A Comprehensive Analysis of the Causes and Predictors of 30-Day Mortality Following Hip Fracture Surgery

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Background: A fracture neck of femur is the leading cause of injury-related mortality in the elderly population. The 30-day mortality figure is a well utilised marker of clinical outcome following a fracture neck of femur. Current studies fail to analyse all patient demographic, biochemical and comorbid parameters associated with increased 30-day mortality. We aimed to assess medical risk factors for mortality, which are easily identifiable on admission for patients presenting with a fractured neck of femur.

Methods: A retrospective review of a prospectively populated database was undertaken to identify all consecutive patients with a fracture neck of femur between October 2008 and March 2011. All factors related to the patient, injury and surgery were identified. The primary outcome of interest was 30-day mortality. Univariate and subsequent multivariate analyses using a backward stepwise likelihood ratio Cox regression model were performed in order to establish all parameters that significantly increased the risk of death.

Results: A total of 1,356 patients were included in the study. The 30-day mortality was 8.7%. The most common causes of death included pneumonia, sepsis and acute myocardial infarction. Multiple regression analysis revealed male gender, increasing age, admission source other than the patient's own home, admission haemoglobin of less than 10 g/dL, a history of myocardial infarction, concomitant chest infection during admission, increasing Charlson comorbidity score and liver disease to be significant predictors of mortality.

Conclusions: This study has elucidated risk factors for mortality using clinical and biochemical information which are easily gathered at the point of hospitalization. These results allow for identification of vulnerable patients who may benefit from a prioritisation of resources.

Keywords: *Hip fractures, Mortality, Risk factors, Epidemiology*

Fragility hip fractures are considered amongst the most prognostically poor consequences of age-related osteoporosis owing to their propensity for complications such as chronic pain, reduced mobility, poor quality of life and mortality. In the year 2000, there were an estimated 1.6 million hip fractures worldwide.[1] With increasing life expectancy and rising numbers of elderly individuals in all geographic populations, the incidence of fragility hip fractures is estimated to reach 6.3 million by the year 2050[2] and will certainly pose a significant health burden worldwide. Death within the first month following fragility hip fracture injuries has been shown to be as high as 13.3% in previous studies.[3] Furthermore, this risk of mortality tends to cluster in the month following surgery but diminishes thereafter.[4]

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Mortality incidence at 30 days has long been recognised as an important care quality indicator for healthcare institutions and has been in longstanding use by the National Hip Fracture Database (NHFD) of the English healthcare system.[5] Identifying modifiable risk factors contributing to mortality can, therefore, play a crucial role in reducing it.[4,6,7] Current literature has identified that age, gender, pre-existing cardiovascular, cerebrovascular or respiratory disease and admission source predispose to mortality.[8-11] A commonly used and validated hip fracture score[12] has also identified several variables contributing to mortality. However, it stratifies mortality risk according to the number of comorbidities rather than severity or type. It also attributes risk of death based on the presence of anaemia to the exclusion of other commonly collected blood parameters. Similarly, other studies have also failed to consider all comorbid and biochemical parameters identifiable at admission in their analysis of risk factors for mortality.[4,6-11] Despite advances in medical and surgical treatments for patients along with the implementation of national evidence-based guidelines for the management of such hip fracture injuries, 30-day mortality rates have shown only a trivial improvement nationally. According to the most recent NHFD reports, the 30-day mortality rates have only improved from 8.1% in 2013 to 8.02% in 2014 and then 7.5% in 2015. It is hence entirely possible that a more thorough and exhaustive analysis of predictors of early mortality may aid in our understanding resulting in improved care.

We, therefore, aimed to perform a comprehensive evaluation of all risk factors for 30-day mortality that are easily obtainable at the point of hospital admission.

METHODS

Hip fracture patient data is prospectively input into the NHFD at our level 1 trauma centre institution by trained personnel. We used this database to identify all consecutive patients admitted over a 3-year period. The clinical data for each patient were then identified and cross referenced with hospital electronic patient records to ensure accuracy.

