

## Original Article

# Laboratory nutritional parameters predict one-year mortality in elderly patients with intertrochanteric fracture

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**Background and Objectives:** The purpose of this study was to investigate the contributing value of nutrition related blood parameters to one-year mortality following intertrochanteric fracture surgery in a Chinese population over the age of 65. **Methods and Study Design:** Nutritional status was evaluated by using admission serum albumin and total lymphocyte count (TLC). One hundred and seventy-four intertrochanteric fracture patients were entered into this study for nutritional status assessment. Gender differences were evaluated by univariate analysis. The predictive value of the variables for one-year mortality was assessed by multiple logistic regression analysis. **Results:** The mean albumin was 31.0 g/L with 73% of patients less than 35 g/L and the mean TLC was  $1.19 \times 10^9$  cells/L with 81% less than  $1.50 \times 10^9$  cells/L. There were no significant differences in albumin ( $p=0.674$ ) or TLC ( $p=0.804$ ) between men and women. Survival information was obtained in 149 patients who received surgical treatment. The general one-year mortality was 31% with 35% in men and 29% in women, respectively. The surviving patients were younger and had higher albumin, TLC and calcium than those who died. However, multivariate analysis identified only serum albumin and TLC as independent and significant risk factors associated with one-year mortality; the optimal cut-off points were 29.5 g/L and  $0.93 \times 10^9$  cells/L, respectively, based on the receiver operating characteristic (ROC) curve. **Conclusions:** Malnutrition is a common phenomenon in an aged Chinese population suffering from intertrochanteric fractures. A lower serum albumin level and total lymphocyte count at admission are significant risk factors to predict the one-year mortality.

**Key Words:** nutritional status, intertrochanteric fractures, mortality, elderly people, albumin

## INTRODUCTION

Intertrochanteric fracture, a subset of hip fracture, is one of the most common injuries in elderly people and, together with femoral neck fracture, presents perhaps the most important public health problem facing orthopaedic surgeons today. Aged people with hip fracture are at considerable risk for premature death<sup>1-5</sup> with increased mortality during the first year after surgery from 8.4% to 36%.<sup>2</sup> Although numerous studies have focused on the risk factors for mortality following hip fracture surgery, there is no conclusive evidence yet what preoperative factors predict postoperative mortality.<sup>6</sup>

Elderly patients with hip fracture are more likely to be malnourished on admission when compared to the age-matched general population.<sup>7-9</sup> Poor nutritional status is known to be both a common causative factor of hip fracture and a predictor of excess mortality following surgical intervention.<sup>10,11</sup> Many methods including anthropometry, the mini-nutritional assessment, nutrition related blood parameters and dietary analysis are used for nutritional status assessment in clinic.<sup>12,13</sup> Serum albumin and total lymphocyte count (TLC) are two of the most important blood markers for nutritional status<sup>14</sup> and have been recognized as prognostic factors of hip fractures.<sup>15-18</sup> Several studies have demonstrated serum albumin<sup>14,16,17,19-21</sup> or

TLC<sup>16,17,22</sup> on admission to be independently predictive of postoperative mortality in aged people with hip fracture. However, most of the studies have not analyzed the different fracture types separately, although the fracture type per se may be influenced by nutrition status<sup>23</sup> and may be predictive of mortality.<sup>24</sup>

The purpose of this study was to assess the nutritional status of intertrochanteric fracture patients from a Chinese population aged over 65 years by preoperative serum albumin and total lymphocyte count. In addition, the relationship between these blood markers and the patients' one-year mortality has been evaluated.

## MATERIALS AND METHODS

### Study design and data collection

All patients were admitted to a university affiliated hospital with an acute intertrochanteric fracture over a 24-

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month period (January 2009–December 2010) and studied retrospectively. This study was approved by the ethics committee of Southeast University affiliated Zhongda Hospital. The basic information of the patients (such as name and identification number) was searched by the diagnosis of intertrochanteric fracture from a discharge registration system. Then the original medical records which contain all laboratory test results of the inpatients were retrieved from the record room of the hospital. Patients younger than 65 years of age, with multiple fractures or malignant pathologic fracture, and those not managed operatively were excluded from the study.

The demographic data (age and gender) and five preoperative blood parameters (serum albumin, TLC, haemoglobin, serum potassium and calcium) were entered into a confidential database (MS Excel™, Microsoft Corp, Seattle, WA). The preoperative serum albumin and TLC results were used as the sole markers of nutritional status. For each patient, 5 mL of Venous blood sample was collected in the morning after admission. The level of TLC and Albumin were detected by automatic blood cell analyzer (sysmex xt-2000i) and biochemical analyzer (Unicel DxC800 synchron) respectively according to the instructions. Values of serum albumin (<35 g/L) and TLC (<1.5×10<sup>9</sup> cells/L) below the lower laboratory reference range were taken to represent malnutrition.<sup>14,16</sup> The proportion of patients with either or both parameters below the normal level was calculated and gender differences in age, blood parameters and mortality were analyzed.

Fracture type and surgical intervention were confirmed according to the operation records. As intramedullary fixation is the first choice of surgical treatment for intertrochanteric fractures in our hospital, a majority of the fractures were stabilized with the gamma nail (GN) or the proximal femoral nail (PFN). The operating procedures were similar, the main difference being the type of implant.<sup>25</sup> All surgeries were performed according to the standard protocols of either GN or PFN by experienced surgeons. Fractures treated with other fixation methods, for example Dynamic hip screw (DHS), were excluded from the study.

As a national database of population death registration system has not been established in China, a telephone follow-up survey was performed one year after the surgery for each case. If the patient was unavailable, a family member or direct caregiver was contacted instead. If the telephone number in the medical record could not get through, a home visit was made according to the family address in the record. If the patient's survival information still could not be obtained, the patient was excluded from

the mortality analysis.

### Statistical analysis

Continuous variables were described as mean±standard deviation. Categorical variables were presented in terms of their frequency. The gender difference in one-year mortality was tested using Pearson Chi squared method. The independent sample *t* test was used to compare the mean level of blood parameters between male and female patients. An univariate analysis of variance was performed on data from patients who survived one year postoperatively and on data from those who did not. The relative contribution of the variables to mortality was identified using a multiple logistic regression analysis with a forward stepwise variable selection. The results of multivariate analyses were expressed in terms of hazard ratio derived from the estimated regression coefficients, with 95% confidence intervals. Statistical analysis was performed using the Statistical Package for the Social Sciences 17.0 version for Windows program (SPSS Inc, Chicago, IL, USA). *p*-values <0.05 were considered significant. The optimal cut-off points of the significant factors were determined using receiver operating characteristic (ROC) curves.<sup>26</sup> This involved plotting the true-positive rate (sensitivity) against the false-positive rate (1-specificity) for possible cut-off scores. Each point on the ROC plot represented a sensitivity/specificity pair corresponding to a particular decision threshold. The highest sensitivity/specificity combination point on the ROC curve represents the optimal cut-off point of the predictors.

### RESULTS

One hundred and seventy four patients with intertrochanteric fracture over the age of 65 years were admitted during the study period. Nutritional and demographic data were available for all 174 patients, of whom 116 (67%) were women and 58 (33%) were men. The gender differences in mean age and blood parameters at admission are shown in Table 1. The only significant difference index is haemoglobin where the level of haemoglobin in male patients is higher than that in female patients. The mean albumin for all patients was 31.0±5.3 g/L (range: 18 to 43; median 31) with an albumin level less than 35.0 g/L occurred in 127 (73%) patients. The mean TLC was (1.19±0.51)×10<sup>9</sup> cells/L [range: (0.29 to 3.47)×10<sup>9</sup> cells/L; median 1.1×10<sup>9</sup> cells/L] with 141 (81%) patients lower than 1.50×10<sup>9</sup> cells/L. Fifty two percent of the patients had both albumin and TLC levels lower than normal.

