Preoperative High-Protein Diet Can Improve The Serum Albumin Levels of Patients Undergoing Total Knee Arthroplasty

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Research Article

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Abstract

Background: Preoperative hypoproteinemia are risk factors for complications in patients undergoing total knee arthroplasty (TKA). However, the relationship between preoperative albumin levels and postoperative use of albumin is unclear, as are the effects of a high-protein diet on preoperative serum albumin levels for these patients.

Methods: We retrospectively enrolled 660 patients who underwent primary TKA from January to December 2019, of whom 97 received postoperative albumin and 563 did not. Logistic and restrictive cubic spline regression analyses were used to explore the relationship between preoperative serum albumin levels and postoperative albumin use. Additionally, 88 patients undergoing primary TKA were educated to follow a high-protein diet during the preoperative waiting period from January to July 2020. From these 88 patients, data from laboratory tests on the day of the outpatient visit and admission were collected and compared to evaluate the effect of high-protein diet on preoperative serum albumin levels.

Results: Higher preoperative serum albumin levels were negatively associated with risk of postoperative albumin use (relative risk 0.725, 95% confidence interval 0.666-0.789), and the risk of needing postoperative albumin decreased with increasing preoperative albumin level with a negative dose-response relationship ($P_{\text{overall}} < 0.001$; $P_{\text{nonlinear}} = 0.186$). After an average of 39.05 ± 22.78 days on a high-protein diet, the albumin levels on admission (46.04 ± 2.49 g/L) were significantly higher than on outpatient (42.79 ± 4.09 g/L), while the biomarkers of liver and kidney function and lipid metabolism did not differ significantly between the two time points.

Conclusions: Preoperative albumin levels were highly associated with postoperative albumin use, showing an obvious dose-response relationship. Preoperative high-protein diet could improve the albumin levels in patients undergoing TKA.

Trial registration: The study was registered in the Chinese Clinical Trial Registry (registration no. ChiCTR2000034978) on July 26, 2020.

Background

Total knee arthroplasty (TKA), a type of total joint arthroplasty (TJA), is a successful surgical treatment for end-stage knee diseases, and its frequency is rapidly increasing with population aging [1, 2]. Malnutrition is a common but often overlooked problem in surgical patients, especially for the elderly [3, 4]. Numerous studies have shown that malnutrition is associated with an increased risk of complications after TKA, including persistent wound drainage, delay of wound healing, superficial surgical site and even deep prosthetic joint infections, as well as intensive care unit admission [5, 6]. Albumin is the most abundant protein in the human plasma, and is considered a reliable and sensitive biomarker of protein status and malnutrition [7, 8]. Albumin, due to its short half-life, is frequently used to assess nutritional status in real time and detect acute nutritional changes [9]. Similar to malnutrition, low serum albumin level is associated with various postoperative complications following TJA, which include pulmonary

infection, renal impaired, superficial and deep infections, myocardial infarction, unplanned intubation, and even mortality [10]. Low serum albumin level is also related to increased treatment costs, longer length of stay, and higher risk of readmission [11].

Human albumin solution (HAS), a blood product, is frequently used to correct hypoproteinemia. However, a study including more than 1 million patients from 510 hospitals in the United States showed that HAS use was associated with an increased risk of thromboembolic, cardiac and pulmonary complications, acute renal failure, and intensive care unit admission [12]. Furthermore, HAS use is quite expensive, placing a substantial financial burden on the health care systems [10]. One study [11] concluded that each 1 g/dL reduction in preoperative serum albumin increased direct costs of TJA on average by 1,282 United States dollars.

Preoperatively correcting hypoalbuminemia and increasing albumin levels may be an effective way to reduce postoperative albumin use, since the elective nature of TKA. Therefore, this study was performed to illustrate the effect of preoperative albumin levels on human albumin use and to determine the effect of high-protein diet during the preoperative waiting period on serum albumin levels in patients scheduled to undergo TKA.

Methods

Study design and patients

This was a single-center retrospective study, and the protocol was approved by the Ethics Committee of West China Hospital of Sichuan University (approval no. 2020-804). The study was registered in the Chinese Clinical Trial Registry (<http://www.chictr.org.cn/edit.aspx?pid=57039&htm=4>; registration no. ChiCTR2000034978). Written informed consent was deemed unnecessary by the ethics committee because the study had no any adverse effect on the rights and health of the subjects, and patient privacy was strictly protected during the study process.

The participants of the study consisted of two cohorts. First, patients (n = 660) who underwent primary TKA due to primary osteoarthritis or rheumatoid arthritis in our hospital from January to December 2019 were enrolled to investigate the effect of preoperative albumin levels on HAS use. Second, patients (n = 88) who underwent primary TKA from January to July 2020 were included to evaluate the effect of a high-protein diet on preoperative serum albumin levels; those patients were educated to eat a high-protein diet during the preoperative waiting period. The criterion for postoperative use of HAS was serum albumin concentration under 35 g/L. Patients were excluded if they had been diagnosed with hemophilia, tuberculous arthritis, liver and/or kidney disease, or if relevant data for them were missing.

Outpatient education and perioperative treatment

When a patient decided to undergo TKA for severe knee primary osteoarthritis or rheumatoid arthritis at the outpatient clinic, admission times were booked. At the same time, the patient's diet and nutritional

status were assessed according to the levels of hemoglobin and serum albumin. If hemoglobin < 140 g/L or albumin < 48 g/L, the patients were informed that they needed to increase the proportion of proteins in their diet during the preoperative waiting period in order to prepare for the surgery. The recommended daily diet was as follows: at least 3 eggs (fried eggs were not recommended) and 50 g lean meat, which contains about 35 g of protein. If they reported poor appetite, patients received drug that promotes gastric motility. In addition, all patients were treated according to multimodal perioperative care pathways described in the Enhanced Recovery after Surgery protocol during the perioperative period [13].

Data collection and study outcomes

For the 2019 cohort, data were collected on demographic characteristics including sex, age, body mass index (BMI); clinical characteristics, including diagnosis primary osteoarthritis or rheumatoid arthritis; comorbidities, including hypertension, diabetes, coronary heart disease, and chronic obstructive pulmonary diseases; results of laboratory tests on the day of admission, including hemoglobin, serum albumin, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), and use of postoperative HAS.

For the 2020 cohort, besides the previously mentioned demographic and clinical characteristics, data were also collected on waiting time before admission; and results of laboratory tests on the day of outpatient visit, including albumin, globulin hemoglobin, hematocrit, biomarkers of liver and kidney function, and lipid metabolism.

Statistical analyses

Continuous variables were presented as mean $\pm$ standard deviation ($\bar{x} \pm SD$), while categorical variables were shown in frequency (proportion). The relationship between HAS use (treated as a binary variable) and preoperative serum albumin levels (treated as a continuous variable) was expressed as relative risk (RR) with 95% confidence interval (CI). A crude model of HAS use regarding the preoperative serum albumin levels was built using univariate analyses. Logistic regression analyses were used to adjust other variables included in our analyses. The correlations among the covariates included in the logistic regression were quantified by Spearman's rank correlation analysis [14]. Furthermore, restrictive cubic spline regression analyses were used to detect the dose-response relationships between serum albumin levels tested on the day of admission and postoperative albumin use [15]. The dose-response was analyzed with R version 3.6.1 (R Foundation for Statistical Computing). The paired-samples T test was used to compare biomarker differences between admission and outpatient. A value of $P < 0.05$ was considered to indicate statistical significance. All data analyses were performed using SPSS version 21 software (IBM, Armonk, NY, USA).

Results

Baseline characteristics of patients

A total of 748 patients were included in our study, of whom 660 patients underwent TKA from January to December 2019, while 88 patients had the procedure from January to July 2020. Among patients from the 2019 cohort, 97 (14.7%) were treated with human albumin. For patients recruited in 2020, the mean preoperative waiting time was 39.05 ± 22.78 days. The baseline demographic and clinical characteristics of the 2019 cohort are shown in Table 1, while those from the 2020 cohort are presented in Table 2.