This project was approved by Leeds General Infirmary Institutional Review Board (Project 668). We collected variables including demographic (age, gender, admission source, and walking ability), biochemical (haemoglobin level, white blood cell count, platelet count, coagulation profile and urea and electrolyte levels) and medical comorbidity data. Patient's preoperative admission source was grouped as one of four categories: patients who were independent in their own home or sheltered accommodation; those who were in a nursing or residential home; those who were already in hospital and had a fall as an inpatient; and those transferred from another hospital. Mobility was categorised into independent walkers; walkers with a single aid (stick or crutch); walkers with two aids (two sticks/crutches or frame); and those who were wheelchair-bound. All patient comorbidity data was identified from hospital records using International Classification of Disease, 10th revision (ICD-10), codes and these were used to calculate the Charlson Comorbidity Index for each patient.[13] The American Society of Anesthesiologists (ASA) grade recorded at the time of surgery was also noted. Other factors analysed included the type of fracture and the time from presentation to hospital to receiving surgical intervention. Fractures were classified as intracapsular undisplaced, intracapsular displaced, intertrochanteric, subtrochanteric or other (if the injury couldn't be distinctively classified). The primary outcome of interest was 30-day mortality following surgery. Causes of death were collected from death certificate entries as well as from coroner's autopsy records and the primary cause of death was used for analysis. Patients that had incomplete datasets or that were managed nonoperatively were excluded from analysis.

All patients were treated on a standardised hip fracture pathway. On presentation, a clinical assessment was performed allowing identification of medical comorbidity data. Blood tests ensured haematological, biochemical and coagulation profiling. A chest radiography and electrocardiography completed the basic cardio-respiratory assessment. Our unit aimed to perform surgery on the day of or the day after presentation of injury in accordance with national health care guidelines.[14]

Following review of imaging by multiple orthopaedic consultants and anaesthetic team at a multidisciplinary trauma meeting, operative management was decided and performed in a theatre with laminar air flow. All operations were performed by or under direct supervision of an orthopaedic consultant. The majority of displaced intracapsular fractures were treated with a cemented hip hemiarthroplasty and undisplaced intracapsular fractures were fixed in situ with screw fixation. Intertrochanteric fractures were fixed with a sliding hip screw, while subtrochanteric fractures were managed with a cephalomedullary device. In accordance with national guidelines, patients that are not cognitively impaired and can mobilise independently or with a single stick were treated with a total hip arthroplasty. After the operation, patients were mobilised fully weight bearing with physiotherapy support.

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Statistical Analysis

To aid clinical interpretation, admission haemoglobin levels and white blood cell counts were categorized as dichotomous variables. Haemoglobin levels were grouped as being less than or more than 10 g/dL—this was done following evidence from a recent study which found haemoglobin < 10 g/dL to be an independent predictor of mortality.[12] White blood cell count levels were grouped

Table 1. Patient Demographics			
Variable	30-Day mortality group	30-Day survivor group	*p*-value
No.	118 (9)	1,238 (91)	
Sex			< 0.001*
Male	49 (42)	320 (26)	
Female	69 (58)	918 (74)	
Age (yr)	86 (65–100)	81 (24–104)	< 0.001*
Fracture type			0.756
Intracapsular-displaced	34 (29)	386 (31)	
Intracapsular-undisplaced	39 (33)	384 (31)	
Intertrochanteric	33 (28)	300 (24)	
Subtrochanteric	7 (6)	96 (8)	
Other	5 (4)	72 (6)	
ASA grade			0.004*
I	13 (11)	106 (9)	
II	24 (20)	336 (27)	
III	53 (45)	647 (52)	
IV	28 (24)	148 (12)	
V	0	1 (0)	
Admission source			< 0.001*
Own home	62 (53)	976 (79)	
Residential/nursing home	42 (36)	202 (16)	
Already inpatient in hospital	5 (4)	29 (2)	
Inpatient from other hospital	1 (1)	3 (0)	
Unknown	8 (7)	28 (0)	
Preinjury walking ability			< 0.001*
Independent	32 (27)	560 (45)	
Single walking stick	26 (22)	238 (19)	
2 Sticks/frame	6 (5)	59 (5)	
Wheelchair/scooter	25 (21)	128 (10)	
Unknown	29 (25)	253 (20)	
Hours to surgery	79 (3–656)	75 (3–774)	0.884

