

Prognostic nutritional index as a risk factor for aseptic wound complications after total knee arthroplasty

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- 1 **Prognostic nutritional index as a risk factor for aseptic wound complications after total knee**
- 2 **arthroplasty**

3 **Abstract**

4 **Background:**

5 Patients with malnutrition have a high risk of postoperative complications in total knee
6 arthroplasty (TKA). Previously, serum albumin and total lymphocyte count were considered
7 preoperative nutritional assessment measures. Prognostic nutritional index (PNI) is calculated by
8 a combination of serum albumin and total lymphocyte count. This study aimed to identify the risk
9 factors for postoperative complications after TKA, including preoperative nutritional assessment,
10 and evaluated preoperative PNI as a predictor of postoperative complications.

11 **Methods:**

12 One-hundred and sixty patients (234 knees) who underwent primary TKA were enrolled
13 consecutively from 2010 to 2018. The serum albumin (g/dL) and total lymphocyte count (/mm³)
14 were examined within 3 months before TKA; thereafter, the PNI was calculated. Postoperative
15 aseptic wound problems, such as skin erosion and dehiscence within 2 weeks and periprosthetic
16 joint infection after TKA were examined.

17 **Results:**

18 Periprosthetic joint infections occurred in 14 knees (6.0%). Postoperative aseptic wound problems
19 within two weeks were significant risk factors of periprosthetic joint infection (odds ratio; 5.10,
20 95% confidence interval [CI]; 1.438–18.093, $p = 0.012$). No significant differences were noted in

21 the patient demographics, such as age, sex, body mass index (BMI), and comorbidities between
22 the positive and negative groups for periprosthetic joint infection, except for the rate of aseptic
23 operative wound problems. Furthermore, postoperative aseptic wound problems were influenced
24 by high BMI (odds ratio; 1.270, 95% CI; 1.111–1.453, $p = 0.000$) and low PNI (odds ratio; 0.858,
25 95% CI; 0.771–0.955, $p = 0.015$).

26 **Conclusions:**

27 Preoperative nutritional status, indicated by PNI and BMI, was associated with postoperative
28 wound problems within two weeks. Periprosthetic joint infection after TKA was associated with
29 early postoperative aseptic wound problems.

30 **Introduction**

31 Total knee arthroplasty (TKA) is commonly performed for patients with severe osteoarthritis and
32 rheumatoid arthritis of the knee. A frequent cause of revision surgery after TKA is periprosthetic
33 joint infection [1-5]. Preoperative risk factors of periprosthetic joint infection should be improved,
34 for example, reduction of body weight [6], control of diabetes mellitus [7], improving
35 malnutrition [8], supplementation of Vitamin D [9], smoking cessation [10]. Furthermore,
36 although several preventive procedures during surgeries including prophylactic intravenous
37 administration of antibiotics, preoperative skin disinfection, and intrawound lavage with a large
38 amount of saline have been performed pre-, intra- and postoperatively, the risk of infection
39 remains. The reported infection rates are approximately 2% to 5% after TKA [1,3-5,11].
40 However, it was reported that patients with malnutrition had a high risk of postoperative infection
41 [8,12,13]. Therefore, it is important to evaluate nutrition for preoperative patients. Previously,
42 prognostic nutritional index (PNI) was used to evaluate nutrition in patients who had heart failure
43 [14] and underwent gastrointestinal surgery [15]. PNI can be easily calculated using serum
44 albumin and total lymphocyte count; it is useful for the nutritional evaluation in patients before
45 surgeries [13,15,16]. In fact, PNI was demonstrated as a predictor of the 5-year overall survival
46 probability after colorectal cancer surgeries and postoperative delirium [16,17]. In the orthopedic
47 field, it was reported that postoperative complications of spine surgeries were associated with the

48 nutritional status of preoperative patients [18,19]. PNI and the modified Glasgow prognostic score
49 were significant predictors of postoperative delirium or surgical site infections after spine
50 surgeries [18,19]. Furthermore, the prevalence of malnutrition in patients undergoing total hip
51 and knee arthroplasty has been reported to be as high as 40% [20]. However, there are no reports
52 on how preoperative nutritional states, such as PNI are related to postoperative periprosthetic joint
53 infection after TKA. The purpose of this study is to identify the risk factors for postoperative
54 complications after TKA, including preoperative nutritional assessment, and evaluated
55 preoperative PNI as a predictor of postoperative complications, such as postoperative wound
56 problems and periprosthetic joint infections.

