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Perioperative Immunonutrition in Elderly Patients Undergoing Total Hip and Knee Arthroplasty: Impact on Postoperative Outcomes

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Abstract

Background: Arthroplasties in elderly patients are surgeries performed to ensure their quality of life. Perioperative care with specific nutrients can improve nutrition status and metabolic response to orthopedic surgeries, such as total knee arthroplasty (TKA) and total hip arthroplasty (THA). *Methods:* Retrospective study with elderly patients divided into 2 groups: control and immunonutrition. The immunonutrition group was instructed to start oral intake of the nutrition supplement 5 days before and to resume it 5 days after arthroplasty (200 mL, 3 times per day). The following were analyzed as primary and secondary outcomes: length of stay (LOS), infectious and noninfectious complications, need for intensive care unit (ICU), transfusion requirement, and C-reactive protein. *Results:* A total of 3015 elderly patients met the inclusion criteria: control group (n = 1398) and immunonutrition group (n = 1617). Overall, 81.2% were women and mean age was 72.6 ± 6.9 years. Immunonutrition group had a shorter LOS in hours (32.0 ± 19.4 vs 56.0 ± 26.4; $P < .001$) and lower rates of infectious complications (2.2% vs 4.6%; $P < .001$). Noninfectious complications and need for ICU also had lower rates in the immunonutrition group. In the logistic regression analysis, immunonutrition reduced the chance of infectious complications by 55% (odds ratio [OR], 0.45; 95% CI, 0.30–0.68; $P < .001$) even after adjusting for variables (OR, 0.45; 95% CI, 0.28–0.71; $P < .001$). *Conclusion:* Perioperative immunonutrition in elderly patients undergoing THA or TKA may shorten postoperative LOS and reduce infectious and noninfectious complications and transfusion requirement. (*JPEN J Parenter Enteral Nutr.* 2021;45:1559–1566)

Keywords

elderly; immunonutrition; infectious complications; length of stay; total knee arthroplasty; total hip arthroplasty

Clinical Relevancy Statement

This article shows the best clinical and surgical outcomes in a group composed for elderly patients who performed specific oral nutrition supplementation with immunonutrients in the perioperative period and were submitted to knee and hip arthroplasties. The conclusion can be reflected as better cost-effectiveness in perioperative care due to reduced hospital length of stay, less infectious and noninfectious complications, and a better quality of life after surgery for elderly patients.

Introduction

Primary total hip arthroplasty (THA) and total knee arthroplasty (TKA) are safe and effective orthopedic surgeries for patients with end-stage osteoarthritis (OA).[1] The prevalence is greater in elderly patients; thus, it is not surprising that the usage rates for joint arthroplasty increase with age.[2,3] OA is the most prevalent joint disease and a leading source of chronic pain and disability in the United States and other developed nations.[4,5]

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Total arthroplasty is a surgical procedure performed to reduce pain, improve function, and correct deformities.[6] The long-term goals of arthroplasty are to relieve pain, increase function, provide stability, and obtain durability. The short-term goals, however, have become the target of aggressive perioperative programs that aim to speed recovery, reduce morbidity and complications, and create an efficient program while maintaining the highest level of patient care.[7,8] Therefore, the success of THA and TKA comprises a group of surgical procedures performed for the management of end-stage arthritis and the improvement of the overall health and quality of life in patients with chronic joint conditions.[9–11]

Among the pillars of success of THA and TKA, we have the preserved nutrition status and immune system, suitable for the patient preoperatively, which are essential to provide an essential source of energy, protein, vitamins, and minerals to have an accelerated recovery after surgery.[12–14] The use of different nutrients to improve the nutrition status and modulate the function of the immune system shows to be necessary in high-metabolic, stressful situations.[15,16]

The advent of nutrition supplements that modulate immunity (containing a mix of immunonutrients, including the amino acids arginine and glutamine, fish oil [ω-3 fatty acids], and nucleotides), when administered perioperatively, may improve wound healing and postoperative inflammation, thus reducing infectious complications and length of stay (LOS) and, therefore, having a positive impact on the quality of life of surgical patients.[13,16]

The prognostic role of metabolic stress in surgical patients encouraged the perioperative administration of energy and proteins (nutrition support) to meet postoperative requirements and prevented a further deterioration of nutrition status after surgery when periods of prolonged fasting and muscle catabolism are expected.[14,17] Nutrition supplements can influence outcomes, particularly in elderly patients, as their functional reserve is limited. Perioperative nutrition support significantly improved postoperative outcomes, such as mortality, morbidity, and LOS, which also translated into relevant economic implications.[1,18,19]

The use of immunonutrients in major gastrointestinal surgeries is well known in the medical literature, with several studies confirming its beneficial results.[16,20,21] Therefore, the goal of this study is to evaluate whether perioperative oral nutrition supplementation (ONS) with immunonutrients can improve postoperative outcomes in orthopedic surgeries, such as primary THA and TKA in elderly patients.