Values are presented as number (%) or mean (range).
ASA: American Society of Anesthesiologists.
*Variables have a *p*-value < 0.15 and were included in the multivariate analysis.

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as being normal (4×10^9/L–12×10^9/L) or abnormal (less than 4×10^9/L or more than 12×10^9/L), in keeping with the widely accepted definition of systemic inflammatory response syndrome.

All factors were initially analysed for risk of mortality with univariate analysis. This assessment involved either using a chi-squared/Fisher exact test for categorical data or the independent t/Mann-Whitney U-test for continuous variables. The impact of these variables were then analysed using a backward stepwise likelihood ratio Cox regression analysis whilst adjusting for covariates. Covariates were included in the multivariate analysis if the univariate analysis resulted in a p-value of < 0.15, in accordance with accepted and published statistical methods.[15] Results were displayed as hazard ratios to aid clinical interpretation. All statistical calculations were performed using IBM SPSS ver. 21 (IBM Co., Armonk, NY, USA).

RESULTS

A total of 1,673 patients were initially identified. After exclusion of 132 duplicates, 44 patients that did not have an operation and 141 incomplete datasets, a total of 1,356 patients were included in the study. The 30-day mortality rate was 8.7% (118/1,356). Of these patients, 89 died during their index admission episode following hip fracture surgery. There were no on-table deaths during surgery. The clinical and demographic data for these patients are summarised in Table 1, grouped by their 30-day mortality status. The commonest cause of death was pneumonia followed by myocardial infarction (MI) (Fig. 1).

On univariate analysis, patients that died within 30 days of surgery were likely to be older, male, functionally less independent and living in a care institution rather that their own home. The mortality group also had a significantly higher incidence of hypertension, chronic obstruc-

tive airways disease (COAD), previous stroke, previous MI, chronic liver disease and chest infection on admission (Table 2). Analysis of admission blood parameters revealed that the mortality group was more likely to have an admission haemoglobin level of less than 10 g/dL, an abnormal white blood cell count, a raised serum potassium level (although the mean potassium level was still within normal range), deranged urea and creatinine levels and a higher international normalized ratio (Table 2).

Following multivariate analysis, the risk factors significant for 30-day mortality included increasing age, male gender, admission source other than patient's own home, admission haemoglobin levels less than 10 g/dL and an increasing Charlson comorbidity score. A history of previous MI, concomitant chest infection during admission and chronic liver disease were the strongest predictors of early mortality with hazard ratios of 2.191, 3.738, and 3.945, respectively (Table 3).

Identification of Risk Factors for Mortality

Table 2 summarises the comorbidities and admission blood parameters that were significant on univariate analysis. Table 3 summarises the outcomes of the multivariate analysis analysing risk factors for 30-day mortality. The causes of death for the 118 patients that died within 30 days of hip fracture surgery are summarised in Fig. 1.