57

58 **Materials and methods**

59 This research has been approved by the Institutional Review Board of the authors' affiliated
60 institutions. From 2010 to 2018, consecutive patients with osteoarthritis of the knee who
61 underwent primary TKA were included in this study. Although posterior-stabilized type implants
62 were used in all TKAs, patellar replacement was not performed in most cases. Patients with
63 rheumatoid arthritis, or previous histories of joint infection, and patients of revision surgery were
64 excluded in this study. The study population included 190 patients (234 knees) with more than 1
65 year follow up (Table 1). There were 48 men (60 knees) and 142 women (174 knees), with an

66 average age of 74.1 ± 7.6 years. The background data of each patient, such as age at surgery, sex,
67 body mass index (BMI), operative time, intraoperative blood loss, and comorbidities were
68 collected. If a patient had at least one disease preoperatively, for example, diabetes mellitus,
69 chronic kidney disease, coronary artery disease, liver cirrhosis, and chronic obstructive
70 pulmonary disease, their comorbidities were considered positive.

71 In blood laboratory data, serum albumin (g/dL) and total lymphocyte count (/mm³) were
72 examined; thereafter, the value of the PNI was calculated as $10 \times \text{serum albumin (g/dL)} + 0.005$
73 $\times \text{total lymphocyte count (/mm}^3\text{)}$ [15]. Blood sampling data were evaluated within 3 months
74 before surgery (mean 6.3 weeks preoperatively, range; 3 – 11 weeks).

75 When operative wound healing took more than 2 weeks without infection, we defined it as the
76 occurrences of postoperative aseptic wound problems including skin erosion and dehiscence. An
77 operative site complication was identified as periprosthetic joint infection according to the
78 International Consensus Meeting on Periprosthetic Joint Infections [21].

79

80 *Procedure of prevention of infection*

81 All patients underwent a standard protocol to prevent infection. Preoperative intravenous
82 administration of antibiotics (cefazolin, 2 g) was started prior to skin incision. Preoperative skin
83 preparation was performed with 10% povidone iodine, and a skin drape with povidone iodine was

84 put on before skin incision. Then, intravenous administration of antibiotics was done once every
85 6 h (cefazolin, 1 g) on the day of surgery. From the day after surgery, cefazolin (1 g) was
86 administered intravenously every 12 h and was continued for 2 days. There were no patients
87 allergic to cefazolin in this study. A suction drain was used for 1 or 2 days after surgery.

88

89 *Statistical analysis*

90 Patients were divided into two groups according to whether they had periprosthetic joint infection
91 or not, and statistical comparison was performed between groups, regarding age, sex, BMI, serum
92 albumin, total lymphocyte count, PNI, operative duration, intraoperative blood loss, and
93 postoperative aseptic wound problems within 2 weeks after TKA. Then, to calculated odds ratio
94 for periprosthetic joint infection, multivariate regression analysis was performed.

95 Furthermore, patients were divided into two groups according to whether they had aseptic
96 operative wound problems or not, and statistical comparison was also performed between groups,
97 regarding age, sex, BMI, serum albumin, total lymphocyte count, PNI, operative duration, and
98 intraoperative blood loss. Then, to calculate the odds ratio for the presence of postoperative
99 aseptic wound problems, multivariate regression analysis was performed.

100 Comparisons of patient's background and surgical data were performed using a t-test. The number
101 of comorbidities and postoperative complications were compared using the chi-square test. If the

102 number of subjects in either cell was less than 5, Fisher's exact test was employed.

103 SPSS version 23 (IBM Corporation, Armonk, New York, USA) was used for statistical analysis.

104 A p-value of 0.05 was considered statistically significant.

105

106 **Results**

107 Patients were followed for a mean of 4.9 years (range, 1.5 to 10 years) after TKA. Periprosthetic
108 joint infections were occurred in 14 knees (6.0%) after mean 4.9 months (range, 1 to 24 months)
109 postoperatively.

110 No significant differences in the patient demographics were observed between the group with
111 periprosthetic joint infection and the group without periprosthetic joint infection, except for the
112 rate of postoperative aseptic wound problems within 2 weeks (Table 2). In multivariate regression
113 analysis, a significant risk factor of periprosthetic joint infection was identified as positive
114 postoperative wound problems within two weeks (odds ratio; 5.10, 95% confidence interval [CI];
115 1.438–18.093, $p=0.012$).