Seven patients receiving non operative treatment and

**Table 1.** Univariate analysis comparing the age and blood parameters between elderly male and female patients with intertrochanteric fracture

Variable	Men	Women	<i>p</i> -value
Age	79.4±7.34	81.8±7.46	0.067
Serum albumin (g/L)	31.1±5.70	30.8±5.00	0.674
Total lymphocyte count (×10 <sup>9</sup> /L)	1.16±0.48	1.18±0.55	0.804
Haemoglobin (g/L)	107±20.1	100±13.2	0.027
Serum potassium (mmol/L)	3.93±0.40	3.84±0.45	0.255
Serum calcium (mmol/L)	2.13±0.12	2.12±0.14	0.975

Variables were reported as mean±standard deviation.

**Table 2.** Univariate analysis comparing survivors and non-survivors 1 year after surgery in elderly intertrochanteric fracture patients

Variable	Die	Live	<i>p</i> -value
Gender, men (%)	18 (35.3)	33 (64.7)	0.399
Age	83.1±7.59	80.0±7.25	0.018
Serum albumin (g/L)	27.7±4.15	32.3±5.06	<0.0001
Total lymphocyte count (×10 <sup>9</sup> /L)	1.00±0.45	1.26±0.54	0.006
Haemoglobin (g/L)	99.7±14.9	104±16.6	0.146
Serum potassium (mmol/L)	3.95±0.50	3.84±0.40	0.173
Serum calcium (mmol/L)	2.09±0.14	2.15±0.12	0.010

**Table 3.** Multiple logistic regression analysis for one-year mortality after surgery in elderly intertrochanteric fracture patients

Variable	Regression coefficient	Standard error	Test statistics
Gender, men	0.554	0.442	1.57
Age	-0.042	0.032	1.71
Serum albumin (g/L)	0.202	0.050	16.0
TLC (×10 <sup>9</sup> /L)	1.361	0.509	7.14
Haemoglobin (g/L)	0.004	0.014	0.067
Serum potassium (mmol/L)	-0.879	0.497	3.12
Serum calcium (mmol/L)	-0.532	1.819	0.085

CI: confidence interval; TLC: total lymphocyte count.

two patients treated with DHS stabilization were excluded from the mortality study. Sixteen patients were lost to follow up one year after surgery leaving survival data for 149 patients (86%). The mean age of the patients was 80.9±7.5 (range: 65 to 97; median 82). Females (n=98; 66%) outnumbered males (n=51; 34%). Forty six patients died within one year postoperatively and the overall mortality rate was 31%. Two patients died of pulmonary infection during their hospital stay and both of them had low albumin and TLC levels at admission. One hundred eleven (74%) patients were malnourished based on albumin levels less than 35.0 g/L of whom 45 (41%) died. Only one patient (3%) died with admission albumin >35.0 g/L (*p*<0.001). There was no difference in one-year mortality between the patients (23%, 6/26) with TLC ≥1.50 ×10<sup>9</sup> cells/L and those (31%, 40/123) with TLC <1.50×10<sup>9</sup> cells/L (*p*=0.344). Demographic characteristics and blood parameters of the survivors and non-survivors are summarized in Table 2. Variables comparison between the two groups (survival at one year post surgery or not) found that age (*p*=0.018), serum albumin level (*p*<0.001), TLC level (*p*=0.006) and serum calcium level (*p*=0.010) had significant differences. However, multiple logistic regression analysis with stepwise variable selection showed that only serum albumin level (*p*<0.001, hazard ratio 1.22) and TLC level (*p*=0.008, hazard ratio 3.90) at hospital admission had significant association with one-year mortality (Table 3).