Spearman's rank correlation analyses showed that the absolute value of the rank correlation coefficient among covariates included in logistic regression analyses ranged from 0.000 to 0.375, which meant that correlations among the variables were low and that variables met the requirements for logistic regression analyses (Fig. 1).

Impact of preoperative albumin levels on human albumin solution use after primary TKA

Several statistical models including different covariates were built to evaluate the impact of preoperative albumin levels at admission on postoperative human albumin use in primary TKA (Table 3). The univariate analysis (crude model) showed that higher preoperative albumin levels were associated with lower risk of postoperative HAS use (RR = 0.720, 95% CI 0.665-0.778, $P < 0.001$). After adjusting for demographic variables (age, sex, and BMI) and clinical characteristics in the logistic regression analysis step-by-step (models 1, 2, and 3), high preoperative albumin levels remained significantly associated with lower risk of postoperative albumin use (Table 3). In addition, a negative dose-response relationship was observed between preoperative serum albumin levels at admission and risk of postoperative albumin use ($P_{\text{overall}} < 0.001$; $P_{\text{nonlinear}} = 0.186$; Fig. 2).

Impact of high-protein diet on preoperative albumin levels in primary TKA

As shown in Table 4, the mean albumin level on the day of admission was significantly higher than the level tested on the day of outpatient visit (46.04 ± 2.49 g/L vs. 42.79 ± 4.09 g/L; $P < 0.001$). In contrast, patients showed no significant differences between admission and outpatient visit in levels of globulin, hemoglobin hematocrit, and fasting blood-glucose, as well as biomarkers of liver and kidney function and lipid metabolism (all $P > 0.05$).

Discussion

Our study is the first to evaluated whether a high-protein diet during the waiting time before admission for primary TKA affects preoperative albumin levels. In our patients, preoperative serum albumin levels were strongly associated with postoperative HAS use in primary TKA and, furthermore, there was a negative dose-response relationship between them. And a high-protein diet during the waiting time before admission for TKA may be a useful tool to improve the albumin levels of these patients and avoid complications after surgery.

Albumin is well known among clinicians for its reliability and sensitivity for assessing nutritional status [16]. Hypoproteinemia can lead to a significantly higher incidence of postoperative complications

including delayed wound healing due to reduced collagen synthesis and protein matrix deposition [17, 18] and superficial or deep infection caused by diminished immune response [19], and adverse events such as myocardial infarction, cardiac arrest, stroke and even mortality in TJA [10, 18]. On the other hand, our study showed that preoperative albumin level was significantly associated with HAS use after TKA, showing a negative dose-response relationship: lower preoperative albumin levels correlated with higher risk of postoperative use of HAS. But HAS use has been associated with higher risk of cardiac, pulmonary, and combined complications, acute renal failure, and unplanned intensive care unit admission [12]. Furthermore, hypoproteinemia was directly associated with increased total costs in revision and primary TJA [11]. Clinicians and policy providers should consider this question for optimizing the nutritional status of patients preoperatively and reducing the risk factors that may increase medical costs in the era of bundled payments for TJA [20].

Serum albumin levels have been associated with long-term mortality in the general population, especially for the elderly [21], and with postoperative course and mortality for patients with geriatric hip fracture [22]. Malnutrition or hypoproteinemia are common in elderly patients, and age and female sex (female) are its independent risk factors, which may be related to associated with their dietary habit of low-quality nutrient intake and/or low economic status [23, 24]. This population accounts for the majority of patients undergoing TKA. Fortunately, compared with emergency operation, the elective nature of TJA allows these patients to have an adequate preoperative nutritional storage for reducing the risk of postoperative HAS use [16, 25]. One study [26] reported that a high-protein diet could improve the overall survival for older adults diagnosed with advanced gastrointestinal cancer. Although serum albumin < 35 g/L is usually considered as malnutrition [27] or hypoproteinemia [28], our study revealed a negative dose-dependent relationship between preoperative serum albumin levels and postoperative HAS use, consistent with a study showing that lower preoperative albumin levels are associated with higher treatment costs [11].

