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Original Article

Serum albumin and total lymphocyte count as predictors of outcome in hip fractures☆

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SUMMARY

Background & aims: Hip fractures are a significant cause of mortality and morbidity in the elderly. Malnutrition is a significant contributor to this, however no consensus exists as to the detection or management of this condition. We hypothesise that results of admission serum albumin and total lymphocyte count (TLC), as markers of Protein Energy Malnutrition (PEM) can help predict clinical outcome in hip fracture patients aged over 60 years.

Methods: This retrospective study evaluated the nutritional status of patients with hip fractures using albumin and TLC assays and analysed their prognostic relevance. Clinical outcome parameters studied were delay to operation, duration of in-patient stay, re-admission and in-patient, 3- and 12-month mortality.

Results: Four hundred and fifteen hip fracture patients were evaluated. Survival data were available for 377 patients at 12 months. In-hospital mortality for PEM patients was 9.8%, compared with 0% for patients without. Patients with PEM had a higher 12-month mortality compared to patients who had normal values of both laboratory parameters (Odds Ratio 4.6; 95% CI: 1.0–21.3). Serum albumin (Hazard Ratio 0.932, 95% CI: 0.9–1.0) and age (Hazard Ratio 1.04, 95% CI: 1.0–1.1) were found to be significant independent prognostic factors of mortality by Cox regression analysis.

Conclusions: These results highlight the relevance of assessing the nutritional status of patients with hip fractures at the time of admission and emphasises the correlation between PEM and outcome in these patients.

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1. Introduction

Hip fractures are a significant cause of morbidity and mortality in the elderly. A one-year mortality of between 14 and 36% was reported.[1–5] Direct cost estimates for hip fracture care in the year after fracture was as much as US$40,000.[6] Reported annual age-adjusted incidence of hip fracture is 43–80 per 100,000 of population.[7] The incidence is projected to increase exponentially over the next 40 years to 6.26 million per annum worldwide because of increased life expectancy and population growth.[8–11]

Protein energy malnutrition (PEM) is associated with an increased rate of infection, bedsores, muscular weakness, poorer respiratory function, hypotrophy of cardiac muscle, and death.[12,13] Preoperative nutritional status has a significant impact on surgical outcome for orthopaedic[14] and other surgical patients.[15,16] For elderly patients, PEM is known to be both a common causative factor of hip fracture and a predictor of poor outcome.[17–22] However, there is no universally accepted definition of PEM and its reported incidence in elderly hip fracture patients varies widely between 9% and 89%.[5,13,17,20,23–29]

Clinical assessment tools for PEM are cumbersome, expensive and have suboptimal sensitivity.[13,30,31] Koval *et al.* and Symeonidis *et al.* used a combination of admission serum albumin and total lymphocyte count (TLC) as independent prognostic factors in hip

Non-standard abbreviations: PEM, protein energy malnutrition; TLC, total lymphocyte count.

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fracture patients.[5,17] They proposed the use of these two rapid and inexpensive tests as surrogate markers of PEM, and advocated their use in routine screening for patients at increased risk of poor outcome.

This study aims to assess the prevalence of PEM using this simple definition and assess whether serum albumin and TLC at admission are correlated with clinical outcome parameters – delay to operation, duration of in-patient stay, re-admission and in-patient, 3- and 12-month mortality for elderly patients undergoing surgery for hip fractures.

2. Materials and methods

All patients admitted to a university teaching hospital with an acute hip fracture over a 21-month period (January 2005 –September 2006) were studied retrospectively. Patients were identified from operating theatre records and the Hospital In-patient Enquiry System (HIPE). Patient clinical (date of admission, date of operation, date of discharge, date of death, re-admission) and demographic (age, gender, domicile (nursing home or home), general practitioner) data were retrieved from the HIPE database and entered into a confidential database (MS Excel™, Microsoft Corp, Seattle, WA). Fracture type and operation were retrieved from operating theatre records. Admission serum albumin and TLC were retrieved from a computerized laboratory database. Patients younger than 60 years of age and those not managed operatively were excluded from the study.

