The risk factors for mortality in elderly patients with hip fractures: postoperative one-year results

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ABSTRACT

Introduction: Hip fractures in the elderly are associated with significant mortality. This study aimed to investigate the risk factors for mortality in elderly patients with hip fractures during a one-year period.

Methods: This was a prospective study which included consecutive isolated nonpathologic hip fractures in 74 (52 female, 22 male) patients in a level-1 trauma centre. These patients were 65 years or older and were ambulatory before the fracture. The patients were treated with hemiarthroplasty. The factors investigated were age, gender, nutritional status determined by blood albumin and total lymphocyte count, haemoglobin levels on the day of admission, mobilisation time after surgery, length of hospital stay, comorbidities, American Society of Anaesthesiologists (ASA) rating of operative risk, and the time period between injury and surgery. The patients were followed up for one year after surgery, or until death.

Results: In total, 15 patients died during the one-year period. Patient survival was 94.6 percent at 3 months, 81.1 percent at 6 months and 79.7 percent at 12 months. There were two in-hospital deaths. The factors significantly associated with mortality were patients with more than two comorbidities, an ASA score of III–IV, a blood albumin level of less than 3.5 g/dl and a total lymphocyte count of less than 1500 cells/ml on admission. Hovewer, after the multivariate analysis, an ASA score of III–IV, low total lymphocyte count, female gender and low haemoglobin levels on admission remained the independent and significant risk factors associated with a one-year mortality.

Conclusion: This study confirms that a high ASA score, female gender, a lower lymphocyte count and low haemoglobin levels on admission are significant factors in assessing the one-year mortality in elderly patients with hip fractures. Predicting these risk factors improves the case management.

Keywords: ASA, hip fracture, mortality risk factors

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INTRODUCTION

Hip fractures in the elderly are associated with significant mortality.[1-8] Most of the deaths occur during the early period after the operation.[3-5,9,10] Since life expectancy has increased, the incidence of hip fractures in elderly people has also risen every year. Hence, defining the risk factors may assist in implementing preventive measures. The total one-year mortality risk ranges from 14% to 36%.[3,5,6] The proposed risk factors include age, gender, nutritional status, anaemia, the type of surgery, an increased time interval between injury and surgery, comorbidities and the American Society of Anaesthesiologists (ASA) score of patients.[5,8,11-14] While age, malnutrition and general health status are well-established risk factors, controversial results have been reported on other risk factors, such as gender and the time interval between injury and surgery.[1,3-5] In some studies, male gender has been suggested to be associated with increased rates of mortality, but others have found there to be no difference between the genders.[1,3,5,13,14] A delay in surgery has been believed to be associated with poor outcomes, and more negative outcomes were reported with operative delay in one study.[8] However, a surgical delay of 24 or 48 hours has been shown to not cause increased mortality at one year post surgery.[12] This study aimed to prospectively investigate the factors affecting the one-year mortality in hip fracture patients aged 65 years or older.

METHODS

In 2006, 115 patients were admitted to our hospital with hip fractures. Out of these, 31 patients were under 65 years old, and pathologic fracture was detected in

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Table I. Characteristics of the patients according to mortality.

