

Malnutrition Assessed Using the Geriatric Nutritional Risk Index Is Associated with Preoperative Incidence of Deep Vein Thrombosis in Japanese Patients Undergoing Total Knee Arthroplasty

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Abstract

Purpose: Few studies have evaluated the association between malnutrition and the risk of preoperative deep vein thrombosis (DVT) in patients undergoing primary total joint arthroplasty. This study aimed to investigate the prevalence of preoperative DVT in Japanese patients undergoing total knee arthroplasty (TKA) and the importance of malnutrition in the risk of preoperative DVT. **Methods:** We retrospectively analyzed 394 patients admitted for primary TKA at our institution between January 2019 and December 2023. All patients scheduled for TKA at our institution had serum D-dimer levels measured preoperatively. Lower-limb ultrasonography was examined to confirm the presence of DVT in patients with D-dimer levels $\geq 1.0 \mu\text{g/mL}$ or who were considered to be at high risk of DVT by the treating physician. Based on the results of lower-limb ultrasonography, all patients were divided into the non-DVT and DVT groups. The incidence of and risk factors for preoperative DVT were investigated, as well as the correlation of DVT with the patient's nutritional parameters. We used two representative tools for nutritional assessment: the Geriatric Nutritional Risk Index (GNRI) and Controlling Nutritional Status Score. **Results:** The mean age was 77.8 ± 6.9 years. Preoperative DVT was diagnosed in 57 of the 394 (14.5%) patients. Multivariate logistic regression analysis showed that advanced age and malnutrition status, assessed using the GNRI, were independent risk factors for preoperative DVT. **Conclusion:** A high incidence of preoperative DVT was observed in patients who underwent TKA. Malnutrition status, as assessed using the GNRI, increased the risk of preoperative DVT. Our findings suggest that cli-

icians should consider these factors when tailoring preventive strategies to mitigate DVT risk in patients undergoing TKA.

Keywords

Malnutrition, Geriatric Nutritional Risk Index, Controlling Nutritional Status Score, Preoperative, Deep Vein Thrombosis, Total Knee Arthroplasty

1. Introduction

Deep vein thrombosis (DVT) is a substantial risk in orthopedic procedures, with total knee arthroplasty (TKA) being particularly susceptible to this complication [1] [2]. Despite advancements in surgical techniques and postoperative care, the prevalence of DVT in patients undergoing preoperative TKA remains challenging. DVT, if left undetected or untreated, can lead to serious consequences, including pulmonary embolism and increased morbidity and mortality rates [1] [3]. Recent literature extensively explores various risk factors for DVT incidence, such as age, comorbidities, and surgical approach [2] [4] [5]. However, a critical knowledge gap remains regarding the association between nutritional status and the prevalence of preoperative DVT, specifically in patients undergoing TKA.

Malnutrition is a known predictor of adverse surgical outcomes [6]-[8]. Several methods are available for detecting malnutrition [9]-[12]. Serological parameters, such as total lymphocyte count and total cholesterol and albumin levels, have been used as markers of nutritional status [9] [10]. In addition, standardized scoring systems, such as the Controlling Nutritional Status Score (CONUT score) [13], Geriatric Nutritional Risk Index (GNRI) [14], Nutritional Risk Screening (NRS2002), Malnutrition Universal Screening Tool, Mini Nutritional Assessment, and, Subjective Global Assessment are useful in defining malnutrition [9]-[12]. The CONUT score and GNRI are often used in clinical practice because they are simpler and more understandable than other nutritional indicators that require expert interviews [11]. In this study, we used two representative tools for nutritional assessment: CONUT score and GNRI.

Existing studies have focused on prophylactic measures and postoperative management, often overlooking the potential influence of preoperative nutritional status on DVT risk. A comprehensive understanding of the effects of nutritional parameters on DVT prevalence is essential to refine preventive strategies and optimize patient outcomes. Despite the recognition of preoperative DVT as a significant problem in orthopedic surgery, including TKA, the specific role of nutritional parameters in this context remains underexplored. To address this gap in the literature, we aimed to determine the prevalence of preoperative DVT in patients undergoing TKA and investigate the association between nutritional parameters and DVT occurrence in Japanese patients.