DISCUSSION

Patients who died within 30 days of hip fracture surgery were likely to have admission haemoglobin levels less than 10 g/dL, be older, be male, have a history of previous myocardial infarction and/or have suffered a concomitant chest infection during their index admission. Chronic liver disease was the strongest risk factor for early death within 30 days of surgery. The overall 30-day mortality rate was
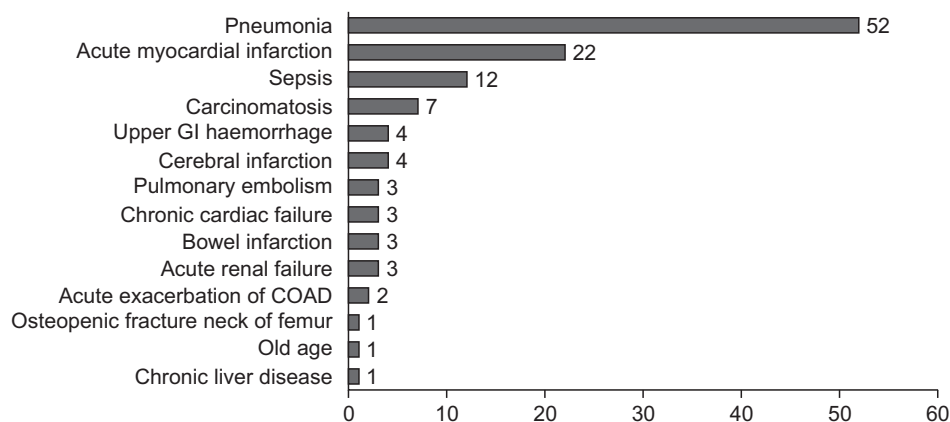
Fig. 1. 30-Day morality causes of death. GI: gastrointestinal, COAD: chronic obstructive airways disease.

Table 2. Univariate Analysis of Risk Factors for 30-Day Mortality

Variable	30-Day mortality group (n = 118)	30-Day survivor group (n = 1,238)	p-value
Comorbidities on admission			
Charlson score	5 (3–9)	4 (0–9)	< 0.001*
Hypertension	13 (11)	30 (2)	< 0.001*
COAD	15 (13)	77 (6)	0.012*
Previous stroke	11 (9)	38 (3)	0.002*
Previous myocardial infarction	12 (10)	27 (22)	< 0.001*
Chest infection during admission	48 (41)	113 (9)	< 0.001*
Chronic heart failure	7 (6)	32 (3)	0.046*
Chronic liver disease	3 (3)	4 (0)	0.017*
Dementia	9 (7)	88 (7)	0.851
Diabetes mellitus	11 (9)	128 (10)	0.874
Neurological disease	2 (2)	26 (2)	1.000
Thyroid disease	5 (4)	71 (6)	0.675
Malignancy	15 (13)	114 (9)	0.248
Alcohol excess	4 (3)	39 (3)	0.785
Urinary tract infection	14 (12)	206 (17)	0.194
Peripheral vascular disease	0	19 (2)	0.400
Cardiovascular disease	7 (6)	25 (2)	0.017*
Connective tissue disorder	0	1 (0)	1.000
Peptic ulcer disease	0	9 (1)	1.000
Chronic kidney disease	33 (28)	87 (7)	< 0.001*
Hemiplegia	2 (2)	15 (1)	0.654
Leukaemia	0	4 (0)	1.000
Blood parameters on admission			
Haemoglobin < 10 g/dL	25 (21)	141 (11)	0.003*
Abnormal white blood cell count	51 (43)	382 (31)	0.007*
Platelet count	119 (93–843)	282 (43–938)	0.435
Sodium	137.8 (123–151)	137.1 (115–151)	0.076*
Potassium	4.5 (2.9–7.0)	4.3 (2.4–7.1)	< 0.001*
Urea	11.5 (2.6–33.8)	8.1 (0.9–35.7)	< 0.001*
Creatinine	139 (58–817)	102 (42–598)	< 0.001*
INR	1.2 (0.9–4.2)	1.1 (0.8–6.3)	0.002*
APTT	30.7 (24–51)	30.5 (19–195)	0.749

Values are presented as mean (range) or number (%).
COAD: chronic obstructive airways disease, INR: international normalized ratio, APTT: activated partial thromboplastin time.
*Variables have a p-value < 0.15 and were included in the multivariate analysis.

