Original Article

Correlation between C-reactive protein/albumin and contralateral hip refracture after total hip arthroplasty in elderly patients with hip fractures

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Background: There is still a risk of refracture of the contralateral hip after total hip replacement, to analyze the expression of C-reactive protein (CRP) and albumin (Alb) in elderly patients with contralateral hip refracture after total hip arthroplasty (THA), and to determine its correlation with the risk of post-surgery refracture and guide the prediction of the risk of contralateral hip fracture in the future.

Methods: The medical records of elderly patients who suffered hip fracture and underwent THA at our hospital between July 2016 and July 2019 were reviewed, and 224 eligible patients were finally enrolled. The patients were divided into the refracture group and the control group according to the incidence of contralateral hip refracture. The baseline data of the two groups were compared, and all relevant laboratory tests were performed before surgery. The serum levels of CRP and Alb were compared, along with the CRP/Alb ratio, between the two groups to establish whether CRP/Alb is a predictor for post-surgery contralateral hip refracture in elderly patients.

Results: Twenty (8.93%) of the 224 patients suffered post-surgery contralateral hip refracture. There were no significant differences in the baseline data of the refracture and control groups ($P>0.05$). However, the patients who experienced refracture had significantly higher CRP levels and lower Alb levels compared with the controls, resulting in an elevated CRP/Alb ratio in the patients with refracture ($P<0.05$). Serum CRP level was negatively correlated to that of Alb ($r=-0.443$, $P<0.001$). The linear regression equation was $Y=2.718–0.598X$, indicating that the CRP/Alb ratio is a risk factor for contralateral hip refracture in elderly hip fracture patients following THA ($P<0.05$). The area under the receiver operating characteristic (ROC) curve of the CRP/Alb ratio as a predictor for post-THA contralateral hip refracture was 0.841 (95% CI: 0.702–0.914). The optimal cutoff value was 1.12, which corresponded to high specificity and sensitivity of 0.782 and 0.945, respectively, and the Youden index was 0.727.

Conclusions: Serum CRP level is closely associated with Alb level in elderly hip fracture patients, and the CRP/Alb ratio is a risk factor for post-THA contralateral hip refracture. Therefore, preoperative measurement of serum CRP/Alb level can assist with predicting the risk of post-THA refracture in elderly hip fracture patients.

Keywords: Hip fracture; elderly patients; total hip arthroplasty (THA); contralateral hip refracture; C-reactive protein/albumin (CRP/Alb); correlation analysis

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Introduction

Despite recent improvements in the one-year survival rates of hip fracture patients after hip replacement and the ability of most patients to recover to their pre-fracture state, the risk of post-surgery hip refracture remains high (1,2). After 1 year, the mortality rate among elderly hip fracture patients with contralateral hip refracture after total hip arthroplasty (THA) is 24.1% (3). C-reactive protein (CRP) is the main inflammatory marker, and it has been used in the prognostic evaluation of many diseases such as orthopedic infections and trauma. Related studies have found that abnormal changes in CRP levels and hip replacement in patients with hip fractures poor prognosis is related (4). Serum albumin levels reflect the nutritional status of patients. Preoperative serum albumin (Alb) expression has been shown to be associated with many postoperative complications (5), and studies have found that hip replacement surgery in elderly hip fracture patients post-adverse prognosis is significantly associated with preoperative serum albumin levels (6). However, the application of the ratio of serum CRP to Alb in hip fracture hip replacement is rare, especially whether the ratio between the two is related to the recurrence of the contralateral hip after operation in elderly hip fracture patients, and there are not many relevant studies. This study focused on the observation of CRP/Alb expression in contralateral hip re-fractures in elderly hip fracture patients after total hip replacement. The aim is to explore the correlation between CRP/Alb expression and contralateral hip re-fractures in patients. The report is as follows.

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/apm-20-855).

Methods

Subjects

The medical records of elderly hip fracture patients who received THA at our hospital between July 2017 and July 2019 were reviewed. The inclusion criteria were as follows: (I) complete medical records and follow-up data available; (II) new, Garden grade III–IV unilateral femoral neck fracture; (III) >60 years old; (IV) non-high-energy traumatic hip fractures caused by walking injuries, sprains, or misstep injuries; (V) total hip replacement surgery performed by the same group of anesthesiologists and chief surgeons; and (VI) normal cognitive function throughout the perioperative and follow-up periods. Patients who met any of the following criteria were excluded: (I) pathological fractures caused by bone tumors or bone cysts; (II) had received conservative treatment; (III) history of hip fractures; (IV) previous contralateral hip surgery; and (V) incomplete follow-up data.