Patient characteristic	No. (%)		p-value
	Survived	Died	
Gender			
Female	41 (78.8)	11 (21.2)	
Male	18 (81.8)	4 (18.2)	[a] $p > 0.05$
Time period between injury and surgery			
≤ 2 days	49 (80.3)	12 (19.7)	[a] $p > 0.05$
> 2 days	10 (76.9)	3 (23.1)	
Comorbidities			
≤ 2	29 (100)	- (0)	[b] **$p < 0.001$**
> 2	30 (66.7)	15 (33.3)	
ASA			
I-II	48 (94.1)	3 (5.9)	[a] **$p < 0.001$**
III-IV	11 (47.8)	12 (52.2)	
Mobilisation time after surgery			
≤ 2	46 (78)	13 (22)	[a] $p > 0.05$
> 2	13 (86.7)	2 (13.3)	
Preoperative ALB			
< 3.5 g/dl	28 (68.3)	13 (31.7)	[b] **$p = 0.006$**
≥ 3.5 g/dl	31 (93.9)	2 (6.1)	
Preoperative TLC			
< 1500 cells/ml	13 (56.5)	10 (43.5)	[a] **$p = 0.002$**
≥ 1500 cells/ml	46 (90.2)	5 (9.8)	
Preoperative nutritional status			
ALB ≥ 3.5 g/dl/TLC ≥ 1500	26 (96.3)	1 (3.7)	
ALB ≥ 3.5 g/dl/ TLC < 1500	20 (83.3)	4 (16.7)	[c] **$p = 0.011$**
ALB < 3.5 g/dl/ TLC ≥ 1500	5 (83.3)	1 (16.7)	
ALB < 3.5 g/dl/TLC < 1500	8 (47.1)	9 (52.9)	

NB. Bold values denote statistical significance.
[a] Using Fisher's exact test; [b] Using Pearson chi-square test; [c] Using Kolmogorov-Smirnov test.
ASA: American Society of Anaesthesiologists; ALB: albumin; TLC: total lymphocyte count

another ten patients. These 41 patients were excluded from the study. The remaining 74 patients (52 female, 22 male), who were 65 years of age or older and ambulatory before fracture, and whose fracture was nonpathologic in origin, were included in the study. Informed consent was obtained from all the patients, and the study was approved by the local ethics committee of the hospital.

In all the patients, the fractures were treated with cemented hemiarthroplasty, followed by a similar postoperative protocol consisting of early mobilisation and ambulation with weight-bearing. The approach was posterior in the lateral decubitis position. Patients were administered cefazolin sodium 1g intravenously four times a day for two days postoperatively. Enoxaparine sodium 0.6 ml was subcutaneously administered once a day for three weeks for thromboemboli prophylaxis, and acetylsalicylic acid 100 mg was administered orally once a day thereafter. After discharge, the patients were examined monthly by the senior author to obtain follow-up information for 12 months postoperatively, or until death. They were interviewed either on routine controls at the hospital or by telephone calls. If the patient was not available, a family member or caregiver was interviewed.

Patient age, gender, the number of comorbidities, total lymphocyte count (TLC), blood albumin (ALB) and haemoglobin (Hb) levels on the day of admission, the length of hospital stay, mobilisation time after surgery, comorbidities, ASA score and time period elapsed between injury and surgery were recorded. To determine the extent to which the time period between injury and surgery affects mortality, the patients were divided into two groups: patients who were operated on within two days after admission and patients who were operated on more than two days after admission. Such an approach has previously been validated.[12]

General health status was defined by the number of pre-existing significant comorbidities, including diabetes mellitus, congestive heart failure, ischaemic heart disease, previous cerebrovascular accident, renal disease, neurological disorders, hypertension and chronic obstructive pulmonary disease. In order to assess to what extent these comorbidies affect the postoperative short-term results, patients were categorised as having ≤ 2 or > 2 comorbidities. The patients were also categorised based on the ASA rating of operative risk.[2] In this system, Grade I indicates a normal, healthy patient, Grade II

Table II. Significant results of Kaplan-Meier survival analysis with log-rank test.

Patient characteristic	No. of patients Died/Total	Mean survival time ± SE	Log Rank χ^2	p-value
ASA				
I-II	3/51	345.9 ± 8.0	23.484	**p < 0.001**
III-IV	12/23	229.2 ± 28.6		
Preoperative ALB				
< 3.5 g/dl	13/41	283.0 ± 18.8	6.986	**p = 0.023**
≥ 3.5 g/dl	2/33	342.7 ± 11.9		
Preoperative TLC				
< 1500 cells/ml	10/23	251.4 ± 28.4	12.026	**p = 0.002**
≥ 1500 cells/ml	5/51	335.9 ± 10.3		
Preoperative nutritional status				
ALB ≥ 3.5 g/dl and TLC ≥ 1500	1/27	350.0 ± 9.8		
ALB ≥ 3.5 g/dl and TLC < 1500	4/24	320.0 ± 18.3	17.375	**p = 0.001**
ALB < 3.5 g/dl and TLC ≥ 1500	1/6	310.0 ± 45.6		
ALB < 3.5 g/dl and TLC < 1500	9/17	230.7 ± 33.4		

NB. Bold values denote statistical significance.
ASA: American Society of Anaesthesiologists; SE: standard error; ALB: albumin; TLC: total lymphocyte count

indicates mild systemic disease, Grade III indicates a severe systemic disease that is not incapacitating, Grade IV indicates a severe incapacitating, systemic disease that is a constant threat to life, and Grade V indicates an amoribund patient. In this study, no patient was assigned to Grade V, and the patients were divided into two categories: Grade I or II and Grade III or IV. Such an approach has been used previously.[11]

Statistical analysis was performed using the Statistical Package for the Social Sciences 13.0 version for Windows program (SPSS Inc, Chicago, IL, USA). The continuous variables are described as average ± standard deviation and median, interquartile range. The categorical variables were presented in terms of their frequency. For a comparison of the means with a normal distribution between the patient groups, Student's *t*-test and One-way ANOVA were used as parametric tests. For a comparison of the means without a normal distribution between the patient groups, Mann-Whitney U-test and Kruskal-Wallis test were used as nonparametric tests. The presence of differences was tested using the Mann-Whitney U-test, and the source of the difference was found with the Kruskal-Wallis test. In order to compare the categorical variables between the patient groups, Pearson's chi-square, Fisher's exact, Kolmogorov-Smirnov and Mantel-Haenszel chi-square tests were used. After the normality assumptions were assessed, a two-way mixed design ANOVA (with independent measures on mortality) was performed with the Greenhouse-Geisser adjustment. The relationships between patient characteristics and survival were analysed by the Kaplan-Meier and Cox Regression Analyses (Forward LR). A p-value of less than 0.05 was regarded as significant.

RESULTS

The mean age of the patients was 77.9 ± 8.3 (range 65–105) years. It was 76.86 ± 8.85 (range 65–105) years for male and 78.29 ± 8.05 (range 65–96) years for female patients. The mean hospitalisation period was 8.1 ± 2.9 (range 4–18) days. The median time period between injury and surgery was one (range 1–13) day. The mean mobilisation time after surgery was 2.2 ± 0.7 (range 0–5) days. 15 (20.3%) patients died during the 12-month period. The mean age for patients who survived and those who died was 78.2 ± 8.4 (range 65–105) and 76.6 ± 8.0 (range 66–98) years, respectively ($p > 0.05$). The characteristics of the patients are summarised according to mortality in Table I. All the patients who died had three or more comorbidities and 12 (80.0%) of them (five ASA III, seven ASA IV) were classified as ASA III-IV ($p < 0.001$).

41 (55.4%) patients were malnourished on hospital admission, based on a preoperative ALB level < 3.5 g dl, and 13 (31.7%) died ($p = 0.006$). 17 (23.0%) patients had both a preoperative ALB level < 3.5 g/dl and TLC < 1500 cells/ml; 9 (52.9%) of these patients died ($p = 0.011$) (Table I). 23 (31.1%) patients were classified as such based on TLC < 1500 cells/ml, and ten (43.5%) of these died ($p = 0.002$). When the ASA score groups were adjusted, the association between the admission levels of TLC < 1500 cells/ml and mortality remained statistically significant ($p = 0.03$) (Mantel-Haenszel common odds ratio 4.947, 95% confidence interval [CI] 1.212–20.182). The mean admission Hb level for patients who survived was 12.29 ± 1.65 g/dl and 10.73 ± 2.04 g/dl for patients who died ($p = 0.003$).

The mean survival time at one year was 309.6 ± 12.2 days (95% CI 285.7–333.5). Patient survival

Table III. Significant results of univariable and bivariable Cox regression analysis.

Patient characteristic	p-value	HR	95% CI for HR
Time period between injury and surgery (days)	0.002	1.351	1.117–1.634
ASA III-IV *(vs I-II)*	< 0.001	11.639	3.275–41.355
Mobilisation time after surgery (days)	0.008	0.189	0.05–0.647
Preoperative ALB (g/dl)	0.008	0.181	0.051–0.640
Preoperative Hg (g/dl)	0.002	0.653	0.501–0.853
Preoperative ALB *< 3.5 g/dl (vs ≥ 3.5 g/dl)*	0.021	5.790	1.306–25.674
Preoperative TLC* *< 1500 cells/ml (vs ≥ 1500 cells/ml)*	0.030	3.371	1.126–10.093
Preoperative nutritional status *(vs ALB ≥ 3.5 g/dl and TLC ≥ 1500)*	0.010		
ALB ≥ 3.5 g/dl and TLC < 1500	> 0.05	4.698	0.525–42.040
ALB < 3.5 g/dl and TLC ≥ 1500	> 0.05	5.049	0.316–80.735
ALB < 3.5 g/dl and TLC < 1500	0.010	18.344	2.321–144.988

* Adjusted for ASA group.
HR: hazard ratio; CI: confidence interval; ASA: American Society of Anaesthesiologists; ALB: albumin; TLC: total lymphocyte count; Hg: haemoglobin

was 94.6% at three months, 81.1% at six months and 79.7% at 12 months. Patients who were malnourished on hospital admission based on ALB < 3.5 g/dl and TLC < 1500 cells/ml and patients with an ASA score III-IV had a lower mean survival time (Table II). When the ASA score groups were adjusted, the association between malnutrition on hospital admission based on a preoperative TLC < 1500 cells/ml and survival time remained statistically significant (Log Rank chi-square = 5.317 p = 0.021).

The results of the univariable and bivariable Cox Regression analysis are presented in Table III. The multivariable analysis with all the variables based on the order of the variables entering the model is presented in Table IV. When the other variables were controlled for, the risk of mortality was significantly increased with admission TLC < 1500 cells/ml (hazard ratio [HR] = 6.275, 95% CI 1.619–24.326), female gender (HR = 7.676, 95% CI 1.412–41.718) and an ASA score of III-IV (HR = 19.328, 95% CI 3.777–98.919). Every one unit increase in the preoperative haemoglobin levels decreased the mortality risk by 49.9% (HR = 0.511, 95% CI 0.353–0.740).

DISCUSSION

High rates of mortality have been previously reported in elderly patients after hip fractures.[1-8] It has been stated that most of the deaths had occurred within three to four months after the hip fracture.[3,4,9] Kenzora et al reported that the overall mortality rate at one year was 14% (58 out of 406).[5] In a large study from Brazil with 606 patients, 130 (21.5%, 95% CI 18.2–24.9) died within one year after admission. In the same study, a sudden rise in mortality was found in the first 30 days after admission, and this remained high until 90 days after admission, followed by a gradual decrease in the mortality rate. Between 91 and 365 days, the mortality rate ceased. The authors proposed in their inclusion criteria that the reason for the early equalisation of mortality risk was not the fracture itself and/or the predominance of older patients.[4] Tosteson et al found that increased mortality was limited to the first six months after hip fracture (HR = 6.28, 95% CI 4.82, 8.19). They also reported no increased mortality during the subsequent follow-up.[10] In contrast with the above studies, Pioli et al conducted a study that included 252 elderly hip fracture patients and reported the death rates as 12.5% at three months, 18.9% at six months and 24% at 12 months.[3] Ahmad investigated elderly hip fracture patients treated with hemiarthroplasty and found the mortality rate to be 4.3% at two weeks, 17.4% at six months and 26% at one year.[12] Bass et al conducted a large sample population-based study investigating the mortality risk factors associated with elderly hip fracture patients. They reported the mortality rates as 8.9% at one month, 15.6% at three months, 21.8% at six months and 29.9% at 12 months.[13] Beringer et al reported the outcomes following proximal femoral fracture in Northern Ireland and found the mortality rates to be 6.9% at one month, 15.6% at four months and 22.3% at 12 months.[14] The current study found the death rates to be 5.4% at three months, 18.9% at six months and 20.3% at 12 months, indicating that there was an increase in mortality in the first six months after admission. Our results are consistent with those of Tosteson et al[10] The mortality rates of some these studies are listed in Table V.

Malnutrition has been reported to be associated with a significant rate of mortality.[11,15-18] Several markers

Table IV. Results of multivariate Cox regression analysis at the end of the 6th month and 1st year.

Patient Characteristic	p-value		HR		95% CI for HR	
	6th mth	1st year	6th mth	1st year	6th mth	1st year
ASA III–IV (vs. I–II)	0.001	< 0.001	16.541	19.328	3.265–83.801	3.777–98.919
Preoperation haemoglobin (mg/dL)	0.001	< 0.001	0.533	0.511	0.369–0.770	0.353–0.740
Preoperation total lymphocyte < 1500 cells/ml (vs ≥ 1500 cells/ml)	0.008	0.008	5.393	6.275	1.394–20.874	1.619–24.326
Female (vs. male)	0.022	0.018	7.108	7.676	1.334 –37.876	1.412–41.718

ASA: American Society of Anaesthesiologists; HR: hazard ration; CI: confidence interval

Table V. Studies showing mortality rates in elderly hip fracture patients.

Research studies	Mortality (%)		
	3 months	6 months	12 months
Pioli et al[3]	12.5%	18.9%	24%
Vidal et al[4]	-	-	21.5%
Kenzora et al[5]	-	-	14%
Tosteton et al[10]	-	20%	-
Ahmad[12]	-	-	26%
Bass et al[13]	15.6%	21.8%	29.9%
Beringer et al[14]	6.9%*	15.6%**	22.3%
Current study	5.4%	18.9%	20.3%

* Mortality occurred at one month.
** Mortality occurred at four months.

have been used to assess the nutritional status.[19-23] Skin antigen testing, nitrogen balance, TLC, ALB, pre-albumin and transferrin levels are among these markers. However, most of them are nonroutine and expensive. The current study used ALB levels and TLC for the assessment of nutritional status. Decreased levels of ALB have been reported to be associated with an increased length of hospital stay, impaired wound healing, increased rates of wound infection, pneumonia and sepsis, an increased incidence of postoperative complications, delayed physical rehabilitation and a decreased likelihood of survival.[3,4,7,11,15,16,24] Koval et al reported that the ALB level was predictive of in-hospital mortality after hip fracture.[11] In the same way, Pioli et al showed that the serum ALB level was a strong independent predictor of in-hospital and late mortality.[3] Incalzi et al investigated the in-hospital mortality rate in elderly hip fracture patients and found that malnutrition was one of the leading factors.[7] In the present study, two patients died during hospitalisation, and both had hypoalbuminaemia and low TLC. Patterson et al found that protein depleted patients had a significantly lower probability of survival one year after hip fracture.[16] In our study, 13 out of 41 patients with ALB < 3.5 g/dl died during the first year, and this result is consistent with the literature. Vidal et al designed a probabilistic study evaluating the mortality rate after hip fracture surgical repair in the elderly, and found the cause of death to be malnutrition in 18 out of 130 patients, who died within one year postoperatively.[4] A decreased number of lymphocytes has been shown to be a significant risk factor for the development of postoperative sepsis and mortality.[25,26] Koval et al reported that a TLC count of less than 1500 cells/ml on hospital admission was predictive for one-year mortality after hip fracture.[11] Contrary to this, Foster et al reported that the TLC count was not predictive of mortality in a series of 40 patients with hip fracture.[17] In the current study, it was found that death rates in patients with TLC < 1500 cells/ml were higher during the first year follow-up, and this result is consistent with the literature. Moreover, in the multivariate analysis, TLC < 1500 cells/ml remained a significant risk factor for mortality as well.

The effect of gender on mortality after hip fracture surgery is debatable.[1,3,5] Pioli et al evaluated mortality rates in hip fracture patients for a one-year period and found male gender to be a significant determinant for mortality. Hovewer, after multivariate analysis, gender did not remain an independent predictor for mortality.[3] Kenzora et al found no significant difference in the mortality rates among the genders in hip fracture patients,[5] while Forsen et al showed in their study that male hip fracture patients had a higher mortality rate than female patients in the first year after the injury.[1] This has been attributed to the more precarious health status of men.[3] Beringer et al also found that female gender was associated with the successful return to home in their patients.[14] Bass et al, in their population-based, large sample of elderly hip fracture patients, found that men had a higher risk for mortality than women. However, their study included pathologic fractures related with metastasis, and they found that the presence of metastatic cancer increased the risk of death by almost four times compared with patients without that diagnosis.[13] In the current study, no difference was found with regard to the gender of the patients at the end of the one-year period. Hovewer, after multivariate analysis, female gender remained a significant risk factor for mortality. This may be due to the frailty of females in our population.

The age of the patient has been reported to be significant in the mortality of patients with hip fracture.[1,5] Kenzora et al found a significantly higher rate of mortality in patients older than 70 years of age.[5] Forsen et al found that female hip fracture patients who were ≥ 85 years of age had excess mortality, especially three months postoperatively,[1] while Beringer et al found that younger age was associated with a successful return to home in their patients.[14] Contrary to these findings, Pioli et al found no association between age and mortality,[3] as in the current study.

Early fracture repair is believed to be associated with a favourable outcome, at least in terms of mobilisation. Although Zuckerman et al reported negative effects of a delay in surgery,[8] the beneficial effects of early surgery have not yet been shown.[5,27] The current study also found no difference in terms of delayed surgery. It is possible that most of the delays were due to the stabilisation of underlying health problems and some medications, which prevented early surgical intervention. In our hospital, these patients were operated on as early as possible.

Anaemia is a common occurence among the elderly and is associated with increased mortality.[28,29] Gruson et al found that the risk of mortality was significantly increased in elderly hip fracture patients with anaemia at six and 12 months after surgery.[28] Halm et al studied the effect of the perioperative Hb level on clinical and functional outcomes in hip fracture patients and found that higher Hb levels were associated with lower odds of death.[29] The current study also found that higher levels of Hb were associated with a lower risk of death. It is not surprising that patients with ASA III and IV had a higher risk of mortality than ASA I and II patients in our study. The survival rate was also shortened in patients with ASA III and IV. ASA is used by anaesthesiologists to assess patients with regard to their surgical risk factors.[2] Kenzora et al found that the number of pre-existing medical conditions was a highly significant risk factor for mortality.[5]

This study had certain advantages. Its prospective consecutive design was its main advantage. There was no patient lost to follow-up. The sample size may seem to be relatively small, but it is felt that the advantages make the study relevant for the information gathered. In conclusion, elderly hip fracture patients have high rates of mortality risk especially in the early period after the injury. This study has shown that ASA III-IV, lower counts of lymphocytes, female gender and relative anaemia appear to be significant independent risk factors that account for a high mortality rate. Identifying these predictive factors may be helpful in improving case management and determining prognosis, especially during the one year after hip fracture management.

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