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Table 3. Multivariate Analysis of Risk Factors for 30-Day Mortality

Variable	p-value	Hazard ratio	95% Confidence interval
Increasing age	< 0.001	1.057	1.030–1.084
Gender (male)	0.005	1.760	1.185–2.615
Admission source other than home	0.002	1.295	1.102–1.521
Admission hemoglobin < 10 g/dL	0.012	1.765	1.131–2.755
Increasing Charlson comorbidity score	0.004	1.249	1.075–1.452
Previous myocardial infarction	0.014	2.191	1.174–4.087
Chest infection during admission	< 0.001	3.738	2.549–5.480
Chronic liver disease	0.024	3.945	1.203–12.938

8.7% (118/1,356 patients). The commonest causes of death were pneumonia and acute myocardial infarction followed by sepsis from other sources. Mortality risk was reduced in patients if they were admitted from their own home. In our cohort, other comorbidities such as diabetes mellitus, admission electrolyte disturbances and malignancy did not increase the risk of 30-day mortality. While increasing ASA grade did not affect early death after hip fracture surgery, an increasing Charlson score did.

Our 30-day mortality rate of 8.7% is comparable with the figure of 7.5% across England and Wales as reported by the NHFD (this figure is case-mix adjusted for multiple variables including age, ASA grade and source of admission, whereas our cohort is an unselected and unadjusted group).[5] Furthermore, our institutional findings compare favourably to those of other developed nations. A study of over 38,000 Danish patients with hip fractures showed the 30-day mortality to be between 9.2% and 10.9%.[16] Elsewhere in the world, this figure is higher, reaching up to 13.3% worldwide as reported by a recent meta-analysis.[3]

Over 60% of patients that died within 30 days after surgery did so as a result of a chest infection and/or an acute MI in our study. In fact, there were four mortalities within 24 hours of surgery resulting from overwhelming chest infection or an acute myocardial infarction. Such patients already have a higher incidence of pre-existing cardio-respiratory disease and the reduced mobility following a hip fracture is known to increase the risk of pneumonia.[17] A chest infection is an independent risk factor for early readmission after hip fracture surgery and is a common postoperative complication.[6,18] The development of a chest infection following hip fracture surgery in our cohort was one of the strongest predictors of 30-day

death after hip fracture surgery with a hazard ratio of 3.738. These findings are in complete agreement with those of a similar study from Japan showing a fivefold increase in early death in hip fracture patients who develop a postoperative pneumonia.[17]

A hip fracture in itself is an independent risk factor for acute myocardial infarction.[19] A recent prospective study of 200 hip fracture patients undergoing surgery found that the incidence of acute myocardial infarction in the perioperative period may in fact be as high as 35.5%– some of these may be completely asymptomatic.[4,20] Due to the high incidence of perioperative myocardial infarction in this cohort, previous authors have made recommendations to routinely measure postoperative cardiac biochemical markers to reduce cardiac-related deaths.[21]

Increasing age, male gender and presentation with injury from a source other than patients' own home were also statistically significant predictors of early mortality in our cohort. Similar findings have also been demonstrated in cohort studies of hip fracture patients looking at early mortality where increasing age, male gender, dementia and residence in an institution were identified as risk factors.[3,22] Mortality amongst men is generally higher than in women[23] and perhaps multifactorial. Factors such as dementia and increasing age likely reflect the patients' poor physiological reserve in withstanding the stress of surgery and its sequelae. Patients admitted from sources other than their own homes are likely to be care-dependent within nursing or care homes with poor mobility and health. In contrast, patients who live in their own homes are more likely to be independent and active resulting in better postoperative outcomes.[24]

