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ORIGINAL ARTICLE

Are albumin and total lymphocyte count significant and reliable predictors of mortality in fractured neck of femur patients?

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Abstract Hip fractures are a significant cause of mortality and morbidity in the elderly. It is important to identify factors that predict an increased mortality following hip fracture. The aim of this study was to identify significant predictors of mortality at 6 and 12 months following hip fractures. Three hundred patients above the age of 65 were identified who were admitted in to the hospital with fracture neck of femur. Two hundred and seventy-four patients were operated and were included into the study. Variables collected were age, gender, significant comorbidities, admission albumin level and admission total lymphocyte count (TLC). Admission time and subsequent time to surgery were also analysed. Our study showed that albumin and TLC were found to be the only clearly significant mortality predictors at 12 months and a delay of up to 4 days to surgery does not significantly increase the mortality at 12 months.

Keywords Total lymphocyte count · Albumin · Mortality · Fractured neck of femur

Introduction

Hip fracture represents the most common cause of injury requiring hospitalisation in patients over the age of 65, with an estimated lifetime incidence of 18 % in women and 6 % in men [1].

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In the UK, there are approximately 70,000 hip fractures a year [2]. This figure is projected to double by 2050 [3, 4]. This would pose growing financial burden on health economy and challenge for the healthcare delivery system. Reported mortality rates following fractured neck of femur range from 14 to 47 % [5]. Recognised risk factors associated with increased mortality following hip fractures include age [6, 7], sex [8], ASA grade [6], nutritional status [9–11], fracture type [6, 12], delay to surgery [6, 13, 14], anaesthetic technique [5] and operator seniority [5]. It is important to recognise factors that predict an increased mortality following hip fracture, as this may allow the surgeon to better manage these patients, by addressing potentially reversible negative prognostic variables. Various published scoring systems like orthopaedic POSSUM score [15], Nottingham Hip Fracture Score [16] and more recently Sernbo [17] have been used to predict mortality in fracture neck of femur patients, but they have limitations in terms of validity, specificity or simplicity.

The aim of this study was to identify significant and reliable predictors of mortality at 6 and 12 months following hip fracture and whether delay in operation adversely affects the outcome.

Patients and methods

A retrospective review of 300 hip fracture patients admitted during a 14-month period to the orthopaedics trauma unit at Wrightington, Wigan and Leigh NHS Foundation Trust was performed. The Trust serves a local population of over 300,000 with more than 750 inpatient beds.

Variables collected were age, gender, significant co-morbidities, admission albumin level and admission total lymphocyte count (TLC). Admission time and subsequent time to surgery were also analysed. Terminally ill and patients with blood dyscrasias were excluded.

Data was then analysed to identify those variables that were significant predictors of mortality at 6 and 12 months.

Data were initially stored in Microsoft Excel™ before being exported to SPSS 16.0™ for analysis. Following preliminary analyses of demographic details, logistic regression analyses were performed to demonstrate any independent variables associated with mortality status at 6 and 12 months. Given the importance of time from injury to operation as a predictor of mortality status in previous studies [6, 13, 18, 19], chi-squared analyses then examined the association between these variables in relation to operations conducted within and beyond the first 3 days post-injury.

Results

A total of 300 consecutive hip fracture cases (240 female; 60 male) admitted over a 14-month period were identified. One case was excluded due to insufficient data, and 15 cases were managed non-operatively and, therefore, excluded from the present study. Of the remaining 284 patients (223 female, 61 male) who constituted the sample, 185 were living in their own home, with 99 being care home residents. Ages ranged from 65 to 104 years, with a mean of 83.0 years ($SD = 7.9$ years). Females ($M = 84.12$ years, $SD = 7.6$ years) were significantly older than males ($M = 79.1$ years, $SD = 8.0$ years), with t (272) = 4.336, $p < .000$, two-tailed, $d = .629$, 95 % CI (2.7, 7.2).

There were 65 in-hospital deaths (22.8 % of the sample), 31 died in orthopaedic ward and 34 after they were moved to rehabilitation and medical wards. One hundred and one patients were dead at 6 months (35.6 %), and 112 dead at 12 months (39.4 %). Table 1 shows means (and standard deviations) for key variables broken down by mortality outcome, at these respective times post-injury. At 6 months, there was a significantly higher male mortality (χ^2 [1, $N = 284$] = 6.736, $p = .009$), though at 12 months this was not significant (χ^2 [1, $N = 284$] = 3.466, $p = .063$). Gender differences in albumin level and TLC were not significant.

For the 231 patients operated upon and discharged, the differences in length of stay associated with mortality outcome at both 6 and 12 months post-injury were not significant.

None of the correlations between the variables shown in Table 1 were of sufficient magnitude for multicollinearity to be a problem within a regression model.

Table 2 shows the results for each independent variable, with only gender, albumin level, and time between injury and operation being significantly associated with 6 months mortality status. The odds ratios show that the males in this sample had a 149.7 % greater likelihood of death 6 months post-injury than females. For each additional day between the injury and operation, there was a 14.2 % greater likelihood of death 6 months post-injury, whilst for each unit g/litre reduction in albumin (normal value 34–48 g/l), there was an 11 % increase likelihood of being dead at 6 months.

TLC was significantly associated with mortality status at 12 months (having not been associated with 6-month outcomes), there being a 30.7 % increase in mortality risk at 12 months with each unit reduction below lower limit of normal, (UNIT—cell count × 10.9/ l, normal range—1.5–4.0). For albumin level, there was a 9.7 % increase in mortality risk at 12 months, with each unit reduction below lower limit of normal (normal value 34–48 g/l).

As time from injury to operation is frequently held to be predictive of mortality outcome, this variable was examined more closely. The 240 patients (84.5 % of the sample) who had received their operation within 3 days post-injury were divided into those receiving operations up to 1 day ($n = 161$) and those receiving operations between 1 and 3 days post-injury ($n = 79$). No significant association was found between these two groups with mortality outcome at either 6 months (χ^2 [1, $N = 240$] = 1.264, ns.) or 12 months (χ^2 [1, $N = 240$] = 0.545, ns.). However, when these 240 patients were compared as a group to the remaining 44 patients receiving operations 4 days or more post-injury, significant associations were found between

Table 1 Means (and *SD*s) for key variables broken down by mortality status at 6 and 12 months, respectively, with one-tailed *p* values

Variables	6-month mortality status			12-month mortality status		
	Alive ($n = 173$)	Dead ($n = 101$)	p	Alive ($n = 162$)	Dead ($n = 112$)	p
Age at time of injury (years)	82.5 (8.3)	84.0 (97.1)	.059	82.3 (8.4)	84.1 (7.0)	.038[a]
Time from injury to operation (days)	1.7 (1.7)	2.5 (2.9)	.007	1.7 (1.7)	2.4 (2.8)	.018[b]
Albumin level (g/dl)	39.6 (4.6)	35.8 (6.5)	.000	39.6 (4.6)	36.1 (6.3)	.000[b]
Total lymphocyte count (units)	1.6 (0.8)	1.3 (0.7)	.009	1.6 (0.8)	1.3 (0.7)	.001[b]

[a] Parametric *t* tests

[b] Mann–Whitney *U* tests

Table 2 Logistic regression results for each independent variable with 6- and 12-month post-injury mortality outcomes as the respective dependent variables

Independent variables	6-month mortality outcomes[a]				12-month mortality outcomes[a]			
	B	Wald χ^2 (1 df)	*p*	Odds ratio	*B*	Wald χ^2 (1 df)	*p*	Odds ratio
Age (years)	.031	2.864	.091	1.032	.031	2.950	.086	1.031
Injury to operation (days)	.133	3.902	.048	1.142	.120	3.254	.071	1.127
Gender[b]	.915	7.165	.007	2.497	.659	3.826	.050	1.932
Albumin level (g/l)	−.116	19.361	.000	0.890	−.102	16.015	.000	0.903
Total lymphocyte count (unit)	−.246	1.761	.184	0.7782	−.367	4.060	.044	0.693
Constant	.168	0.007	.934	1.183	.384	0.037	.847	1.468

[a] Coded 1 = alive, 2 = dead

[b] Coded 1 = female, 2 = male

time to operation and mortality outcome at 6 months (χ^2 [1, $N = 284$] = 6.829, $p = .009$) and 12 months (χ^2 [1, $N = 240$] = 5.431, $p = .020$), with more patients surviving in the group receiving operations up to 4 days post-injury than would be expected under the null hypothesis.