2. Materials and Methods

2.1. Patient Population

This study included 409 patients with knee osteoarthritis who were admitted to our hospital for primary TKA between January 2019 and December 2023. A total of 394 patients were included, after excluding 15 patients who had undergone arthroplasty within 3 months or who had missing preoperative laboratory data.

Patients scheduled for TKA at our institution had serum D-dimer levels measured preoperatively, and lower-limb ultrasonography was performed to confirm the presence of DVT in patients with D-dimer levels $> 1.0 \mu\text{g/mL}$ or those deemed at high risk for DVT by the treating physician. None of the patients had symptoms suggestive of DVT, such as increased calf circumference, calf pain or presence of Homans's sign, at the time of the index procedure. The patients' age, sex, body mass index (BMI), the American Society of Anesthesiologists Physical Status classification [15], and data from the medical records and medical condition were collected. Preoperative laboratory data, such as total lymphocyte count and total cholesterol, albumin, and D-dimer levels, were also collected. The CONUT score and GNRI were used for objective nutritional assessment. In all cases, the Kellgren–Lawrence grade was assessed as a preoperative radiographic parameter using anteroposterior whole-leg standing radiographs.

This study received ethical approval from the Medical Research Ethics Committee of our institution under protocol number R23-079.

2.2. Malnutrition Assessment

In this study, we used two representative tools for nutritional assessment: CONUT score and GNRI. In a previous study, the GNRI was calculated using the following formula: $\text{GNRI} = [1.489 \times \text{serum albumin concentration (g/L)}] + (41.7 \times [\text{body weight (kg)}/\text{ideal body weight (kg)}])$ [14]. Ideal body weight was identified using height and BMI (22.0 kg/m^2). In the present study, the all subjects were classified into two groups indicating different risk levels of nutritional-related complications: $\text{GNRI} \geq 98$, the normal group; $\text{GNRI} < 98$, the malnutrition group. The CONUT score was obtained based on serum albumin concentration (g/L), total cholesterol concentration (mg/dL), and total lymphocyte count [13]. In the present study, we defined a CONUT score of ≥ 2 as the malnutrition group and a CONUT score of < 1 as the normal group with no risk of malnutrition.

2.3. Diagnosis of DVT

Lower-limb ultrasonography using an Aplio 300 ultrasound system (Canon Medical Systems, Tokyo, Japan) was performed as previously reported [16]. Briefly, ultrasonography was performed with compression and color Doppler imaging in B-mode for the common femoral, femoral, popliteal, and calf veins bilaterally. DVT was diagnosed by intravascular filling defects, the absence of venous flow,

venous incompressibility, which were then co-diagnosed by two experienced sonographers. DVT in the more proximal part of the popliteal vein was defined as the proximal type, and DVT in calf veins as the distal type. Those with both proximal and distal DVT were considered to be of the mixed type.

2.4. Statistical Analyses

GraphPad Prism version 10 (GraphPad Software, San Diego, CA, USA) was used for statistical analysis. Data are expressed as means \pm standard deviations. Univariate analysis was performed first to determine the inputs to the multivariate regression model. Quantitative variables were analyzed by a Student's t-test, and qualitative variables were compared by a Fisher's exact test. Subsequently, factors with a *p*-value < 0.1 were introduced into the multivariate logistic regression analysis to examine the independent risk factors for preoperative DVT. A *p*-value $p < 0.05$ were considered statistically significant. The results are presented as odds ratios (ORs) and 95% confidence intervals (95% CIs).

3. Results

In total, 394 patients were included in this retrospective study. **Figure 1** showed a flowchart of the preoperative DVT evaluation. The relevant demographic and clinical characteristics of the patients are presented in **Table 1**.