116 There were significant differences in BMI and PNI between the group with operative wound
117 problems within 2 weeks postoperatively and the group without operative wound problems (Table
118 2). Based on the above results, the significant risk factors of postoperative aseptic wound
119 problems were identified as BMI (odds ratio; 1.270, 95% CI; 1.111–1.453, $p=0.000$), and PNI

120 (odds ratio; 0.858, 95% CI; 0.771–0.955, $p=0.015$) in multivariate regression analysis.

121

122 **Discussion**

123 The most important finding of the present study was that postoperative wound problems were
124 significantly associated with preoperative BMI and PNI, and early postoperative wound problems
125 influenced periprosthetic joint infection after TKA.

126 There were several reports that BMI was associated with postoperative complications after TKA:
127 for example, infection, sepsis, and renal insufficiency [8,22-24]. Based on our study, BMI should
128 be considered as a predictor of postoperative wound problems.

129 To the best of our knowledge, this study is the first to investigate the relationship between
130 preoperative nutritional status using PNI and postoperative wound problems affecting
131 periprosthetic joint infection after TKA. Previously, the values of serum albumin, prealbumin,
132 and transferrin were commonly measured for evaluation of preoperative malnutrition. Several
133 reports showed that low albumin, prealbumin, and transferrin were associated with postoperative
134 infection, wound complications, increased length of hospital stay, and death [8,25-29]. However,
135 there were also several controversial reports that various serological markers related to
136 malnutrition status were questionable for use in predicting postoperative complications [20,30-
137 32]. Rai et al. showed that preoperative malnutrition, as assessed by low levels of serum albumin,

138 serum transferrin, and total lymphocyte count, did not necessarily lead to delayed wound healing
139 [20]. Morey et al. reported that the values of serum albumin level and total lymphocyte count
140 were highly questionable as a surrogate of malnutrition for predicting wound complications after
141 TKA [31]. We considered that all parameters for malnutrition should be subnormal if,
142 theoretically a patient is malnourished. In the present study, when we considered isolated serum
143 albumin level or total lymphocyte count as malnutrition parameters respectively, then 32.4% of
144 patients were interpreted as malnourished; when both serum albumin level and total lymphocyte
145 count were defined as malnutrition dependently, just 2.0% of patients were termed as
146 malnourished. Morey et al. also reported that when they considered serum albumin level or total
147 lymphocyte count as malnutrition parameters respectively, then 21% of patients were interpreted
148 as malnourished; in contrast, when both serum albumin level and total lymphocyte count were
149 defined as malnutrition dependently, only 1.6% of patients were termed as malnourished [31].
150 Therefore, we assume that the prevalence rate of malnutrition in TKA patients can be changed
151 considerably by using the different definitions of parameters. In this study, serum albumin and
152 total lymphocyte count were not directly associated with operative wound problems and
153 periprosthetic joint infection. However, PNI which was calculated by a combination of serum
154 albumin and total lymphocyte count affected early postoperative wound problems. This result of
155 PNI may be unique for the prediction of postoperative complications after TKA.

156 There are some limitations to this study. First, we evaluated only serum albumin and total
157 lymphocyte count levels as serological markers. However, serum albumin and total lymphocyte
158 count were commonly assessed in previous studies. Furthermore, a novel contribution of this
159 study is the calculation of PNI, which was associated with early postoperative aseptic wound
160 problems after TKA. Second, laboratory examinations immediately after surgery, including serum
161 albumin and total lymphocyte count levels, were not evaluated. Postoperative complications
162 might be associated with nutrition status after surgery. However, in this study, we tried to detect
163 preoperative factors of periprosthetic joint infection and aseptic wound problems. Third, there
164 was an unfair patient population with women dominating. Our results might not be applied to
165 other studies with different populations relative to our study. However, more women patients
166 undergo TKA than men in Japan. In addition, we avoided its confounding effect by using
167 multivariate regression analysis.

168 Despite of presence of multiple causes for periprosthetic joint infection after TKA, aseptic
169 operative wound problems in the early phase after TKA were associated with incidence of
170 periprosthetic joint infection. Furthermore, preoperative BMI and PNI are significant risk factors
171 for early postoperative wound problems, and preoperative nutritional assessment may be
172 important for avoiding postoperative complications. Therefore, in patients with high BMI or low
173 PNI, careful attention regarding operative wound condition after TKA is required.

174

175 **Declarations**

176 **Funding** This study was not externally funded.

