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Original Article

# Association between preoperative lumbar skeletal muscle index and postoperative nausea and vomiting in patients undergoing pylorus-preserving pancreatoduodenectomy: a retrospective study

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**Background:** Sarcopenia is associated with postoperative complications; however, its impact on the quality of postoperative recovery, such as postoperative nausea and vomiting (PONV) and pain, remains unclear. We investigated the association of preoperative lumbar skeletal muscle mass index (LSMI) with PONV, postoperative pain, and complications.

**Methods:** Medical records of 756 patients who underwent pylorus-preserving pancreatoduodenectomy (PPPD) were retrospectively reviewed. The skeletal muscle areas were measured on abdominal computed tomography (CT) images. LSMI was calculated by dividing the skeletal muscle area by the square of the patient's height. We analyzed the correlations between preoperative LSMI calibrated with confounding variables and PONV scores, PONV occurrence, pain scores, rescue analgesic administration, postoperative complications, and length of hospital stay.

**Results:** The median (1Q, 3Q) LSMI was 47.72 (40.74, 53.41) $cm^2/m^2$. The incidence rates of PONV according to time period were as follows: post-anesthesia care unit, 42/756 (5.6%); 0–6 h, 54/756 (7.1%); 6–24 h, 120/756 (15.9%); 24–48 h, 46/756 (6.1%); and overall, 234/756 (31.0%). The incidence of PONV was inversely correlated with LSMI 24–48 h post-surgery and overall. LSMI and PONV scores were negatively associated 6–24 h and 24–48 h post-surgery. There was no association between LSMI and postoperative pain scores, rescue analgesic administration, complications, or length of hospital stay.

**Conclusions:** Preoperative LSMI was associated with PONV in patients undergoing PPPD. