fitted Aalen additive risk models adjusted for age, gender, CCI, income, and educational level in order to validate the findings derived from Cox regression models. The level of statistical significance was set at $p < 0.05$ in all analyses. The R software package (version 3.0.2) together with the "rms", "Gmisc", and "timereg" packages were used (Harrel 2012).

Characteristics of the study population

The initial database contained 152,173 individuals, but cases younger than 60 and cases older than 99 years were excluded together with their respective controls (n = 8,956). Thus, the final study population consisted of 143,217 individuals with 24,699 cases who had received a THA due to a femoral neck fracture and 118,518 controls matched for age, sex, and place of residence (Figure 1, see Supplementary data). End of follow-up was defined as the date of death or emigration, or December 31, 2012, whichever came first. The median observation time for the entire cohort was 5.3 years (4.6 for THA cases and 5.4 for controls).

There was a higher proportion of females (75%) than males (25%) in the study population, and the majority were between 70 and 79 years old (42% of the population). Most individuals in the study population had no associated comorbidities

Table 1. Baseline demographic information on the study population of 143,217 individuals (arthroplasty cases and controls)

Description of the study population	Controls n	%	THA patients n	%
Sex				
Male	29,827	25	6,259	25
Female	88,691	75	18,440	75
Age				
60–69	21,443	18	4,453	18
70–79	49,985	42	10,304	42
80–89	42,171	36	8,852	36
90–99	4,919	4.2	1,090	4.4
CCI [a]				
0	100,957	85	16,131	65
1–2	14,467	12	6,998	28
> 2	3,094	2.6	1,570	6.4
Income [b]				
1st quarter	31,487	27	6,408	26
2nd quarter	30,658	26	6,828	28
3rd quarter	29,182	25	6,393	26
4th quarter	27,178	23	5,068	21
Education				
None [c]	10,913	9.2	2,242	9.1
9 years	62,262	53	13,426	54
High school	31,621	27	6,556	27
University	13,722	12	2,475	10

[a] CCI: Charlson comorbidity index.
[b] First quarter had the lowest income.
[c] No school education or level of education unknown.

(82%). 15% had a CCI of 1–2, and 3.3% had a CCI of 3 or more. Most of the population (53%) had only up to 9 years of school education, 27% had completed high school, 11% had a university degree, and the remaining 9.2% had less than an elementary school education or an unknown level of education (Table 1).

In the group of THA cases, 4.5% had received a later contralateral THA but contralateral procedures were disregarded in our analyses. Cemented fixation of the THA was performed in the vast majority of hips (94.8%), only 0.8% were operated with uncemented implants, and the remaining hips (4.2%) had hybrid or reversed hybrid fixation (a combination of a cemented cup with an uncemented stem or vice versa). The proportion of individuals with a CCI of 1–2 was considerably higher in the cases (28%) than in the controls (12%), and the proportion of cases with a CCI of more than 2 was also higher in the cases than in the controls (p < 0.001). The proportion of individuals with a personal income above the third quartile was higher in the controls than in the cases (23 vs. 21%, p < 0.001). There was a slightly higher proportion of control individuals with a university degree (12% vs. 10% in the cases, p < 0.001).

Ethics

Ethical approval was granted by the Regional Ethical Review Board in Gothenburg (approval number 2013: 360/13).

Table 2. Crude survival for different time intervals with 95% confidence intervals, for controls and THA patients

	Controls Survival	95% CI	THA patients Survival	95% CI
30-day survival	99.6	99.5–99.6	98.1	97.9–98.3
60-day survival	99.1	99.1–99.2	97.1	96.9–97.3
180-day survival	97.3	97.3–97.4	94.4	94.1–94.7
365-day survival	94.6	94.4–94.7	90.9	90.5–91.2

Results

Early mortality for any reason in arthroplasty patients and controls

Crude survival in THA patients was lower than in control individuals. 90-day survival after the index date was 96.3% (95% CI: 96.0–96.5) for THA cases and 98.7% (95% CI: 98.6–98.8) for control individuals. This was equivalent to a 3.0-fold (95% CI: 2.7–3.2) increase in the crude risk of death within the first 90 days after the index date for THA patients relative to control individuals. Crude survival after 30, 60, 90, 180, and 365 days for THA cases and controls is given in Table 2. Crude survival stratified by age groups is given in Table 3 (see Supplementary data). The adjusted HR for the risk of death within the first 90 days after the index date was 2.2 (95% CI: 2.0–2.4) for THA cases relative to control individuals (Table 4). In this model (with adjustment for age, sex, comorbidities, and socioeconomic background), the most pronounced increase in risk was associated with the presence of a CCI of 3 or more (HR = 8.4, 95% CI: 7.5–9.4). An age of 90 years or more was also associated with a robust increase in the risk of 90-day mortality (HR = 4.8, 95% CI: 4.2–5.5). Higher levels of education were associated with a reduction in risk; individuals with a university degree had the lowest HR for the risk of death within 90 days of the index date (HR = 0.5, 95% CI: 0.4–0.6). Income had smaller effects on the adjusted risk of 90-day mortality.

The unadjusted survival for female THA patients without any comorbidity according to the CCI and an age of 70–79, compared to their appropriate controls, is shown in Figure 2A. For comparison, Figure 2B depicts the unadjusted survival in males aged between 80 and 89 with a CCI of 3 or more, for THA cases and controls. Male sex, advanced age (80–89 years), and high CCI (≥ 3) were associated with a considerably higher early mortality—in both cases and in controls (Figure 2).

The Aalen additive risk models confirmed an increase in the adjusted risk of early mortality for hip fracture patients treated with a THA compared to control individuals (Figure 3, see Supplementary data).

Information on ASA grade was available for 24% of all arthroplasty cases. 11% of patients with information on ASA grade available were graded ASA 1, 53% were graded ASA 2,

Survival (%) – healthy women aged 70–79

A

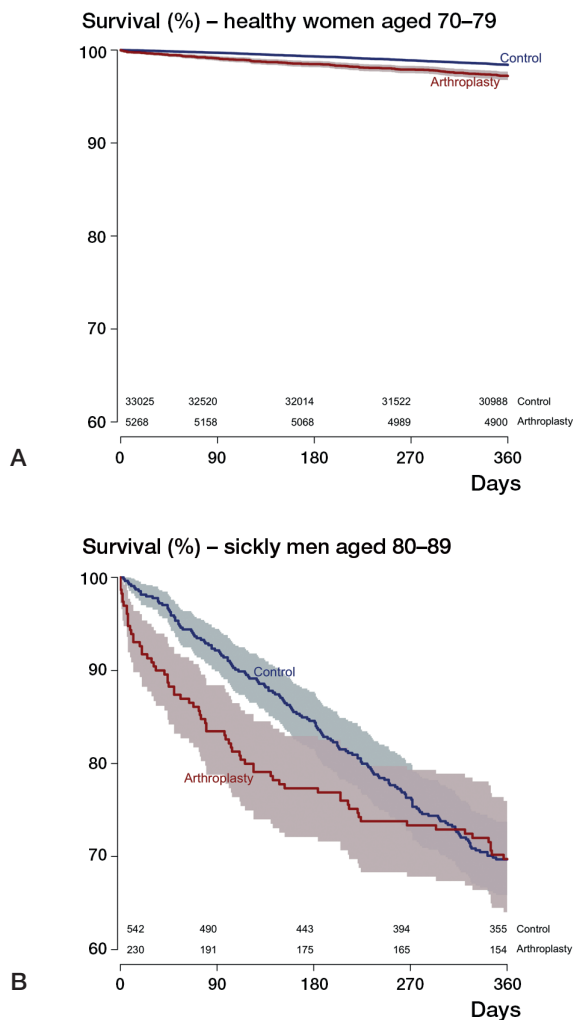## Survival (%) – sickly men aged 80–89

B

Figure 2. Unadjusted first-year survival functions of THA patients and controls. A. Females aged 70–79, CCI = 0. B. Males aged 80–89, CCI = 3 or more. 95% confidence intervals are shaded, but they may appear so narrow as to be indistinguishable. Numbers at risk: A: 5,268 THA patients and 33,025 controls; B: 230 THA patients and 542 controls.