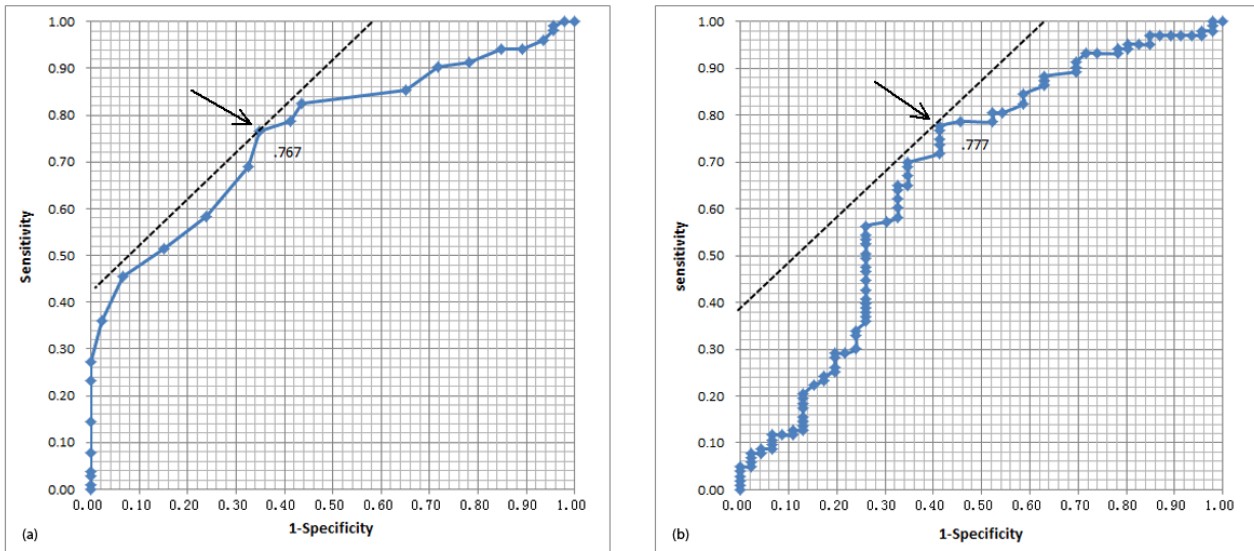
Based on the ROC curves, the optimal cut-off points for serum albumin level and TLC level were 29.5 g/L (sensitivity 76.7%; specificity 65.2%) and 0.925×10<sup>9</sup> cells/L (sensitivity 77.7%; specificity 58.7%) respectively (Figure 1). If the patients were classified based on their albumin level at 30.0 g/L, the one-year mortality in patients with albumin equal or higher than 30.0 g/L (16.8%, 16/95) was significantly lower than those below 30.0 g/L (55.6%, 30/54, *p*<0.001). When the patients were classified based on their TLC level at 1×10<sup>9</sup> cells/L,

the mortality in patients with TLC equal or higher than 1.00×10<sup>9</sup> cells/L (18.2%, 16/88) was significantly lower than those below 1.00×10<sup>9</sup> cells/L (49.2%, 30/61, *p*<0.001).

## DISCUSSION

The incidence of hip fracture is increasing, paralleling the increased longevity of the global population.<sup>27</sup> Almost 9 of 10 hip fractures occur in patients older than 65 years and approximately half will be intertrochanteric fractures. Many studies have investigated the mortality of hip fractures in elderly patients and most include all types of hip fractures grouped together. It is generally known that intertrochanteric fracture patients are slightly older and sicker than femoral neck fracture patients.<sup>28</sup> Survival studies focusing on fracture type have demonstrated that intertrochanteric fracture patients have a higher postoperative mortality rate than those with femoral neck fracture.<sup>24,28,29</sup> Since so many differences exist in patient characteristics, surgical management and outcomes between femoral neck fracture and intertrochanteric fracture, it is reasonable to single out the specific fracture group for risk predictor evaluation. Here, we focus on the relationship between the nutritional status and long term mortality following surgery in an aged Chinese patients group admitted with a femur intertrochanteric fracture. We found a high rate of malnutrition among these patients based on the serum albumin and TLC levels at admission, and we demonstrated that both of these parameters can significantly predict one-year mortality in this patients group.

The increased prevalence of poor nutritional status among older adults with hip fractures compared to the general population has been well documented.<sup>7-11,13,14,16,18-21</sup> Malnutrition combined with the catabolic response to trauma or surgery, leads to muscle wasting and has been associated with post-operative complications,<sup>18</sup> increased length of stay<sup>15,17</sup> and mortality.<sup>14,19-21</sup> However most of



**Figure 1.** Receiver operating characteristic curves for (a) serum albumin level and (b) total lymphocyte count. Black arrows indicate the optimal cut-off points of 29.5 g/L for serum albumin level and  $0.925 \times 10^9$  cells/L for total lymphocyte count corresponding to the highest sensitivity/specificity combination. Dotted line indicates reference line (0 diagnostic efficiency).