In our patients, about 35 g of dietary protein (about 0.5 g/kg body weight) were added to the daily diet, which resulted in an increase of about 3.2 g in serum albumin from the day of outpatient visit to admission (an average of 39.05 ± 22.78 days). Several studies have evaluated the effects of a high-protein diet. One study [29] reported that a high-protein diet (1.07–1.60 g/kg body weight/day) lasting for 6–12 months was an effective and safe way to reduce weight: the high protein produced satiety and increased energy expenditure. Furthermore, high-protein diets lasting for 12 weeks could significantly improve body composition in women with normal-weight obesity, reducing the waist circumference, fat mass, and body fat percentage and increasing lean body mass [30]. Interestingly, high-protein diets could also improve skeletal muscle mass in patients with gastrointestinal cancer [31], which may be relevant to our patients, since skeletal muscle mass is also important for recovery of function after TKA [32]. Future studies should evaluate the effect of high-protein diets on quadriceps muscle strength, which will provide more evidence for preoperative high-protein diet combined with muscle exercise for the patients planning to undergo TKA.

Our study showed that a high-protein diet had no significant impact on biomarkers of liver, kidney, or lipid metabolism. Tischmann et al. [33] revealed that a high-protein diet lasting for approximately 34 months

had no significant effect on the biomarkers of cardiometabolic health and vascular function in overweight participants. In contrast, a previous study [34] reported that high-protein diets can decrease the levels of low-density lipoprotein, total cholesterol, and triglycerides as well as mitigate insulin resistance in patients with type 2 diabetes mellitus. The differences with our study may be associated with the metabolic disorder in diabetic patients and shorter duration of our study.

Our study presents several limitations. First, we excluded patients with renal and hepatic diseases, and therefore the safety of a high-protein diet for these patients must be assessed because of its potential effects on renal function [29, 35]. Second, although we asked patients to fast for 6-8 hours before blood collection, some patients, especially at outpatients visit, may have failed to follow it, which would affect our laboratory test results. Third, although we educated patients in detail, some patients may not have strictly followed our suggestions during the preoperative waiting period. Finally, large randomized controlled studies are needed to compare the effect of a high-protein diet on the rate of HAS use and its consumption. Despite these limitations, we believe that the current study provides new ideas for preoperative nutritional management for patients planning to undergo TKA.

Conclusion

Lower preoperative serum albumin levels were associated with increased risk of postoperative HAS use and there was a negative dose-response relationship between them. Given the elective nature of TKA, a high-protein diet during the waiting time before surgery admission may be a useful way to improve the albumin levels in these patients. Future high-quality studies are needed to confirm these findings.

Abbreviations

BMI: body mass index

CI: confidence interval

CRP: C-reactive protein

ESR: erythrocyte sedimentation rate

HAS: human albumin solution

TJA: total joint arthroplasty

TKA: total knee arthroplasty

ALB: albumin

CHD: coronary heart disease

COPD: chronic obstructive pulmonary disease

Hb: hemoglobin

Pre-op: preoperative

Declarations

Ethics approval and consent to participate

The Ethics Committee of West China Hospital of Sichuan University approved the study (approval no. 2020-804). Written informed consent was deemed unnecessary by the hospital's institutional review board. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and analysed during the current study are not publicly available due to some of them remain unpublished and confidential but are available from the first or corresponding author on reasonable request

Competing interests

No conflict of interest exists in the submission of this manuscript, and manuscript is approved by all authors for publication.

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Authors' contributions

H X and L L: Applied for ethical and registered this study, drafted the work and revised it critically for important intellectual content. JW X and D W: collected data, analyzed and interpreted data for the work. ZY H: participated in final approval of the version to be published. ZK Z: contributions to the conception and design of the work, and revised the manuscript. All authors read and approved the final manuscript.

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A statement of the location where the work was performed

The work was performed in Department of Orthopaedic surgery, West China Hospital, Sichuan University.

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Tables

Table 1. Baseline characteristics of patients who underwent routine primary TKA in 2019.

Baseline characteristic	No albumin (n=563)	Albumin use (n=97)	All (n=660)
Demographic characteristic			
Age (years)	67.33±8.55	69.44±7.86	67.64±8.48
Female	447 (79.4)	79 (81.4)	526 (79.7)
BMI (kg/m ²)	25.90±3.53	25.50±4.00	25.84±3.60
Diagnosis			
Primary osteoarthritis	529 (95.0)	85 (87.6)	614 (93.0)
Inflammatory arthritis	34 (6.04)	12 (12.3)	46 (6.97)
Comorbidity			
Hypertension	250 (44.4)	35 (36.1)	285 (43.2)
Diabetes	66 (11.7)	11 (11.3)	77 (11.7)
COPD	18 (3.20)	3 (3.09)	21 (3.18)
CHD	13 (2.31)	2 (2.06)	15 (2.27)
Preoperative laboratory test			
ALB (g/L)	43.23±2.48	40.36±3.48	42.85±2.84
Hb (g/L)	134.33±15.28	133.00±12.87	134.13±14.95
CRP (mg/L)	4.11±3.44	5.01±5.02	4.24±3.73
ESR (mm/h)	23.65±16.84	28.82±18.65	24.40±17.19

Values are n (%) or mean ± SD.

Abbreviations: ALB: albumin; BMI: body mass index; CHD: coronary heart disease; COPD: chronic obstructive pulmonary disease; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; Hb: hemoglobin.

Table 2. Baseline characteristics of patients who underwent routine primary TKA from January to August 2020.

Baseline characteristic	No albumin (n=88)
Demographic characteristic	
Age (year)	64.32±10.88
Female	63 (71.6)
BMI (kg/m ²)	26.11±3.92
Diagnosis	
Primary osteoarthritis	81 (92.0)
Inflammatory arthritis	7 (7.95)
Comorbidity	
Hypertension	37 (42.0)
Diabetes	10 (11.4)
COPD	5 (5.68)
CHD	5 (5.67)
Preoperative waiting time (days)	39.05±22.78

Values are n (%) or mean ± SD.

Abbreviations: BMI: body mass index; COPD: chronic obstructive pulmonary disease; CHD: coronary heart disease.

Table 3. Logistic regression analyses of preoperative albumin level and HAS use after primary TKA.

Model	Risk of postoperative albumin use	
	Risk ratio (95% confidence interval)	P
Crude model	0.720 (0.665-0.778)	<0.001
Model 1	0.772 (0.665-0.784)	<0.001
Model 2	0.722 (0.664-0.785)	<0.001
Model 3	0.725 (0.666-0.789)	<0.001

Model 1: adjusted for age, sex, body mass index and diagnosis.

Model 2: adjusted as in model 1 + hypertension, type 2 diabetes, chronic obstructive pulmonary disease, and coronary heart disease.

Model 3: adjusted as in model 2 + preoperative hemoglobin, C-reactive protein, and erythrocyte sedimentation rate.

Table 4. The effect of high-protein diet on different biomarkers in patients undergoing primary TKA from the 2020 cohort.