Table 4. Crude and adjusted risk of 90-day mortality with 95% confidence intervals. The adjusted hazard ratio (HR) for each variable was derived from a model adjusting for the other variables included in the model (i.e. gender, age, Charlson comorbidity index (CCI), personal income, and education). By definition, reference groups had an HR of 1

Risk of 90-day mortality	Crude HR	95% CI	Adj. HR	95% CI
Case [a]				
Arthroplasty	2.96	2.72–3.21	2.18	2.00–2.37
Sex [b]				
Female	0.69	0.63–0.75	0.71	0.65–0.78
Age [c]				
60–69	0.53	0.44–0.64	0.58	0.48–0.70
80–89	2.64	2.39–2.90	2.32	2.10–2.56
90–99	6.23	5.47–7.10	4.80	4.16–5.55
CCI [d]				
1–2	4.03	3.69–4.41	3.14	2.87–3.44
> 2	10.4	9.36–11.6	8.41	7.52–9.41
Income [e]				
2nd quarter	1.04	0.94–1.15	1.02	0.92–1.13
3rd quarter	0.88	0.79–0.98	0.95	0.85–1.06
4th quarter	0.57	0.50–0.65	0.84	0.73–0.97
Education [f]				
9 years	0.46	0.42–0.51	0.74	0.66–0.83
High school	0.31	0.27–0.35	0.57	0.49–0.66
University	0.24	0.20–0.29	0.50	0.41–0.61

[a] Reference = controls.
[b] Reference = male.
[c] Reference = 70–79
[d] Reference = 0.
[e] Reference = first quarter (lowest income).
[f] Reference = No school education or level of education unknown.

and the remaining 36% were ASA 3 or above. ASA grade was entered into a multivariable Cox regression model together with the covariates age group, sex, income, and education level, and—by definition—only arthroplasty cases were included in the model. The adjusted risk of death within 90 days from the date of surgery was higher for ASA grade 2 than for grade 1, but not statistically significantly so, with an HR of 2.5 (95% CI: 0.9–7.0) (Table 5). The adjusted risk of death within 90 days was, however, quite dramatically increased for patients with ASA grade 3 or more, with an HR of 9.5 (95% CI: 3.5–25.8) compared to patients with ASA grade 1.

Early mortality in different time periods in arthroplasty patients and controls

In order to detect time trends in the comorbidity burden and in early postoperative mortality in patients with femoral neck fractures who underwent THA, we divided the observation period into thirds. It became apparent that patients with a CCI of 1 or more became more frequent from period to period (Table 6, see Supplementary data). When assessing unadjusted 90-day survival in fracture patients who underwent THA in different time periods, we found only minor changes during the observation period. From 1992 to 1998, 90-day survival was 96.2% (95% CI: 95.7–96.6) in cases, whereas it was 96.7% (95% CI: 96.3–97.1) from 1999 to 2005 and 95.9% (95% CI: 95.4–96.3) from 2006 to 2012. A multivariable Cox regression model was fitted to calculate the risk of death within 90 days during the periods investigated, with adjustment for age, sex, medical comorbidity, income, and education. Compared to the first time period (1992–1998), the adjusted HR for the risk of death within the first 90 days after the index procedure was 0.8 (95% CI: 0.7–1.0) for patients operated 1999–2005, and it was 1.0 (95% CI: 0.8–1.2) for those operated 2006–2012.