these studies were based on patients from developed western countries. The nutritional status of hip fractured patients from a developing country such as China with a different healthcare delivery system is still unclear. In the present study, we employed admission serum albumin and TLC level as markers of nutrition assessment. Both of them are routine preoperative laboratory tests in our hospital and numerous studies have used a combination of albumin and TLC levels to identify whether the patients are under a state of protein energy malnutrition.<sup>14,16,19</sup> According to the widely accepted reference value, 35.0 g/L for albumin and  $1.50 \times 10^9$  cells/L for TLC, we observed 73% of the patients included in this study with a low albumin level, 81% with a low TLC level and 52% with both under the reference values. The incidence of malnutrition is much higher than that reported by Koval et al. They evaluated nutritional status of 490 hip fracture patients aged 65 years and older in the United States, and reported 18% patients with low albumin, 57% with low TLC, and only 9% having both parameters below the normal value.<sup>16</sup> More recently, another study from Ireland using serum albumin and TLC as the sole markers in hip fracture patients aged over 60 years, and reported 66% patients with low albumin level, 74% with low TLC level, and 51% with both low albumin and TLC levels.<sup>26</sup> The proportion of intertrochanteric fracture in both studies was about 50%, but neither had analyzed the difference of nutritional status by fracture type. Although the data from Ireland are comparable to the present study, we admit that the regional difference of nutritional status in aged people is unavoidable because of the inconsistency in economy, culture, hygiene and diet. We did not find any gender differences in age or nutritional status and it is not surprising that male patients have a higher mean haemoglobin level than women. Because previous studies have demonstrated a relationship between low haemoglobin level and increased mortality in hip fracture patients,<sup>22,30</sup> we included this parameter in the current study. However, we failed to discover haemoglobin level as a predictor of

one-year mortality in this patient group.

Mortality rate observed in this study is comparable with those reported in literature for hip fracture where the one-year mortality range from 8.4% to 36%.<sup>21</sup> One prospective study among elderly women with a hip fracture was conducted to determine whether the survival outcome differed by fracture type. They revealed one-year mortality in intertrochanteric fracture patients at 28% which was markedly higher than their 11% mortality in femoral neck fracture patients.<sup>24</sup> The relationship of fracture type and mortality in geriatric hip fracture patients was not specifically addressed in a systematic review by Butler et al.<sup>31</sup> Thus, the impact of fracture type to postoperative mortality in hip fracture patients needs further evaluation. Several investigators have demonstrated the predictive value of serum albumin and TLC on postoperative mortality in hip fracture patients. Koval et al<sup>16</sup> found that an albumin level below 35.0 g/L was predictive for increased length of stay and in-hospital mortality and a total lymphocyte count below  $1.50 \times 10^9$  cells/L was predictive for one-year mortality. They also reported that patients with abnormal albumin and total lymphocyte counts were 3.9 times more likely to die within one year after surgery. In a similar study by O'Daly et al, survival analysis of 200 patients with hip fracture showed patients with low albumin and TLC levels were more likely to die within 12 months but only serum albumin and age were found to be significant independent prognostic factors.<sup>14</sup> On the contrary, a study from Singapore evaluating the risk factors for mortality in elderly patients with hip fractures revealed patients with low albumin and TLC level had a lower mean survival time. However, the albumin level lost its predictive value of mortality after multivariate analysis.<sup>28</sup> Recently, a systematic review and meta-analysis concluded that low albumin and TLC just had moderate or limited evidence in predicting mortality following hip fracture surgery<sup>6</sup> which indicates that further studies are needed to reevaluate their predictive values.