General information

A total of 224 elderly hip fracture patients (105 males and 119 females) who underwent THA were enrolled. The patients had a mean age of 71.12±6.0 [60–85] years old. The mean duration between fracture and surgery was 4.02±1.61 [1–7] days. All patient data were collated and reviewed after informed consent was obtained from the patients. The study complied with the relevant medical ethics regulations.

Study methods

Grouping

All patients were followed up for a period of 1 year after THA. In the event of a patient experiencing a new trauma or fracture-related symptoms during this period, they were admitted to the hospital to undergo imaging tests and consultation. The patients with or without confirmed contralateral hip fracture were assigned to the refracture group and the control group, respectively.

Baseline data collection

Preoperative baseline data was collected using a questionnaire which took into account variables such as gender, age, fracture classification, time from fracture to surgery, and comorbidities (e.g., diabetes, hypertension, heart disease, chronic lung disease, or systemic diseases). Surgical information including operation time, anesthesia classification, and intraoperative blood loss was also recorded.

Laboratory tests

After fasting overnight, peripheral blood (5 mL) was collected from the basilic vein of the patients, and routine hematological indices, including white blood cell, platelet, and red blood cell counts and hemoglobin levels, were measured using an automated blood analyzer. The blood samples were centrifuged at 3,000 rpm for 15 minutes to collect serum. Subsequently, serum CRP and Alb levels were measured using the specific ELISA kits (Shenzhen Jingmei Biotech Co. Ltd., China), and the CRP/Alb ratio was calculated.

Table 1 Comparison of baseline data between the refracture group and the control group

Baseline data	Refracture group (n=20)	Normal group (n=204)	Statistics	P
Gender (number of cases)	–	–	–	–
Male/female	9/11	96/108	χ^2=0.031	0.860
Age	72.02±7.11	70.90±6.11	t=0.771	0.442
Time from fracture to surgery (days)	4.24±1.52	3.97±1.48	t=0.777	0.438
Fracture classification (number of cases)	–	–	–	–
Operation time (hours)	2.69±1.01	2.60±0.95	t=0.402	0.688
ASA anesthesia classification (number of cases)	–	–	–	–
I/II/III	5/7/8	20/30/30	Z=0.141	0.874
Intraoperative blood loss (mL)	421.45±40.32	420.51±36.75	t=0.108	0.914
White blood cell count ($\times10^9$/L)	8.83±3.41	9.01±3.65	t=0.212	0.833
Platelet count ($\times10^9$/L)	200.02±51.12	205.21±50.24	t=0.440	0.660
Red blood cell count ($\times10^{12}$/L)	3.51±0.71	3.71±0.75	t=1.143	0.254
Hemoglobin (g/L)	111.24±14.41	108.12±13.12	t=0.716	0.478
Femoral neck bone density (g/cm^2)	0.66±0.08	0.67±0.06	t=0.689	0.492

Statistical analysis

Data were processed using SPSS20.0 statistical software [IBM Corporation (SPSS Co.)] and tested for normal distribution. The normally distributed measurable data were expressed as $\bar{x}$±s and compared using the independent samples *t*-test. Count data were expressed as percentages and compared using the χ^2 test. Binary Logistic regression analysis was used to test the effect of CRP/Alb on contralateral hip re-fracture after total hip replacement. The area under the receiver operating characteristic (ROC) curve was calculated to assess the predictive value of CRP/Alb. Statistical significance was indicated when P<0.05.

Results

Incidence of refracture

Of the 224 elderly hip fracture patients who underwent THA, only 20 (8.93%) experienced contralateral hip refracture.

Comparison of baseline data between the refracture and control groups

There were no significant differences in gender, age, time from fracture to surgery, fracture classification, comorbidities, surgical conditions, white blood cell count, platelet count, red blood cell count, hemoglobin, and bone density between the refracture and control groups (P>0.05; *Table 1*).

Preoperative serum CRP and Alb levels, and CRP/Alb ratio differed between the two groups

The refracture group had significantly higher preoperative serum CRP levels, lower Alb levels, and a higher CRP/Alb ratio compared to the controls (P<0.05; *Table 2*).