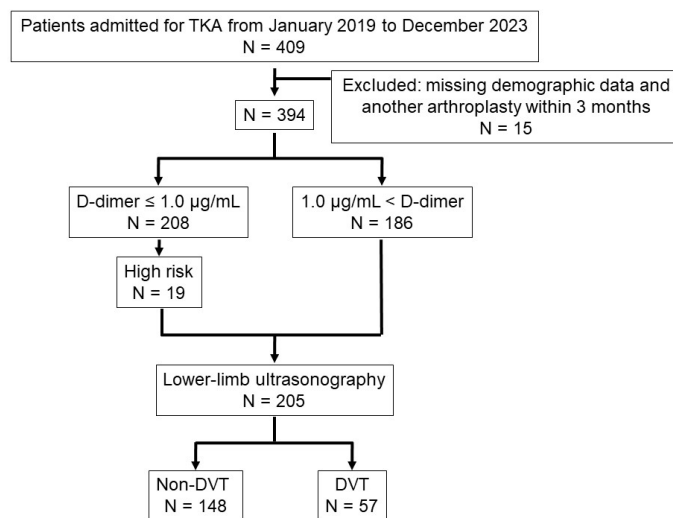


Figure 1. Flowchart demonstrates participants' selection in the study.

Table 1. Patient demographics.

| Variables | Total n = 394 |
|--------------------------|------------------|
| Age (years) | 77.8 \pm 6.9 |
| Sex (male/female) | 68/326 |
| BMI (kg/m ²) | 25.9 \pm 3.9 |

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| | |
|--------------------------------|--------------|
| KL grade 1, 2/3, 4 | 28/366 |
| ASA-PS 1, 2/3, 4 | 363/31 |
| Total lymphocyte count | 1812 ± 739 |
| Albumin level (g/dL) | 4.1 ± 0.4 |
| Total cholesterol (mg/dL) | 206.8 ± 36.9 |
| D-dimer (µg/mL) | 1.6 ± 1.6 |
| Nutrition status (CONUT score) | 85/309 |
| Malnutrition/normal | |
| Nutrition status (GNRI) | 58/336 |
| Malnutrition/normal | |

Values are expressed as the means ± standard deviations. BMI, body mass index; KL, Kellgren-Lawrence; ASA-PS, American Society of Anesthesiologists Physical Status; CONUT score, Controlling Nutritional Status Score; GNRI, Geriatric Nutritional Risk Index.

The mean age was 77.8 ± 6.9 years. This study included 68 males (17.3%) and 326 females (82.7%). Preoperative diagnoses included degenerative osteoarthritis of the knee in 350 (88.8%), rheumatoid arthritis in 29 (7.4%), and avascular necrosis of the knee in 15 (3.8%) patients. Malnutrition identified by the CONUT score and GNRI accounted for 21.6% (85/394) and 14.7% (58/394) of cases, respectively. Of the 394 patients, 186 (47.2%) had preoperative elevated D-dimer levels and 57 (14.5%) had DVT. In patients with elevated D-dimer levels, the positive predictive value was 30.5% (57/186). Among the 57 patients with preoperative DVT, unilateral and bilateral thromboses were observed in 36 (63.2%) and 21 (36.8%) patients, respectively. There were 52 patients with distal DVT (91.2%), three patients with proximal DVT (5.3%), and two patients with mixed DVT (3.5%). All were asymptomatic.

Univariate analysis demonstrated that advanced age, BMI, elevated D-dimer levels, and malnutrition status (GNRI < 98) were significantly correlated with preoperative DVT ($p = 0.005$, $p = 0.02$, $p = 0.03$, and $p = 0.0008$, respectively). The univariate analysis of demographics is shown in **Table 2**.

Table 2. Univariate analysis of preoperative DVT risk between the non-DVT and DVT groups.

| Variables | Non-DVT group n = 148 | DVT group n = 57 | <i>p</i> -value |
|--------------------------|--------------------------|---------------------|-----------------|
| Age (years) | 78.6 ± 6.4 | 81.4 ± 5.5 | 0.005 |
| Sex (male/female) | 33/115 | 9/48 | 0.20 |
| BMI (kg/m ²) | 25.9 ± 3.8 | 24.5 ± 3.4 | 0.02 |
| KL grade 1, 2/3, 4 | 12/136 | 2/55 | 0.20 |