Methods

Study Design and Setting

This is a retrospective observational cohort study, with data collected from elderly patients with indication for primary elective TKA and THA surgeries performed in a single geriatric center of orthopedic surgery from January 2014 to December 2018. The elderly patients who met inclusion criteria were reported in the study and divided into 2 groups: control (that is, a historical control without immunonutrition protocol, from January 2014 to August 2016) and immunonutrition (with immunonutrition perioperative protocol, from September 2016 to December 2018).

The patients in the immunonutrition group received ONS with Impact immunonutrients (Nestlé Health Science, Epalinges, Switzerland) in preoperative medical appointments (30 bottles of 200 mL each) and were instructed to start the daily oral intake 5 days before the arthroplasty and to resume it for another 5 days after the surgery procedure. The dose used was 200 mL, 3 times per day (600 mL per day). The ONS intake control was made during hospital admission for the surgical procedure when patients provided a form with the percentage of acceptance in the 5 days prior to arthroplasty.

The inclusion criteria were age $\geq$60 years, indication for elective orthopedic-cemented or uncemented surgery with TKA or THA, patients with oral intake only, a volume ingestion $\geq$50% of the ONS with immunonutrients, and only primary total arthroplasty. Exclusion criteria were patients who evolved with clinical instability and a requirement for prolonged fasting in the postoperative period, patients with a need for urgent and/or emergency orthopedic surgery, patients allergic to components of the ONS with immunonutrients, patients using enteral or parenteral nutrition therapy, and patients undergoing revision arthroplasty. The inclusion and exclusion criteria flow charts are shown in Figure 1.

In the preoperative period, all patients (historical control and immunonutrition group) received an abbreviation for fasting according to the Enhanced Recovery After Surgery protocol. In the postoperative period, all patients received medication for prophylaxis of venous thromboembolism (unfractionated heparin), compression stockings, early mobilization allowing full-weight bearing, pain control, and respiratory physiotherapy as part of a recovery, fast-track institutional protocol. Thus, both groups received the same preoperative and postoperative treatment, except for the immunonutrition supplements in the latter group.

The study was reviewed and approved by the local research ethics committee in according to the Certificate of Presentation for Ethical Appreciation (CPEA 20295019.8.0000.8114). All procedures were performed following the Declaration of Helsinki.

Variables and Measures

Data of interest were collected for analysis of the elderly patients undergoing primary TKA and THA: demographic data (gender and age); anthropometric data, such as weight

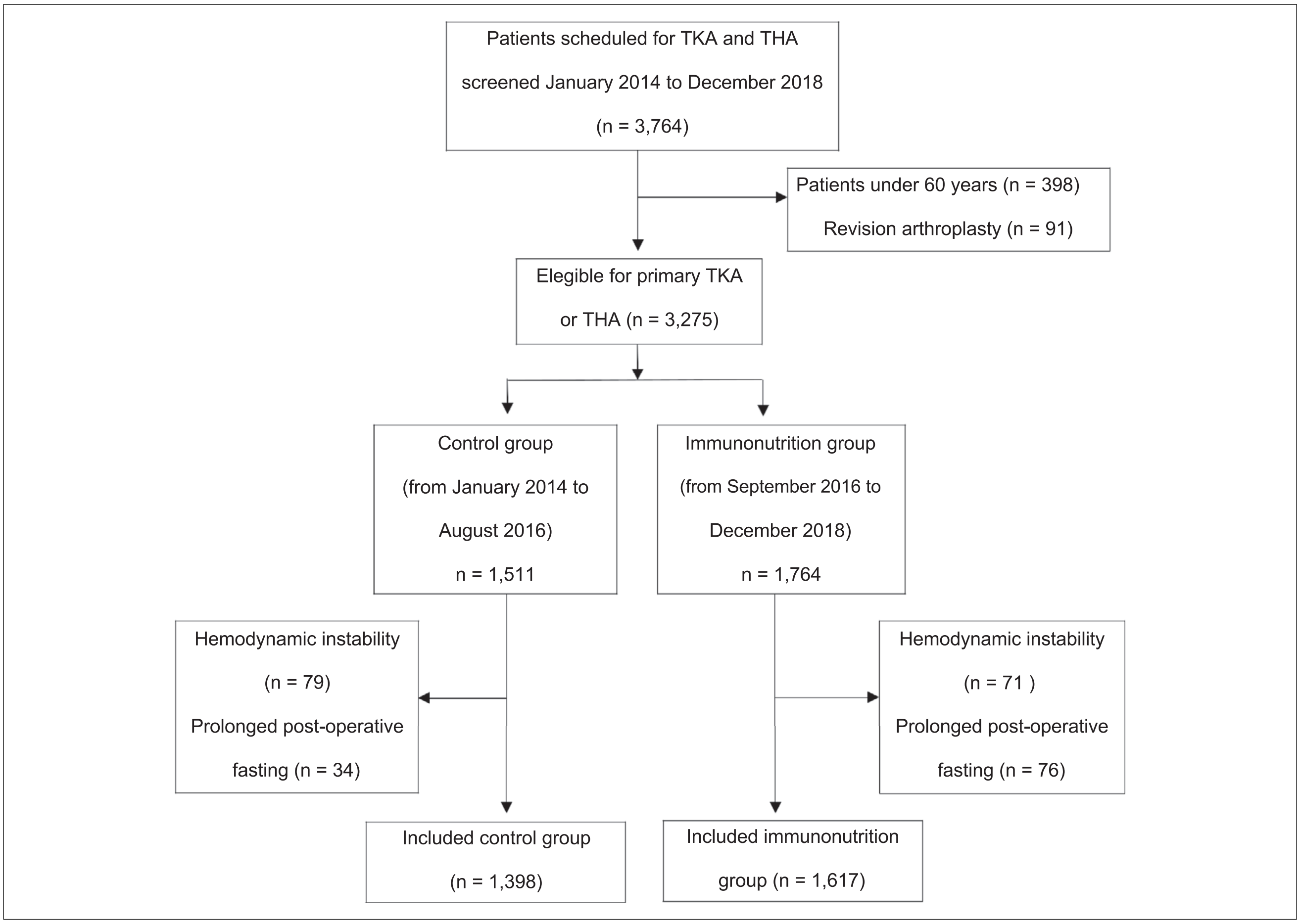

Figure 1. Flow chart describing inclusion and exclusion criteria of the control group and immunonutrion group. THA, total hip arthroplasty; TKA, total knee arthroplasty.

(kilograms), height (meters), body mass index (BMI), and calf circumference (CC); type of primary elective arthroplasty (knee or hip); whether the arthroplasty was cemented or uncemented; and laboratory data (blood count and C-reactive protein [CRP] measurement between 12 and 24 hours after surgery). BMI was calculated as weight divided by height (in meters squared). Obesity was defined as a BMI $\geq$ 30.

Between the control and immunonutrition groups, the primary outcomes were LOS (in hours) and presence of infectious complications (surgical site infection and/or prosthetic joint infection). Secondary outcomes were the need for immediate postoperative care in the intensive care unit (ICU), the requirement for blood transfusion in the postoperative period, the presence of noninfectious complications (deep venous thrombosis, hematoma, surgical wound dehiscence, acute kidney failure, or prosthesis dislocation), and mortality.

Infectious complications, noninfectious complications, and mortality were assessed within 90 days after arthroplasty. The follow-up routine was at 30 and 90 days after surgery for both groups. The average number of days that these complications appeared in the follow-up after surgery in each group was determined.

Statistical Analysis

First, for the descriptive analysis, variables were tested for normality by using the Shapiro-Wilk test ($P > .05$ for normality). For variables with a normal distribution, data were expressed as mean and SD, and categorical data were expressed as a percentage of proportion. The comparison of percentage distribution of categorical variables was performed by using the Pearson χ^2 test. For variables with a normal distribution, the comparison of absolute means between independent groups was performed by using the Student *t*-test. Correlations between groups in quantitative variables were studied by using Pearson and Spearman coefficient of correlation. Generalized linear models appropriate to the distribution of each variable were used. To

Table 1. Baseline Characteristics of Elderly Patients Undergoing Primary THA and TKA.

Variable	Control, n = 1398	Immunonutrition, n = 1617	*P*
Age, y	72.9 ± 6.7	72.4 ± 7.1	.074
Gender (%)			
Female	1159 (82.9)	1289 (79.7)	.029
Male	239 (17.1)	328 (20.3)	
BMI	30.6 ± 4.8	30.7 ± 5.2	.528
CC, cm	38.6 ± 4.1	37.6 ± 4.1	<.001
Type of surgery (%)			
TKA	894 (63.9)	954 (59.0)	.006
THA	504 (36.1)	663 (41.0)	
Cemented surgery (%)			
No	355 (25.4)	677 (41.9)	<.001
Yes	1043 (74.6)	940 (58.1)	

Data are expressed as mean and SD. BMI is calculated as weight in kilograms divided by height in meters squared.
BMI, body mass index; CC, calf circumference; THA, total hip arthroplasty; TKA, total knee arthroplasty.

Table 2. Characteristics of Elderly Patients Submitted to Primary THA and TKA, With Infectious Complications.

Variable	Infectious complications No, n = 2915	Yes, n = 100	*P*
Age, y	72.6 ± 6.9	74.1 ± 7.5	.044
Gender (%)			
Female	2364 (81.1)	84 (84.0)	.548
Male	551 (18.9)	16 (16.0)	
BMI	30.6 ± 5.0	30.8 ± 4.7	.736
CC, cm	38.0 ± 4.2	38.0 ± 3.9	.890
Type of surgery (%)			
TKA	1778 (61.0)	70 (70.0)	.087
THA	1137 (39.0)	30 (30.0)	
Cemented surgery (%)			
No	1003 (34.4)	29 (29.0)	0.311
Yes	1912 (65.6)	71 (71.0)	

Data are expressed as mean and SD. BMI is calculated as weight in kilograms divided by height in meters squared.
BMI, body mass index; CC, calf circumference; THA, total hip arthroplasty; TKA, total knee arthroplasty.

identify the independent factors associated with primary and secondary outcomes, multivariate logistic regression analysis was performed before and after adjustments for the variables. Potentially confounding variables was adjusted for age, gender, BMI, CC, type of arthroplasty, and cemented or uncemented surgery. The effects of measure were presented in crude and adjusted forms for baseline variables. Statistical significance was set at $P < .05$ and at a 95% CI. Observational data were statistically analyzed by using R 3.6.3 software (R Foundation, 2020).

Results

Baseline characteristics of 3015 elderly patients undergoing primary TKA or THA, according to the control group (n = 1398) and immunonutrition group (n = 1617), are shown in Table 1.

According to demographic and anthropometric data from all patients, 81.2% were women, mean age was 72.6 ± 6.9 years, and mean BMI was 30.6 ± 5.0. The prevalence of obesity (BMI ≥ 30) was 53.9%. Comparing the characteristics of the 2 groups, there was a significant difference between gender and measurement of the CC. Although the proportion of women was higher in both groups, an even greater proportion was observed in the control group when compared with the immunonutrition group (82.9% vs 79.7%; $P = .029$). The mean CC was significantly higher in the control group (38.6 ± 4.1 vs 37.6 ± 4.1; $P < .001$). The BMI comparison between groups had no significant difference (30.6 ± 5.0 vs 30.7 ± 5.2; $P = .528$).

The type of surgery, TKA or THA, and cemented or uncemented surgery also had a significant difference between groups ($P = .006$ and $P < .001$, respectively). Arthroplasty performed on the knee joint and cemented surgery were more frequent in the control group.

Table 2 demonstrates that 3.3% had infectious complications (n = 100) and shows the association between baseline characteristics of all patients and the presence of infectious complications. There was a significant difference only with the age variable. Patients with infectious complications had a higher mean age when compared with patients with no complications ($P = .044$).

Noninfectious complications occurred in 4.0% of all patients, and Table 3 shows the characteristics of patients who presented these complications (n = 121). The most common noninfectious complications were acute kidney failure (1.1%), wound dehiscence (0.9%), deep venous thrombosis (0.7%), hematoma (0.7%), and prosthesis dislocation (0.6%). A higher mean age and a higher difference of proportion of male elderly patients was reported in the group with noninfectious complications, as compared with the group without noninfectious complications, with statistically significant difference ($P = .030$ and $P = .002$, respectively).

The average number of days that infectious and noninfectious complications appeared after total arthroplasties, during the follow-up within 90 days, were not significantly different between the control group and immunonutrition group. All infectious and noninfectious complications occurred within the 30-day follow-up period in both groups.

Regarding primary outcomes, the immunonutrition group had shorter LOS in hours (32.0 ± 19.4 vs 56.0 ± 26.4; $P < .001$) and had lower rates of infectious complications (2.2% vs 4.6%; $P < .001$) compared with the control group (Table 4). The mean LOS in the immunonutrition group

Table 3. Characteristics of Elderly Patients Submitted to Primary THA and TKA, With Noninfectious Complications.

	Noninfectious complications		
Variable	No, n = 2894	Yes, n = 121	*P*
Age, y	72.6 ± 6.9	74.1 ± 7.7	.030
Gender (%)			
Female	2363 (81.7)	85 (70.2)	.002
Male	531 (18.3)	36 (29.8)	
BMI	30.6 ± 5.0	30.1 ± 5.2	.269
CC, cm	38.0 ± 4.2	37.9 ± 4.4	.906
Type of surgery (%)			
TKA	1778 (61.4)	70 (57.9)	.485
THA	1116 (38.6)	51 (42.1)	
Cemented surgery (%)			
No	985 (34.0)	47 (38.8)	.320
Yes	1909 (66.0)	74 (61.2)	

Data are expressed as mean and SD. BMI is calculated as weight in kilograms divided by height in meters squared.
BMI, body mass index; CC, calf circumference; THA, total hip arthroplasty; TKA, total knee arthroplasty.

Table 4. Primary and Secondary Outcomes of Elderly Patients Undergoing Primary THA and TKA.