Early mortality for cardiovascular reasons in arthroplasty patients and controls

The proportion of individuals who died for cardiovascular reasons within 90 days of the index date was lower in the controls (0.4%) than in the THA cases (0.8%; p < 0.001). The adjusted risk of death for cardiovascular reasons within 90 days was

Table 5. Crude and adjusted risk of 90-day mortality with 95% confidence intervals in the subgroup of arthroplasty patients for whom information on ASA grade was available. The adjusted hazard ratio (HR) for each variable was derived from a model adjusting for the other variables included in the model (i.e. gender, age, Charlson comorbidity index (CCI), personal income, and education). By definition, reference groups had an HR of 1

Risk of 90-day mortality	Crude HR	95% CI	Adj. HR	95% CI
ASA [a]				
2	2.94	1.08–8.03	2.55	0.93–7.04
> 2	12.5	4.66–33.4	9.53	3.52–25.8
Sex [b]				
Female	0.54	0.47–0.61	0.48	0.36–0.62
Age [c]				
60–69	0.82	0.65–1.04	0.79	0.53–1.18
80–89	2.03	1.74–2.37	1.65	1.22–2.24
90–99	4.44	3.57–5.52	3.11	2.00–4.82
Income [d]				
2nd quarter	1.06	0.89–1.26	1.18	0.80–1.75
3rd quarter	0.95	0.79–1.13	0.97	0.66–1.45
4th quarter	0.76	0.62–0.93	1.12	0.73–1.71
Education [e]				
9 years	0.61	0.51–0.73	2.20	0.54–8.94
High school	0.45	0.36–0.56	1.75	0.43–7.20
University	0.37	0.28–0.51	1.38	0.32–5.88

[a] Reference = ASA grade 1.
[b] Reference = male.
[c] Reference = 70–79 years.
[d] Reference = first quarter (lowest income).
[e] Reference = No school education or level of education unknown.

higher in THA patients (HR = 1.6, 95% CI: 1.4–1.9) (Table 7, see Supplementary data). A CCI of 3 or higher was again associated with a great increase in the risk of cardiovascular death within 90 days, with an HR of 4.2 (95% CI: 3.2–5.3) compared to individuals with no comorbidities according to the CCI.

Admissions to hospital care in arthroplasty patients and controls

14% of the entire study population was admitted to hospital care within 90 days of the index date (i.e. the date of insertion of the THA. The index date for the non-surgery control individuals was defined as the date of surgery for each corresponding case). Hospital admission within the first 90 days was more common in THA patients (44%) than in control individuals (7.7%; p < 0.001) (i.e. the hospital admission baseline of the general population at a certain age over a given time period). 1.4% of the study population was admitted to hospital for cardiovascular reasons within 90 days of the index date. A higher proportion of THA patients than control individuals were admitted within 90 days for cardiovascular reasons (1.9% vs. 1.3%; p < 0.001).

After adjustment for age, medical comorbidity, and socioeconomic background, THA cases had a quite dramatically

increased risk of admission to hospital care for any reason within 90 days from the index date compared to control individuals (HR = 6.8, 95% CI: 6.6–7.0), but THA patients only had a slightly higher adjusted risk of admission for cardiovascular reasons (HR = 1.1, 95% CI: 1.0–1.3) (Table 8, see Supplementary data).

Discussion

The main findings on early mortality

We found that hip fracture patients treated with THA had more than twice the (adjusted) mortality of a matched control population within the first 90 days of the index date. The 90-day mortality increased quite dramatically with advancing age and increased burden of medical comorbidities, both in cases and in controls. The risk of early death for cardiovascular reasons was considerably higher in THA patients than in controls.

The main aim of this study was to investigate the effect of age and comorbidity on early postoperative mortality after THA performed because of femoral neck fracture. Traditionally, the hip fracture itself contributes to the increased risk of mortality, but mortality after hip fractures is also interpreted as being the result of a deterioration in general health (i.e. an increase in medical comorbidity and increased frailty). Our findings support this interpretation, with quite a dramatically reduced survival in both patients and controls for those with a CCI of 3 or more. Our findings highlight the importance of including comorbidity in future analyses.