Continued

| | | | |
|--------------------------------|--------------|--------------|--------|
| ASA-PS 1, 2/3, 4 | 9/139 | 5/52 | 0.34 |
| Total lymphocyte count | 1743 ± 629 | 1914 ± 1116 | 0.17 |
| Albumin level (g/dL) | 4.0 ± 0.4 | 4.0 ± 0.4 | 0.25 |
| Total cholesterol (mg/dL) | 205.2 ± 37.0 | 207.3 ± 37.0 | 0.72 |
| D-dimer (µg/mL) | 2.1 ± 1.7 | 2.8 ± 2.5 | 0.03 |
| CONUT score | 1.0 ± 1.2 | 0.9 ± 1.4 | 0.70 |
| Nutrition status (CONUT score) | | | |
| Malnutrition/normal | 36/112 | 13/44 | 0.49 |
| GNRI | 101.6 ± 6.2 | 100.0 ± 6.5 | 0.12 |
| Nutrition status (GNRI) | | | |
| Malnutrition/normal | 21/127 | 21/36 | 0.0008 |

Values are expressed as the means ± standards deviation. DVT, deep vein thrombosis; BMI, body mass index, KL, Kellgren-Lawrence; ASA-PS, American Society of Anesthesiologists Physical Status; CONUT score, Controlling Nutritional Status Score; GNRI, Geriatric Nutritional Risk Index.

The results of multivariate logistic regression analysis showed that advanced age (OR, 1.09; 95% CI, 1.03 - 1.15; $p = 0.005$) and malnutrition status (GNRI < 98) (OR, 2.47; 95% CI, 1.12 - 5.42; $p = 0.02$) were independent risk factors for preoperative DVT in patients undergoing TKA. Although an elevated D-dimer level tended to be more relevant to the incidence of preoperative DVT, this difference was not statistically significant (OR, 1.18; 95% CI, 0.99 - 1.41; $p = 0.07$). The results of the multivariate logistic regression analysis are shown in **Table 3**.

Table 3. Multivariate analysis of preoperative DVT risk between the non-DVT and DVT groups.

| Variables | Odds ratio (95% CI) | <i>p</i> -value |
|--------------------------|---------------------|-----------------|
| Age (years) | 1.09 (1.03 - 1.15) | 0.005 |
| BMI (kg/m ²) | 0.94 (0.85 - 1.03) | 0.21 |
| D-dimer | 1.18 (0.99 - 1.41) | 0.07 |
| Nutrition status (GNRI) | | |
| Malnutrition /normal | 2.47 (1.12 - 5.42) | 0.02 |

Values are expressed as the means ± standards deviation. DVT, deep vein thrombosis; BMI, body mass index; GNRI, Geriatric Nutritional Risk Index; CI, confidence interval.

4. Discussion

Given that preoperative DVT is likely to lead to postoperative venous thromboembolism risk, it is highly relevant to analyze the prevalence of preoperative DVT and its risk factors. In the present study, we focused on the association

between nutritional parameters and the prevalence of preoperative DVT in Japanese patients undergoing primary TKA.

In the present study, 14.5% of the patients who were scheduled for TKA had preoperative DVT, even before the surgery. Multivariate analysis identified advanced age and malnutrition (GNRI < 98) as independent preoperative risk factors for DVT, whereas malnutrition as assessed by the CONUT score was unrelated to risk factors. While advanced age and elevated D-dimer levels have been associated with the prevalence of DVT in several studies [17]-[19], the observed association between malnutrition, as assessed using the GNRI, and preoperative DVT is a novel contribution, suggesting that nutritional status plays a role in thrombotic risk even prior to surgery. These findings emphasize the importance of a thorough risk assessment before TKA and guide clinicians in tailoring preventive strategies based on individual patient nutritional characteristics using the GNRI.