Outcomes	Control, n = 1398	Immunonutrition, n = 1617	*P*
LOS, h	56.0 ± 26.4	32.0 ± 19.4	<.001
Infectious complications (%)	65 (4.6)	35 (2.2)	<.001
Noninfectious complications (%)	76 (5.4)	45 (2.8)	<.001
ICU (%)	96 (6.9)	104 (6.4)	.630
Transfusion (%)	300 (21.5)	104 (6.4)	<.001
Hb, g/dL	9.6 ± 1.5	11.2 ± 1.5	<.001
Ht (%)	28.4 ± 4.2	33.4 ± 4.4	<.001
CRP, mg/dL	83.2 ± 72.0	37.5 ± 54.8	<.001
Mortality 90-day (%)	9 (0.6)	4 (0.2)	.110

CRP, C-reactive protein; Hb, hemoglobin; Ht, hematocrit; ICU, intensive care unit; LOS, length of stay; THA, total hip arthroplasty; TKA, total knee arthroplasty.

was 42% lower than that in the control group. Secondary outcomes, such as noninfectious complications and the requirement for postoperative transfusion, also had lower proportions in the immunonutrition group, with a statistically significant difference. CRP measured after surgery had lower mean value in the immunonutrition group ($P < .001$) and was 55% lower than that in the control group.

The logistic regression analysis is demonstrated in Table 5 and shows that patients in the immunonutrition group had a 55% reduction in the chance of infectious complications (odds ratio [OR], 0.45; 95% CI, 0.30–0.68; $P < .001$). Even after adjusting for baseline variables (age, gender, BMI, CC, type of arthroplasty, and cemented or uncemented surgery), the effect still remained with the same magnitude. For noninfectious complications, the immunonutrition group reduced the chance of complications by 50% (OR, 0.50; 95% CI, 0.34–0.72; $P < .001$), and the measure of effect also remained after adjusting for baseline variables.

The elderly patients in the immunonutrition group showed a 75% reduction in the chance of blood transfusion in the postoperative period (OR, 0.25; 95% CI, 0.20–0.32; $P < .001$). In the adjusted model, this reduction was 76%, without major variations (OR, 0.24; 95% CI, 0.19–0.31; $P < .001$). The measures of effect on the requirement for ICU and 90-day mortality were not significantly different between groups.

Discussion

Our study reported that elderly patients undergoing primary TKA or THA who received nutrition supplements with immunonutrients in perioperative care had shorter LOS and lower rates of infectious complications compared with the control group. There was a 55% reduction in the chance of infectious complications and mean LOS was 42% lower in the immunonutrition group. In addition, the immunonutrition group reduced the chance of secondary outcomes, such as noninfectious complications and the need for blood transfusion, by 50% and 76%, respectively, in an adjusted logistic regression model.

It has long been known that in any surgical procedure, the body reacts with the release of stress hormones, such as cortisol, catecholamines, and glucagon. Those hormones are released quite quickly and cause changes to metabolism by mobilizing substrates from all energy storages, including glucose from glycogen, fat from fat deposits, and protein mainly from muscles.[14] At the same time, the inflammatory system is also activated in injuries. Therefore, cytokines are released, among which tumor necrosis factor α and interleukin 6 have been identified in the metabolic responses and increased production of acute-phase proteins, such as CRP.[22]

Metabolic response to surgery causes hyperinflammation, oxidative stress, and immune impairment, which increase the risk of postoperative infections.[13,23] Therefore, the aim of immunonutrition is to modulate the metabolic response after surgery by using specific nutrition substrates with metabolic effects in patients with high risk to develop postoperative infections, regardless of their baseline nutrition status.[12,16,20]

Although immune dysfunction in surgical patients is multifactorial, recent studies suggest that the immune system may be modulated by the use of specific nutrients (immunonutrients), such as arginine, ω-3 fatty acids, and nucleotides, which have the ability to ensure the defense

Table 5. Logistic Regression Model for Crude and Adjusted Measures of Effect of the Primary and Secondary Outcomes.

				95% CI				95% CI		
Variable	Control, n = 1398	Immunonutrition, n = 1617	Crude OR[a]	Lower	Upper	P	Adjusted OR[b]	Lower	Upper	P
Infectious complications	65 (4.6%)	35 (2.2%)	0.45	0.30	0.68	<.001	0.45	0.28	0.71	<.001
Noninfectious complications	76 (5.4%)	45 (2.8%)	0.50	0.34	0.72	<.001	0.50	0.33	0.76	<.001
ICU	96 (6.9%)	104 (6.4%)	0.93	0.70	1.24	.630	1.03	0.75	1.42	.860
Transfusion	300 (21.5%)	104 (6.4%)	0.25	0.20	0.32	<.001	0.24	0.19	0.31	<.001
90-day mortality	9 (0.6%)	4 (0.2%)	0.38	0.10	1.18	.110	0.36	0.09	1.27	.120

ICU, intensive care unit; OR, odds ratio.
[a]Crude odds ratio.
[b]Adjusted odds ratio for gender, age, BMI, CC, type of arthroplasty, and cemented or uncemented surgery.

mechanisms and intestinal barrier function and to modulate the inflammatory response.[24,25] There is evidence suggesting that supplements with immunomodulatory agents improve postoperative immunological response and speed up recovery from the immunodepression following surgical trauma and reduce the incidence of infectious complications.[21,26]

Alito et al published the only study in which immunonutrition was used in orthopedic patients and concluded that patients who underwent arthroplasties and who received perioperative preparation with immunonutrients had a shorter LOS and lower values of CRP collected in the third postoperative day.[8] However, this study was led with a few patients (n = 32), and they were not exclusively elderly. Therefore, by then, there was no impact study to justify and recommend the use of perioperative preparation with immunonutrition in elderly patients undergoing orthopedic surgery.