Preoperative serum CRP and Alb levels were negatively correlated in the elderly patients with hip refracture

Pearson's correlation coefficient demonstrated that serum CRP level was negatively correlated with Alb level in the elderly hip fracture patients (r=–0.443, P<0.001). The correlation scatterplot is shown in *Figure 1*.

Linear binary logistic regression analysis of the effect of pre-operative CRP/Alb ratio on contralateral hip re-fracture in elderly hip fractures

The preoperative CRP/Alb ratio was used as a covariate, and the recurrence of contralateral hip fracture in elderly

Table 2 Comparison of preoperative serum CRP and Alb levels, and CRP/Alb ratio between the refracture and control groups ($\bar{x}\pm s$)

Group	n	CRP (mg/L)	Alb (g/L)	CRP/Alb
Refracture group	20	45.21±5.93	32.94±3.38	1.47±0.27
Normal group	204	30.02±5.55	37.83±2.79	1.02±0.24
t	–	11.611	7.335	7.913
P	–	<0.001	<0.001	<0.001

CRP, C-reactive protein; Alb, albumin.

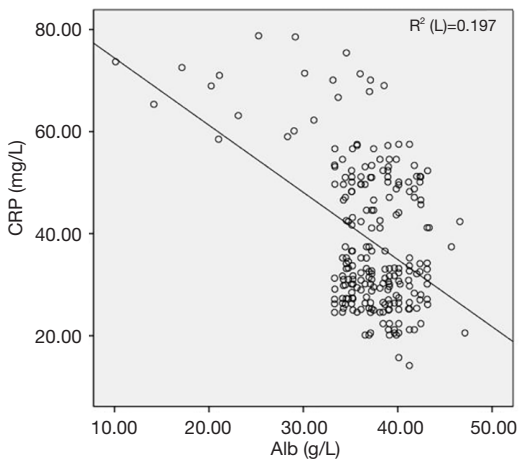

Figure 1 Correlation scatterplot of preoperative serum CRP and Alb levels in elderly patients with hip fractures. CRP, C-reactive protein; Alb, albumin.

hip fracture patients was used as the dependent variable (1 = occurred, 0 = not occurred). The results of binary logistic regression analysis showed that high CRP/Alb ratio may be a risk factor for contralateral hip re-fracture after total hip replacement in elderly hip fracture patients (P<0.05; *Table 3*).

Preoperative CRP/Alb ratio has a high predictive value for contralateral hip refracture in elderly hip fracture patients

A ROC curve was plotted with incidence of post-THA hip refracture as the state variable. The area under the curve for the CRP/Alb ratio was 0.841 (95% CI: 0.702–0.914), and the optimal cutoff value was 1.12. The corresponding specificity and sensitivity were 0.782 and 0.945, respectively, and the Youden index was 0.727 (*Figure 2*); thus, preoperative CRP/Alb has high predictive ability for post-THA refracture.

Discussion

Older patients carry a higher risk of contralateral hip refracture following hip arthroplasty due to bone loss. Besalduch *et al.* (7) reported an incidence of 10.8% for post-surgery contralateral hip fractures in the elderly population, which is close to the 8.4% observed in a similar Chinese study (8). The incidence of post-THA contralateral hip refracture in our cohort was 8.93%, which is consistent with these findings. Because of the increased risk of death for patients with post-surgery contralateral hip fracture, it is vital that the causative and predictive factors with relatively high specificity and sensitivity are identified, so that refracture can be prevented and treated early (9,10). Despite the results of previous studies showing satisfactory prediction of the risk of post-surgery contralateral hip refracture through acute physiological and chronic health evaluation systems, surgical severity, physiological ability, and surgical invasiveness scores (11,12), the complexity and diversity of these indices often limit their application in a clinical setting, especially in primary hospitals. Therefore, a simpler and more effective laboratory-based indicator is urgently needed to predict and evaluate this risk.