Several studies have reported that the incidence of preoperative DVT in patients who underwent primary TKA ranges from 5.5% to 15.8% [17]-[20], which is approximately the same as or lower than that reported in our study. Sato *et al.* [17] and Wakabayashi *et al.* [19] reported that the prevalence rates of preoperative DVT in patients who underwent TKA were 14.7% and 15.8%, respectively, which are comparable to those of the present study, whereas Sun *et al.* [20] and Xiong *et al.* [18] reported lower prevalence rates of 5.5% and 6.9%, respectively. Differences in patient background, such as average age and race, may help to explain the variability in the incidence of preoperative DVT reported in the literature. In particular, the average age of the patient population in this study was approximately 10 years older than that in their studies because our hospital specializes in the elderly. Given the high incidence of preoperative DVT, preoperative screening is crucial to prevent subsequent thromboembolic complications.

Malnutrition is a known predictor of adverse surgical outcomes [6]-[8]. Low albumin levels have long been recognized as an effective indicator of malnutrition status [21]. However, recent reports have been doubtful of its use as an indicator of nutritional status, as it is more likely to be related to inflammation or hydration status rather than nutritional status [10] [22]. In this study, we used two representative malnutrition screening tools, the CONUT score and GNRI, which are simple and easy for clinicians to use. The CONUT score and GNRI were originally developed to assess nutritional status and related morbidity in hospitalized patients and mortality in patients with cancer but have now been validated in several settings, including orthopedic conditions, such as in patients with trauma and prosthetic [6] [8] [16] [23] [24].

The GNRI is a simple index of nutritional status that can be calculated using only serum albumin level, height, and weight [14], and has the advantage that it mitigates the effects of hydration. Previous studies have validated the GNRI for assessing nutritional status and predicting complications in surgical patients [6] [8] [16] [23]. Furthermore, recent reports suggest that GNRI correlates with

frailty and sarcopenia [25] [26]. Our results showed that low albumin levels and malnutrition, defined by the CONUT score, were not significantly associated with preoperative DVT risk, whereas malnutrition assessed by the GNRI was an independent risk factor. Therefore, as a modifiable risk factor, early nutritional intervention may be of benefit to the malnutrition group identified by the GNRI. Moreover, these results suggest the need to combine serum albumin levels with a more stable measure, such as body weight.

Although the CONUT score is calculated solely from laboratory data, such as serum albumin concentration, cholesterol levels, and lymphocyte count, the GNRI considers anthropometric measures, such as height, weight, and BMI. Body composition is also associated with muscle mass, and associations between GNRI and muscle mass have been reported in recent years. Cerera *et al.* [27] reported that GNRI correlated with grip strength and arm muscle area, those are one of the diagnostic criteria for sarcopenia, whereas Xiang *et al.* reported an association between low GNRI and low muscle mass [28]. Shiroma *et al.* evaluated the association between sarcopenia and malnutrition status as assessed by both the GNRI and CONUT scores and reported that the GNRI had superior diagnostic power in the diagnosis of sarcopenia [25]. Moreover, Shin *et al.* reported an association between lower extremity muscle weakness and DVT prevalence in post-TKA patients [29]. Given previous reports that low GNRI is associated with muscle mass and the incidence of preoperative DVT in malnourished patients assessed by the GNRI in the present study, pump dysfunction due to lower extremity muscle weakness and poor quality may contribute to DVT incidence.

The strength of our study is its focus on the preoperative phase, during which interventions to reduce the risk of DVT can be strategically implemented. Nutritional status, a modifiable factor, is a potentially influential variable that may be helpful in emphasizing the importance of a thorough risk assessment before TKA and guiding clinicians in tailoring preventive strategies based on individual patient characteristics.

This study has some limitations. First, this is the single-center retrospective comparative design, which may have affected the generalizability of the results. Future studies using a multicenter approach are warranted to validate and expand upon our findings. Second, the incidence of preoperative DVT in this study may be underestimated because lower-limb ultrasonography was not performed in all patients.

In conclusion, this study sheds light on the association between nutritional parameters and the occurrence of preoperative DVT in Japanese patients undergoing primary TKA. A high preoperative DVT rate was observed in patients undergoing TKA. Advanced age and malnutrition, as assessed using the GNRI, were the risk factors for preoperative DVT. Our findings suggest that clinicians should consider these factors when tailoring preventive strategies to mitigate DVT risk in patients undergoing TKA.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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