According to the European Society of Parenteral and Enteral Nutrition guidelines for surgery, based on a grade A level of evidence, immunonutrition is already indicated for all patients undergoing operation for digestive cancer 5–7 days prior to surgery, regardless of the patient's nutrition status. Immunonutrition should be continued in the postoperative phase in malnourished patients for 5–7 days or until patients are able to resume oral intake, covering ≥60% of their requirements.[12,16]

Regarding the LOS, our study showed a reduction of 1 day (24 hours) in the immunonutrition group, even in a fast-track program. A large number of investigations report that LOS after arthroplasty can be reduced from 4–12 days to 1–3 days, with no significant increase in the incidence of complications when it is part of a fast-track program.[27–29] At the same time, studies show that perioperative nutrition can benefit the vast majority of patients submitted to hip or knee arthroplasty, including the elderly ones.[18,26,30]

A systematic review and meta-analysis showed that preoperative low serum albumin level, total lymphocyte count, or serum transferrin levels correlate with poor postoperative outcomes and wound complications after TKA or THA.[31] Since these lab tests are markers of systemic inflammation and do not correlate with nutrition status, the increase in complications in these patients is most likely due to the presence of severe systemic inflammation prior to surgery rather than malnutrition. The improved clinical outcomes after TKA or THA when immunonutrition is administered preoperatively and postoperatively may be due to the down regulation of systemic inflammation, which is supported by our finding of a significantly lower CRP level in the immunonutrition group compared with the control group (Table 4). It is less likely that the improved clinical outcomes are related to any changes in the patient's nutrition status with the immunonutrition supplementation.

Another finding in our study was the high prevalence of elderly women (81.2%) and obesity by BMI (53.9%). Remember that we did not use a validated tool to assess nutrition status, although there was no difference in BMI between the 2 groups. It is known that OA is more common in obese women than in men, and the prevalence of OA increases steeply with age.[5] With the aging of the population, and the increase in obesity throughout the world, it is anticipated that the burden of OA will become a major problem for health systems globally.[32–34]

Although there is an extensive literature on the relationship between the chronic inflammatory state of obese patients and postoperative complications in orthopedic surgery, there has been an increasing emphasis on medical comorbidities, often concomitant impaired immunity.[35] Interestingly, there has been recent evidence that the co-prevalence of micronutrient and protein deficiencies may be paradoxically associated with increasing BMI.[36] A prospective study reported that obese TKA patients were 6.7 times more likely to sustain a prosthetic joint infection, whereas obese THA patients had a 4.2 times higher risk.[37,38] Also, obese patients have double the risk of developing surgical site infections.[39]

In our study, the CC in the control group was significantly higher than that in the immunonutrition group (38.6 ± 4.1 vs 37.6 ± 4.1; $P < .001$), but this finding does not show us that the immunonutrition group had worse anthropometric measures, since both groups had their averages above the cutoff points validated for the Brazilian population for normal muscle mass assessed by CC as an anthropometric measure (men > 34 cm and women > 33 cm).[40] In addition, both groups had a mean BMI in the obesity range and were not significantly different. So, we did not feel the differences in CC between the 2 study groups significantly affected our findings or conclusions.

Therefore, the central principle of perioperative immunonutrition is to reduce complications, shorten the hospital LOS, improve patient satisfaction (providing pain relief and functional improvement), save costs, and promote faster recovery, since OA is a very prevalent chronic comorbidity in the elderly population and a serious problem for healthcare systems worldwide.[41–43]

Our study has some limitations. First, this study was retrospective, and, since it was not a double-blind study, it could contribute to some form of bias. Therefore, the integrity of the information in medical records was limited regarding the outcomes of infectious and noninfectious complications. The documentation was also limited in reporting the use of immunosuppressants and other agents that modify the metabolic response associated with lower immunity and poor nutrition status. Second, we only control the ONS intake preoperatively, and all patients ingested $\geq 50\%$ of the total daily volume, but not all patients were able to ingest the entire volume of postoperative supplements. Third, the previous comorbidities of the elderly patients were not reported and could interfere with the occurrence of postoperative complications. The last limitation refers to the study design, as it is a historical control (meaning the treatments were not carried out at the same time) and other procedures in the care of these patients may have been modified over time, changing the clinical outcomes although both groups received the same treatment, except for the specific ONS in the immunonutrition group.

Conclusion

In light of the increasing number of joint-replacement surgeries, it is important to understand the effectiveness of perioperative protocols used to improve postoperative results and ensure quality of life to elderly patients. These findings allow us to conclude that the use of perioperative immunonutrition protocol in elderly patients undergoing primary, elective THA and TKA, regardless of baseline BMI, may shorten the postoperative LOS and reduce infectious and noninfectious complications, the need for blood transfusion, and acute-phase proteins.