Interestingly, in our cohort, the presence of diabetes mellitus, malignancy and admission electrolyte imbalances

did not significantly increase the risk of 30-day mortality. In our centre, patients with diabetes mellitus are assessed on admission for current anti-hyperglycaemic treatment and prescribed the appropriate inpatient anti-hyperglycaemic treatment immediately. This includes adjustable rate intravenous insulin therapy if the patient usually requires insulin or if the blood glucose readings are unusually high. The patient's glucose levels are monitored regularly and they are placed back on their usual treatment once they are eating and drinking normally after their operation. Acute electrolyte imbalances, if severe enough, are similarly treated in an aggressive manner on admission and the hip fracture surgery is delayed until the patient is deemed anaesthetically fit to undergo the operation. We believe this strict inpatient diabetic and electrolyte control is responsible for the lack of association between diabetes mellitus and 30-day mortality in this cohort.

Increasing ASA grade also did not significantly increase the risk of mortality. However, a higher Charlson score was associated with increased mortality. This likely reflects the fact that the ASA grade may be more subject to higher interobserver variability.[25] The Charlson comorbidity scoring system, however, scores specific diagnoses and is a more robust and reproducible system.[26] Our results are in accordance with a previously pooled analysis of over 500,000 hip fracture patients which also demonstrated that a high admission Charlson score was a preinjury predictor of mortality.[27]

Chronic liver disease was the strongest predictor of 30-day mortality in our cohort with a hazard ratio of 3.98. Although only one patient died directly from chronic liver disease (and, therefore, hepatorenal failure), the statistical analysis concluded that patients with long-term liver disease are at much higher risk of 30-day mortality from any cause. It is known that chronic liver disease also increases the risk of cardiovascular disease. These results are echoed by the findings of a similar Australian study which showed liver disease to be an overwhelmingly strong predictor of inpatient mortality amongst hip fracture patients with a hazard ratio of 4.75.[28] It has previously been suggested that such patients have an increased susceptibility to infection which has also been demonstrated in the elective setting following arthroplasty surgery.[29] The mechanisms behind the increased surgical risk in patients with liver disease are poorly understood; however, dysregulation of metabolic homeostasis and the imbalance of oxidative and antioxidative processes have been implicated as underlying mechanisms leading to morbidity and mortality.[30]

Our study is strengthened by the inclusion of a large number of patients and is unique in that it provides risk factors not previously found in literature for a number of reasons. Previous studies have omitted blood parameters as risk factors. The fact that anaemia is a risk factor for myocardial infarction and that chest infection may result in hyponatremia strengthens our reasons for including blood results as variables in our analysis. We also examined specific comorbidities for association with early mortality as well as Charlson score which is a weighted score based on specific diagnoses and has previously been used in similar patient cohorts. Other studies looking at mortality following hip fractures have previously used comorbidity counts which can be vague and have high interobserver errors.

This study is limited by its retrospective design and, therefore, does not offer the robustness of data offered by prospective data collection. However, we are confident that due to the cross-referencing of data between the NHFD and multiple local hospital records, we obtained an accurate dataset. The NHFD is a prospectively populated audit database with accurate data input by trained trauma coordinators at our centre. In addition, we used multivariate analysis to investigate a large cohort of patients analysing many parameters that can influence mortality–this minimises the confounding effect of covariates.

A specific limitation that we faced was that we did not have complete body mass index data on all patients and, therefore, this was not included in the final analysis. Although this could impact mortality, any such effect is likely to be indirect due to the sequelae of a high body mass index such as diabetes mellitus and ischaemic heart disease. These factors were independently analysed in this study for association with mortality.

In conclusion, increasing age, male gender, admission source and admission haemoglobin of less than 10 g/dL predispose to early mortality. A previous history of myocardial infarction, concomitant chest infection during index admission and chronic liver disease are the strongest predictors of 30-day mortality in hip fracture patients. The Charlson comorbidity score allows indexing of patient comorbidities in a more robust manner than a simple comorbidity count and is also an independent predictor of early mortality. A multidisciplinary approach to the care of these patients should be undertaken from the point of admission with physicians supporting early medical optimisation of cardiorespiratory, metabolic and liver functions.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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