Studies have revealed that the concurrence of a fracture and trauma or infection is closely associated with the severity of the fracture. CRP, a reliable marker of trauma/infection-related inflammation, is an important indicator of orthopedic infection following surgery (13,14). A recent study showed that an elevated level of preoperative CRP is a primary risk factor of post-THA death in older patients with hip fractures (15), indicating that it may also be associated with increased incidence of post-surgery contralateral hip refracture. Serum Alb is an important indicator of protein/energy consumption and is routinely used to evaluate perioperative nutritional status (16). As a standard laboratory test, several studies have used serum Alb detection as a prognostic indicator in elderly patients

Table 3 Linear regression analysis of the effect of CRP/Alb ratio on contralateral hip refracture in elderly hip fracture patients

Item	B	Standard error	Wald	P	OR	95% CI of B
Constant	6.589	1.830	12.948	<0.001	–	–
CRP/Alb	4.902	1.421	11.906	0.001	134.604	8.312–217.783

CRP, C-reactive protein; Alb, albumin.

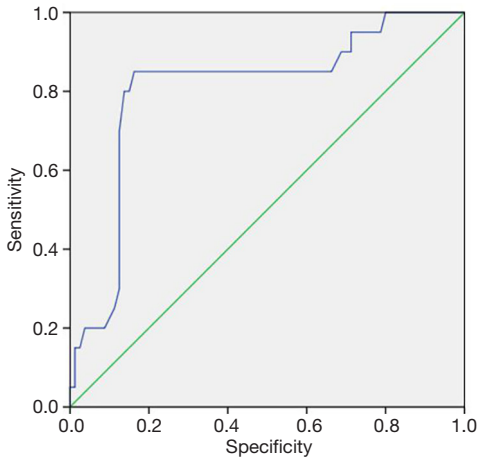

Figure 2 ROC curve showing the predictive value of preoperative CRP/Alb ratio for contralateral hip refracture in elderly hip fracture patients. ROC, receiver operating characteristic; CRP, C-reactive protein; Alb, albumin.

with hip fractures. Low perioperative serum Alb level is a major factor affecting the length of hospital stay, recovery of normal activities, and the risk of postoperative death among such patients; this is evidenced by the correlation between poor nutritional status during the perioperative period and slower postoperative recovery (17,18). Thus, low serum Alb level is also a factor potentially related to the incidence of post-surgery contralateral hip refractures.

As indicators of the immunological and nutritional status respectively, CRP and Alb levels have limited clinical utility when applied separately. In fact, the ratio of CRP to Alb is more accurate as an indicator of both inflammatory and nutritional status compared to either index (19,20). Because the level of perioperative or postoperative detection may be affected by the operation itself or medication during the perioperative period, this study mainly observes the impact of the preoperative CRP/Alb on patients, and has ensured the credibility of the results. The results of this study showed that compared with the normal group, the patients in the contralateral hip re-fracture group had higher preoperative blood CRP levels, lower Alb levels, and higher CRP/Alb ratio, and the contralateral hip re-fracture group patients showed higher CRP and Alb levels. Negative correlation, that was, with the increase of CRP, the Alb of the patient decreased. It was speculated that the increase in systemic inflammatory response before surgery may be the cause of poor nutritional status. As the nutritional status continued to deteriorate, the systemic inflammatory response also increased, both Interactions were causal to each other and therefore affect the prognosis. Linear regression analysis indicated that the CRP/Alb ratio is a potential risk factor for post-THA contralateral hip refracture in elderly hip fracture patients, and its high predictive value was confirmed by ROC curve analysis. Altogether, these findings suggest that preoperative serum CRP and Alb levels, and the CRP/Alb ratio can predict the risk of post-surgery contralateral hip refracture in older people, this risk can be reduced by nutritional fortification and attenuation of systemic inflammatory response before surgery. However, this study also has certain limitations. First, the study was a retrospective single-center study with limited medical record data, especially the small sample size of the contralateral hip re-fracture group. Second, the study did not fully consider other factors. The possible impact and the results obtained may deviate from the actual. These limitations should also be verified by prospective, large sample and long-term research in the future.

In summary, serum CRP level is correlated with Alb level in elderly hip fracture patients, and the CRP/Alb ratio is a risk factor for post-THA contralateral hip refracture. Therefore, to predict the risk of post-THA contralateral hip refracture, the preoperative serum CRP/Alb ratio should be measured in elderly hip fracture patients.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All patient data were collated and reviewed after informed consent was obtained from the patients. The study complied with the relevant medical ethics regulations. The Affiliated Hospital of North Sichuan Medical College [2017ER (A) 034].

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