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Statement of Authorship

T. J. M. Gonçalves, S. E. A. B. Gonçalves, and N. Nava equally contributed to the conception and design of the research; V. C. Jorge contributed to the design of the research; A. M. Okawa and V. A. Rocha contributed to the acquisition and analysis of the data; L. C. H. Forato, V. A. O. Furuya, and S. S. Martins contributed to the analysis of the data; D. Oksman contributed to the acquisition, analysis, and interpretation of the data. All authors drafted the manuscript, critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

References

1. Daigle ME, Weinstein AM, Katz JN, Losina E. The cost-effectiveness of total joint arthroplasty: a systematic review of published literature. *Best Pract Res Clin Rheumatol*. 2012;26(5):649-658.
2. Alexiou KI, Roushias A, Varitimidis SE, Malizos KN. Quality of life and psychological consequences in elderly patients after a hip fracture: a review. *Clin Interv Aging*. 2018;13:143-150.
3. Schwartz AJ, Chang YH, Bozic KJ, Etzioni DA. Evidence of pent-up demand for total hip and total knee arthroplasty at age 65. *J Arthroplasty*. 2019;34(2):194-200.
4. Murray CJ, Atkinson C, Bhalla K, et al. The state of US health, 1990–2010: burden of diseases, injuries, and risk factors. *JAMA*. 2013;310(6):591-608.
5. Cross M, Smith E, Hoy D, et al. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. *Ann Rheum Dis*. 2014;73(7):1323-1330.
6. Driesman A, Paoli AR, Wiznia DH, et al. Total joint arthroplasty is associated with a decreased risk of traumatic falls: an analysis of 499,094 cases. *J Am Acad Orthop Surg*. 2020;28(20):838-846.
7. Berend KR, Lombardi AV, Jr., Mallory TH. Rapid recovery protocol for peri-operative care of total hip and total knee arthroplasty patients. *Surg Technol Int*. 2004;13:239-347.
8. Alito MA, de Aguilar-Nascimento JE. Multimodal perioperative care plus immunonutrition versus traditional care in total hip arthroplasty: a randomized pilot study. *Nutr J*. 2016;15(1):34.
9. Ethgen O, Bruyère O, Richy F, Dardennes C, Reginster JY. Health-related quality of life in total hip and total knee arthroplasty. A qualitative and systematic review of the literature. *J Bone Joint Surg Am*. 2004;86(5):963-974.
10. Schwartz AJ, Bozic KJ, Etzioni DA. Value-based total hip and knee arthroplasty: a framework for understanding the literature. *J Am Acad Orthop Surg*. 2019;27(1):1-11.
11. Ibrahim MS, Khan MA, Nizam I, Haddad FS. Peri-operative interventions producing better functional outcomes and enhanced recovery following total hip and knee arthroplasty: an evidence-based review. *BMC Med*. 2013;11(1):37.
12. Mariette C. Immunonutrition. *J Visc Surg*. 2015;152(Suppl 1):S14-S17.
13. Braga M. The 2015 ESPEN arvid wretlind lecture. Evolving concepts on perioperative metabolism and support. *Clin Nutr*. 2016;35(1):7-11.
14. Ljungqvist O, Soop M, Hedstrom M. Why metabolism matters in elective orthopedic surgery: a review. *Acta Orthop*. 2007;78(5):610-615.