Based on the ROC curve results, we get an optimal cut-

off level of 30.0 g/L for albumin and  $1.0 \times 10^9$  cells/L for TLC, respectively. It helps to identify, pre-operatively, those patients who will be at high risk following surgery. In a prospective study, Foster et al<sup>19</sup> reported a mortality rate of 70% in hip fracture patients with albumin less than 30.0 g/L, compared with a mortality rate of 18% in those  $\geq 30.0$  g/L. They suggested a more aggressive approach to nutritional support for those with a serum albumin below 30.0 g/L. Similar results were obtained later in another prospective cohort study including 248 hip fracture patients aged 70 and older, in which Pioli et al found that albumin  $< 30.0$  g/L was the only significant predictor of in-hospital mortality.<sup>20</sup> More recently, a survival study in Japan revealed a different albumin cut-off point of 36.0 g/L for predicting the 4-year postoperative mortality in hip fracture patients.<sup>21</sup> However, the patients included in this study were younger and seemed having a good nutrition situation with a mean albumin level of 35.4 g/L. We believe that the different health level of the patients leads to the different cut-off point value and the warning line should be established based on the local data.

There are several limitations in this study. First, it is a retrospective study, and thus completeness of medical records was limited with regard to preoperative comorbidities, functional status and cognitive level which were found to be significant factors of one year mortality.<sup>3,20,22</sup> Future studies should include a comprehensive assessment of patient characteristics to investigate the strength of albumin and TLC as predictors of mortality in hip fractured patients. The unmeasured differences in medical therapies may contribute to the results. Likewise, nutritional intervention is also very important. It has been shown to modify nutritional parameters and albumin levels, but it still not regularly managed for the hip fractured patients in our hospital. The impact of surgical delay was not included, because surgical decision does not always completely depend on the patients' condition. In the health delivery system of China, patients sometimes had to wait for an extra bed before admission, even for an emergency traumatic case. Sometimes the surgery had to be postponed, because all members of the patient's family did not reach a consensus. The multivariate Cox regression should be a better statistical approach for survival analysis if we can get the exact death time of the patients. The postoperative complication, the functional outcome and the cause of death were not recorded in this study which is essential for a fracture repair. The relationship between the nutritional status and functional recovery will be studied in the future and is not the purpose of this study.

In conclusion, serum albumin and TLC are useful clinical markers for nutritional assessment and effective predictors of one-year mortality in aged patients with intertrochanteric fracture. In combination, they provide valuable information, helping to identify those patients who are candidates for interventions which might reduce their risk of premature death. Whether a strategy of nutritional support to improve serum albumin could improve survival rate in these high-risk patients warrants further evaluation.

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#### AUTHOR DISCLOSURES

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## Original Article

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### 血液营养指标能够预测高龄股骨粗隆间骨折患者术后一年死亡率

**背景和目的：**观察术前营养相关的血液指标对中国 65 岁以上股骨粗隆间骨折患者内固定术后一年死亡率的预测价值。**方法和研究设计：**将入院时患者血清白蛋白水平及全血淋巴细胞计数作为评价患者营养状况的主要指标，共 174 例高龄股骨粗隆间骨折患者纳入了本研究并进行了营养评估，采用单变量分析方法比较营养指标的性别差异，采用多变量 logistic 回归分析评估不同指标对患者术后一年死亡率的预测价值。**结果：**术前平均白蛋白水平为 31.0 g/L，其中 73% 的患者低于正常水平 35 g/L；术前平均淋巴细胞计数水平为  $1.19 \times 10^9$  cells/L，其中 81% 的患者低于正常水平  $1.50 \times 10^9$  cells/L。不同性别患者的白蛋白和淋巴细胞计数没有显著差异，接受手术治疗并获得最终随访的 149 例患者，总体死亡率为 31%，其中男性患者为 35%，女性患者为 29%。相对于死亡的患者，存活的患者更年轻、术前具有更高的白蛋白、淋巴细胞计数和血钙水平。然而多因素回归分析显示只有白蛋白水平和淋巴细胞计数是预测患者一年内死亡的独立危险因素。受试者操作特征曲线显示白蛋白和淋巴细胞计数两项指标的临界值分别为 29.5 g/L 和  $0.925 \times 10^9$  cells/L。**结论：**营养不良在中国高龄股骨粗隆间骨折人群中是一个普遍现象。患者入院时的血清白蛋白水平和血液淋巴细胞计数对患者术后一年的死亡率具有预测价值。

**关键词：**营养状况、股骨粗隆间骨折、死亡率、老年人、白蛋白