Admission serum albumin levels and TLC results were used as the sole markers of nutritional status. Values of serum albumin ($<$3.5 g/dL) and TLC ($<$1500 cells/mm^3) below the lower laboratory reference range were taken to represent PEM.[5,17] Both of the nutritional parameters were examined individually and together as predictors of outcome. As previously described,[5,17] a 2 $\times$ 2 table was constructed for the four possible combinations of normal and abnormal values for serum albumin and TLC:

(i) Group A: preoperative albumin $\geq$ 3.5 g/dl; TLC $\geq$ 1500 cells/mm^3
(ii) Group B: preoperative albumin $\geq$ 3.5 g/dl; TLC $<$ 1500 cells/mm^3
(iii) Group C: preoperative albumin $<$ 3.5 g/dl; TLC $\geq$ 1500 cells/mm^3
(iv) Group D: preoperative albumin $<$ 3.5 g/dl; TLC $<$ 1500 cells/mm^3

Where only one, or neither test were performed preoperatively, patients were studied as a comparison group, E.

Primary outcome was assessed according to six clinical outcome parameters:

a) Waiting time to operation ($<$48, or $\geq$48 h)
b) Duration of in-patient hospital stay ($\leq$30, or $>$30 days) from time of surgery
c) Re-admission to hospital $\leq$3 months from time of surgery
d) In-hospital mortality
e) 3-month postoperative mortality from time of surgery
f) 12-month postoperative mortality from time of surgery

Where 3- and 12-month survival date were unavailable from the HIPE system, the patient's General Practitioner was contacted to ascertain this information. Date of death was determined from the Civil Registration Database in the Office of the Registrar General. This is a statutory computerized national database for all records related to life events, including death, in the Republic of Ireland. If this information could not be obtained, patient status was recorded as 'unknown' and the patient was excluded from this analysis.

All operations were performed either by, or under the direct supervision of a consultant surgeon. The preferred operative intervention was to use a hemiarthroplasty for intracapsular fractures and a dynamic hip screw (DHS) for extracapsular fractures.

2.1. Statistical analysis

Both nutritional parameters were examined as predictors of each outcome. Qualitative variables were compared using Pearson chi^2 or Fisher's exact test and reported as frequency (%). Quantitative variables were compared using the non-parametric Mann–Whitney *U* or Kruskal–Wallis tests and reported as median $\pm$ interquartile range (IQR). The effects of the four possible combinations of the two nutritional status variables (Groups A–D) were examined as predictors of outcome by multivariate logistic regression analysis. Further, the effects of having low preoperative albumin count (Groups C and D) and the effects of low total lymphocyte count (Groups B and D) were investigated as part of the multivariate analysis. Regression models were adjusted for age, gender and domicile. Additionally, rates of survival were calculated by the Kaplan–Meier method and compared using the log-rank test.[32] All demographic and clinical variables (Table 1) were included as explanatory variables in a Cox proportional-hazards regression analysis.[33] The results of the multivariate analyses were expressed in terms of hazard ratio derived from the estimated regression coefficients, with 95% confidence intervals. Statistical analyses were performed using SPSS 16.0 (SPSS Inc, Chicago, IL, USA). *P*-values $<$ 0.05 were considered significant.

3. Results

Four hundred and fifteen patients over the age of 60 years underwent operative intervention for hip fracture over the study period. Clinical and demographic data were available for all 415 patients. Survival data were available for 377 patients at 12 months (91% follow-up) (Table 1). Thirty-eight patients for whom survival data were not available were excluded from analysis.

The median patient age was 83 (76–88) years. Females (n = 294; 78%) outnumbered males (n = 83; 22%). Thirty-seven percent of patients were resident in a nursing home at the time of fracture. Nursing home patients were more likely to be female (p = 0.042), older (p $<$ 0.001) and have a shorter duration of in-patient stay (p = 0.003). Overall, one hundred and ninety-two patients (51%) had an intracapsular fracture and 185 (49%) had an extracapsular fracture. Median length of hospital stay was 10 (6–18) days and median time to operation was one (0–1) day. Fourteen percent of patients (n = 51) were re-admitted to hospital, for treatment of a medical condition, within 3 months of their operation. Twenty-four patients (6%) died acutely in hospital, 54 (14%) were dead at 3 months, and 96 (26%) were dead within 12 months of their operation.

Two hundred patients (53%) had both a TLC and serum albumin levels taken at admission, while 177 (47%) had not. For the 200 study patients who had both, low albumin levels were recorded for 131 (66%) patients. A low TLC level occurred in 148 patients (74%). Patients who had low levels of albumin (Groups C and D) were older than those who did not (Groups A and B) (p = 0.017). Patients who had low levels of TLC (Groups B and D) were also older than those who did not (Groups A and C) (p = 0.023). Patients resident in nursing homes were more likely to have lower albumin at admission (p = 0.033).

The demographics of the patients who had known albumin and TLC values at admission did not differ significantly from that of patients who did not have both of these investigations performed. The type of fracture and surgical procedures performed did not differ significantly between both groups. The only outcomes which

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