177 **Conflict of interest** The authors declare that they have no conflict of interest.

178 **Ethical approval** This research has been approved by the Institutional Review Board of the
179 authors' affiliated institutions.

180

181 **Reference**

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278 **Table 1**
 279 Demographic characteristics of the patients.
 280

	190 patients (234 knees)
Age (yr)	74.1 ± 7.6
Sex (men/women)	48 (60 knees)/142 (174 knees)
Body height (cm)	155.6 ± 10.4
Body weight (kg)	58.1 ± 11.7
BMI (kg/m ²)	24.0 ± 4.0
Preoperative serum albumin (g/dL)	4.2 ± 0.3
Preoperative total lymphocyte count (/mm ³)	1813.7 ± 555.5
Preoperative PNI	50.7 ± 4.7
Operative duration (min)	155.4 ± 35.3
Intraoperative blood loss (g)	127.7 ± 120.6
Comorbidities	
Diabetes mellitus	45 (19.2%)
Chronic kidney disease	26 (11.1%)
coronary artery disease	9 (3.4%)
liver cirrhosis	6 (2.6%)
chronic obstructive pulmonary disease	6 (2.6%)
Postoperative aseptic wound problems within 2 weeks	20 (8.5%)
Periprosthetic joint infection	14 (6.0%)

281
 282 Values are presented as numbers, mean and standard deviation, or percentage.
 283 BMI, body mass index
 284 PNI, prognostic nutritional index

285 Table 2
 286 Comparison between patients with and without periprosthetic joint infection
 287

	Patients without periprosthetic joint infection (n=220)	Patients with periprosthetic joint infection (n=14)	
Age (yr)	74.1 ± 7.1	77.2 ± 5.9	<i>p</i> =0.115
Sex (men/women)	54/166	6/8	<i>p</i> =0.227
Body height (cm)	152.0 ± 8.5	152.7 ± 7.6	<i>p</i> =0.788
Body weight (kg)	60.6 ± 11.5	64.4 ± 7.0	<i>p</i> =0.226
BMI (kg/m ²)	26.1 ± 3.8	27.6 ± 3.0	<i>p</i> =0.145
Serum albumin (g/dL)	4.2 ± 0.3	4.1 ± 0.4	<i>p</i> =0.593
Total lymphocyte count (/mm ³)	1825.2 ± 566.8	1633.4 ± 378.3	<i>p</i> =0.214
PNI	50.8 ± 4.8	49.1 ± 3.9	<i>p</i> =0.220
Operative duration (min)	155.0 ± 35.0	161.5 ± 40.1	<i>p</i> =0.505
Intraoperative blood loss (g)	125.9 ± 119.7	156.3 ± 135.3	<i>p</i> =0.365
Comorbidities	78 (35.5%)	6 (42.8%)	<i>p</i> =0.785
Postoperative aseptic wound problems within 2 weeks	16 (7.3%)	4 (28.6%)	<i>p</i> =0.022

288
 289 Values are presented as number of sex, mean (standard deviation), and the rate (%) of
 290 comorbidities and complications.
 291 BMI, body mass index
 292 PNI, prognostic nutritional index

Table 3

Comparison between patients with and without postoperative aseptic wound problems within 2 weeks

	Patients without aseptic operative wound problems (n=214)	Patients with aseptic operative wound problems (n=20)	
Age (yr)	74.3 ± 6.9	74.2 ± 8.5	<i>p</i> =0.950
Sex (men/women)	56/158	4/16	<i>p</i> =0.736
BMI (kg/m ²)	25.8 ± 3.5	29.3 ± 4.8	<i>p</i> <0.001
Serum albumin (g/dL)	4.1 ± 0.3	4.1 ± 0.4	<i>p</i> =0.327
Total lymphocyte count (/mm ³)	1834.8 ± 554.4	1616.0 ± 541.7	<i>p</i> =0.096
PNI	51.0 ± 4.6	48.2 ± 5.7	<i>p</i> =0.015
Operative duration (min)	154.1 ± 35.0	166.4 ± 36.8	<i>p</i> =0.142
Intraoperative blood loss (g)	125.2 ± 117.0	152.3 ± 149.0	<i>p</i> =0.345
Comorbidities (%)	73 (34.1%)	11 (55.0%)	<i>p</i> =0.105

Values are presented as number of sex, mean (standard deviation), and the rate (%) of comorbidities.

BMI, body mass index

PNI, prognostic nutritional index