Discussion

Treatment of hip fractures represents a significant and ongoing challenge for orthopaedic surgeons. The incidence of concurrent medical co-morbidities amongst this patient group is high, with 66 % of patients presenting with an ASA grade of 3 or greater [4]. Consequently, the need for appropriate pre-operative stabilisation, and recognition and reversal of negative prognostic variables is fundamental to their optimal clinical management. The risk surgery represents to this patient group is further potentiated given only 42–58 % of hip fracture patients have any form of pre-operative medical assessment [4, 20].

Comparing our case mix with National Hip Fracture Database [4], the cohort was well matched to national averages. Approximately 80 % of cases were female; mean ages were 79 and 84 years for men and women, respectively [4]. Only 65 % of patients in our series were admitted from home, compared to a national average of 76 %, possibly indicating a frailer local population [4].

The variables associated with mortality at 6 months were male gender, reduced albumin and delay to surgery. Whilst male gender initially was significant in prediction of mortality at 6 months, this was not significant at 12 months. Similarly, the increased risk presented with each day's delay to surgery noted at 6 months was lost at 12 months, in those patients who had surgery within 4 days. TLC was a significant predictor of mortality at 12 months, there being a 30.7 % increased likelihood of mortality with each unit reduction in TLC. Similarly, reduced albumin levels were a significant predictor of mortality both at 6 and 12 months, with a 9.7 % increase in mortality risk at 12 months, with each reduction in g/litre albumin.

Our findings suggest that both albumin and TLC levels can be used as a predictor of those patients most at risk of death following hip fracture. These can act as indicators of protein energy malnutrition (PEM) and poor nutritional status [21, 22, 23–27]. Calculating patient's degree of PEM can be cumbersome and we feel a single measure of albumin and TLC is reliable predictor of 1-year mortality as a surrogate marker of PEM. This may represent an area for further clinical optimisation both pre- and post-operatively.

Our results, in contrast to others, do not identify any significant association between mortality and those patients operated on within 24 h versus those operated on within 4 days. There is still considerable debate as to the benefit of early operative intervention, and in fact, whether surgery after 24 or 48 h constitutes a surgical delay [28]. Indeed, one study has reported that surgery within 24 h increases mortality risk [7].Whilst the initial guidelines produced by the British Orthopaedic Association advises surgery within 48 h [20], recent key recommendation on hip fracture from National Institute for Health and Clinical Excellence suggests that surgery should take place on the day or the day after injury [29]. Our findings, however, do not show any increased risk of mortality in those patients having surgery within 4 days of injury, though do show significant increases in mortality in those having surgery after this. Additionally, our results do not show any significant association between hospital length of stay and mortality. Average length of stay was 19 days in keeping with the National Hip Fracture Database average (23 days; range 12–58) [4].

Conclusion

Admission albumin and TLCs were found to be the only clearly significant predictors of mortality at 12 months.

These are both simple and inexpensive tests, which we believe should be used, in conjunction with a thorough clinical assessment and examination, to identify patients at significant risk of mortality. More work is necessary to identify the causative link between reduced albumin, TLC and mortality in this patients group, in the hope that pre-operative correction of these variables may improve patient outcome.

Kieffer et al. [30] have found that the single measure of albumin is a very accurate predictor of 1-year mortality in patients with fractured neck of femur and recommend routine measurement on admission in these patients for surgical planning. Findings from our study support their conclusion with the addition that operative delay up to 4 days does not adversely affect the final outcome in this group of patients.

Therefore, with regards to timing of operation in this patient group, our findings suggest that a delay of up to 4 days does not significantly increase the mortality at 12 months. Timely operation on the basis of preoperative optimisation and clinical judgement as part of a multidisciplinary team should guide treatment, in keeping with national recommendations [4, 20].

Conflict of interest We, authors of this article, certify that there is no actual or potential conflict of interest in relation to this article.

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