15. Martindale RG, McClave SA, Taylor B, Lawson CM. Perioperative nutrition: what is the current landscape? *JPEN J Parenter Enteral Nutr*. 2013;37(5 Suppl):5s-20s.
16. Weimann A, Braga M, Carli F, et al. ESPEN guideline: clinical nutrition in surgery. *Clin Nutr*. 2017;36(3):623-650.
17. Morán López JM, Piedra León M, García Unzueta MT, et al. Perioperative nutritional support. *Cir Esp*. 2014;92(6):379-386.
18. Burgess LC, Phillips SM, Wainwright TW. What is the role of nutritional supplements in support of total hip replacement and total knee replacement surgeries? a systematic review. *Nutrients*. 2018;10(7):820.
19. Greene KA, Wilde AH, Stulberg BN. Preoperative nutritional status of total joint patients. Relationship to postoperative wound complications. *J Arthroplasty*. 1991;6(4):321-325.
20. Waitzberg DL, Saito H, Plank LD, et al. Postsurgical infections are reduced with specialized nutrition support. *World J Surg*. 2006;30(8):1592-1604.
21. Marik PE, Flemmer M. Immunonutrition in the surgical patient. *Minerva Anestesiol*. 2012;78(3):336-342.
22. Neumaier M, Braun KF, Sandmann G, Siebenlist S. C-reactive protein in orthopaedic surgery. *Acta Chir Orthop Traumatol Cech*. 2015;82(5):327-331.
23. Kwong LM, Kistler KD, Mills R, Wildgoose P, Klaskala W. Thromboprophylaxis, bleeding and post-operative prosthetic joint infection in total hip and knee arthroplasty: a comprehensive literature review. *Expert Opin Pharmacother*. 2012;13(3):333-244.
24. Enomoto TM, Larson D, Martindale RG. Patients requiring perioperative nutritional support. *Med Clin North Am*. 2013;97(6):1181-200.
25. Chow O, Barbul A. Immunonutrition: role in wound healing and tissue regeneration. *Adv Wound Care (New Rochelle)*. 2014;3(1):46–53.
26. Evans DC, Martindale RG, Kiraly LN, Jones CM. Nutrition optimization prior to surgery. *Nutr Clin Pract*. 2014;29(1):10-21.
27. Jorgensen CC, Petersen PB, Kehlet H. Days alive and out of hospital after fast-track total hip and knee arthroplasty: an observational cohort study in 16 137 patients. *Br J Anaesth*. 2019;123(5):671-678.
28. Berg U, Berg M, Rolfson O, Erichsen-Andersson A. Fast-track program of elective joint replacement in hip and knee-patients' experiences of the clinical pathway and care process. *J Orthop Surg Res*. 2019;14(1):186.
29. Berg U, BüLow E, Sundberg M, Rolfson O. No increase in readmissions or adverse events after implementation of fast-track program in total hip and knee replacement at 8 Swedish hospitals: an observational before-and-after study of 14,148 total joint replacements 2011–2015. *Acta Orthop*. 2018;89(5):522-527.
30. Botella-Carretero JI, Iglesias B, Balsa JA, Arrieta F, Zamarrón I, Vázquez C. Perioperative oral nutritional supplements in normally or mildly undernourished geriatric patients submitted to surgery for hip fracture: a randomized clinical trial. *Clin Nutr*. 2010;29(5):574-579.
31. Gu A, Malahias MA, Strigelli V, Nocon AA, Sculco TP, Sculco PK. Preoperative malnutrition negatively correlates with postoperative wound complications and infection after total joint arthroplasty: a systematic review and meta-analysis. *J Arthroplasty*. 2019;34(5):1013-1024.
32. Grotle M, Hagen KB, Natvig B, Dahl FA, Kvien TK. Obesity and osteoarthritis in knee, hip and/or hand: an epidemiological study in the general population with 10 years follow-up. *BMC Musculoskelet Disord*. 2008;9(1):132.
33. Leyland KM, Judge A, Javaid MK, et al. Obesity and the relative risk of knee replacement surgery in patients with knee osteoarthritis: a prospective cohort study. *Arthritis Rheumatol*. 2016;68(4):817-825.
34. Sloan M, Premkumar A, Sheth NP. Projected volume of primary total joint arthroplasty in the U.S., 2014 to 2030. *JBJS*. 2018;100(17):1455-1460.
35. Reyes C, Leyland KM, Peat G, Cooper C, Arden NK, Prieto-Alhambra D. Association between overweight and obesity and risk of clinically diagnosed knee, hip, and hand osteoarthritis: a population-based cohort study. *Arthritis Rheumatol*. 2016;68(8):1869-1875.
36. Fu MC, D'Ambrosia C, McLawhorn AS, Schairer WW, Padgett DE, Cross MB. Malnutrition increases with obesity and is a stronger independent risk factor for postoperative complications: a propensity-adjusted analysis of total hip arthroplasty patients. *J Arthroplasty*. 2016;31(11):2415-2421.
37. Namba RS, Paxton L, Fithian DC, Stone ML. Obesity and perioperative morbidity in total hip and total knee arthroplasty patients. *J Arthroplasty*. 2005;20(7 Suppl 3):46-50.
38. Antonelli B, Chen AF. Reducing the risk of infection after total joint arthroplasty: preoperative optimization. *Anthroplasty*. Published August 1, 2019. https://doi.org/10.1186/s42836-019-0003-7
39. Yuan K, Chen HL. Obesity and surgical site infections risk in orthopedics: a meta-analysis. *Int J Surg*. 2013;11(5):383-388.
40. Barbosa-Silva TG, Bielemann RM, Gonzalez MC, Menezes AM. Prevalence of sarcopenia among community-dwelling elderly of a medium-sized South American city: results of the COMO VAI? study. *J Cachexia Sarcopenia Muscle*. 2016;7(2):136-143.
41. Deng QF, Gu HY, Peng WY, et al. Impact of enhanced recovery after surgery on postoperative recovery after joint arthroplasty: results from a systematic review and meta-analysis. *Postgrad Med J*. 2018;94(1118):678-693.
42. Konopka JF, Lee YY, Su EP, McLawhorn AS. Quality-adjusted life years after hip and knee arthroplasty: health-related quality of life after 12,782 joint replacements. *JB JS Open Access*. 2018;3(3):e0007.
43. Wallace IJ, Worthington S, Felson DT, et al. Knee osteoarthritis has doubled in prevalence since the mid-20th century. *Proc Natl Acad Sci U S A*. 2017;114(35):9332-9336.