Baseline mortality of course varied depending on age group, with the nonagenarians having a roughly 5-fold increase in adjusted 90-day mortality compared to the prevailing age group of individuals aged 70–79. A report on a small number of nonagenarians who were operated on with hemiarthroplasty for femoral neck fracture described a 1-year mortality of 24% (Sanz-Reig et al. 2012), and a small retrospective study on THA performed for femoral neck fracture in octogenarians found a 30-day mortality of 3% (Kieffer et al. 2014). The functional benefits of THA compared to hemiarthroplasty become evident after several years, and THA appears to be more suitable for those with a longer life expectancy (Hedbeck et al. 2011).

The impact of comorbidity on the risk of early postoperative death

We found that short-term mortality was strongly influenced by the degree of medical comorbidity, with a roughly 8-fold increase in the risk of death within 90 days from the index date in individuals with a CCI of 3 or more, compared to individuals without any comorbidity according to the Charlson classification. Our observation is supported by findings on 4,323 femoral neck fractures that were treated with a THA (Jameson et al. 2012). A high degree of medical comorbidity is therefore strongly associated with a high risk of early postopera-

tive death, and is a warning flag indicating that a treatment other than THA (i.e. hemiarthroplasty or closed reduction and percutaneous internal fixation in suitable fractures) should be considered as an alternative in such patients.

In the present study, the adjusted risk of death for cardiovascular reasons was considerably higher in THA patients than in control individuals, but the adjusted risk of admission to hospital for cardiovascular reasons within 90 days from the index date was only slightly higher for THA cases than for controls. Our findings are in accordance with the results of a study on the risk of 90-day cardiac events in non-fracture patients operated with a THA (Singh et al. 2011).

The comorbidity measurement most commonly used in daily clinical practice is the ASA score, a 6-category physical status evaluation system. We therefore performed an exploratory analysis of the subcohort of THA patients where there was information on ASA grade. Arthroplasty patients with an ASA grade of 3 or more had a 9-fold greater risk of death within 90 days than patients with an ASA grade of 1. It would be interesting to compare the value of different measures of medical comorbidity such as the CCI, ASA, and Elixhauser comorbidity index for prediction of early postoperative mortality in hip fracture patients, but this is beyond the scope of the present work.

Strengths and weaknesses of the study

In order to understand the risk of death after hemi- or total arthroplasty in patients who have had hip fracture, comorbidities, socioeconomic factors, and patient selection must be known. In THA cases in particular, few—if any—studies have adjusted for these important confounders. The present study has yielded data on the largest cohort to be investigated so far, and has enabled a unique comparison between early mortality in patients treated with THA due to femoral neck fracture and mortality in matched controls of similar age taken from the general population. Our results were validated by fitting Aalen additive risk models, which confirmed the increase in the adjusted risk of early mortality in hip fracture patients treated with THA relative to that in control individuals (Figure 3, see Supplementary data).

Since a very small proportion of the THA patients included in our study had received uncemented implants, the estimation uncertainty when adding the fixation mode as a covariate into regression models was large (data not shown), precluding valid conclusions. On the other hand, the risk of excess mortality induced by cementation must be weighted against the increased risk of periprosthetic fracture and subsequent revision surgery that appears to be associated with uncemented fixation (Jameson et al. 2012, Langslet et al. 2014).

A further weakness of our study design is its inability to compare early mortality in femoral neck fracture patients treated with a THA to that in patients treated with a hemiarthroplasty. These patients were not included in our database, but such a study would be very interesting to perform.

Conclusion

We found a more than doubled adjusted risk of death within 90 days after THA operation due to femoral neck fracture compared to matched controls. The adjusted risk of death for cardiovascular reasons, one of the main reasons of death in this population, was also considerably higher in THA patients than in controls. Risk factors for early mortality are higher age, medical comorbidity defined according to the comorbidity index described by Charlson, ASA grade 3 and above, male sex, income below the first quartile, and a lower level of education. Our findings indicate that THA surgery for femoral neck fracture is comparatively safe in patients under the age of 80 and with few or no comorbidities, whereas treatment strategies other than THA might be a better alternative in more frail and older patients, but this should be investigated further.

Supplementary data

Figures 1 and 3, and Tables 3, and 6–8 are available on the website of Acta Orthopaedica (www.actaorthop.org), identification number 10159.

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