Biomarker	Outpatient visit (n=88)	Pre-operative (n=88)	P values
Nutritional status			
Albumin (g/L)	42.79±4.09	46.04±2.49	<0.001*
Globulin (g/L)	28.29±4.59	27.64±3.81	0.158
Hemoglobin (g/L)	134.63±12.59	136.34±11.48	0.069
HCT (L/L)	0.41±0.38	0.42±0.32	0.585
Liver function			
Total bilirubin (μmol/L)	10.29±3.98	10.57±3.98	0.569
Direct bilirubin (μmol/L)	3.01±1.49	2.91±1.11	0.496
Indirect bilirubin (μmol/L)	7.24±2.97	7.65±3.14	0.273
Total bile acid (μmol/L)	4.17±2.11	3.67±2.77	0.157
ALT (IU/L)	27.55±20.31	24.08±13.76	0.107
AST (IU/L)	23.21±5.95	22.61±7.65	0.438
ALP (IU/L)	97.17±29.17	93.26±25.48	0.090
GGT (IU/L)	35.45±30.92	33.68±26.85	0.473
Kidney function			
Serum urea (μmol/L)	5.69±1.72	5.94±1.78	0.082
Serum creatinine (μmol/L)	66.66±17.58	66.53±16.37	0.876
eGFR (ml/min/1.73 m ²)	88.22±18.82	88.69±17.04	0.493
Serum uric acid (μmol/L)	316.58±103.51	310.40±109.96	0.549
Lipid metabolism			
Triglyceride (mmol/L)	1.57±0.60	1.47±0.84	0.261
Cholesterin (mmol/L)	4.88±0.90	5.01±0.96	0.150
HDL-C (mmol/L)	1.35±0.35	1.39±0.34	0.103
LDL-C (mmol/L)	2.82±0.69	2.92±0.69	0.118
Other			
Creatine kinase (IU/L)	101.36±63.63	91.56±41.43	0.079
Lactic dehydrogenase (IU/L)	196.59±26.02	192.02±38.81	0.438
HBDH (IU/L)	155.17±22.89	150.65±32.98	0.329

Values are mean ± SD, unless otherwise noted.*: P < 0.05.

Abbreviations: ALP: alkaline phosphatase; ALT: alanine transferase; AST: aspartate transferase; eGFR: estimated glomerular filtration rate; GGT: glutamyl transpeptidase; HCT: hematocrit; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; HBDH: hydroxybutyrate dehydrogenase.

Figures

Variables	Pre-op ESR	Pre-op CRP	Pre-op Hb	CHD	COPD	Diabetes	Variables
Pre-op ALB	1	0.285	-0.260	-0.020	0.007	-0.009	Pre-op ESR
Sex	0.000	1	-0.043	-0.089	-0.034	-0.045	Pre-op CRP
Age	0.000	-0.042	1	-0.046	-0.037	-0.118	Pre-op Hb
BMI	0.019	0.000	-0.016	1	0.030	0.040	CHD
Diagnosis*	-0.144	-0.079	-0.235	-0.223	1	-0.012	COPD
Hypertension	0.074	0.067	0.247	0.126	-0.046	1	Diabetes
Diabetes	0.086	0.090	0.103	0.051	-0.044	0.121	--
COPD	-0.037	-0.037	0.029	0.021	-0.016	0.051	--
CHD	0.001	0.001	0.065	0.004	-0.042	0.093	--
Pre-op Hb	0.096	-0.375	-0.050	0.245	-0.221	0.010	--
Pre-op CRP	-0.154	0.058	-0.066	0.092	0.240	-0.002	--
Pre-op ESR	-0.129	0.240	0.073	-0.074	0.188	0.071	--
Variables	Pre-op ALB	Sex	Age	BMI	Diagnosis	Hypertension	--

Figure 1

Spearman's rank correlations between covariates included in the logistic regression analyses.

Variables	Pre-op ESR	Pre-op CRP	Pre-op Hb	CHD	COPD	Diabetes	Variables
Pre-op ALB	1	0.285	-0.260	-0.020	0.007	-0.009	Pre-op ESR
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Pre-op ESR	-0.129	0.240	0.073	-0.074	0.188	0.071	--
Variables	Pre-op ALB	Sex	Age	BMI	Diagnosis	Hypertension	--

Figure 1

Spearman's rank correlations between covariates included in the logistic regression analyses.

Figure 2

Dose-response relationship between preoperative serum albumin level and risk of HAS use.

Figure 2

Dose-response relationship between preoperative serum albumin level and risk of HAS use.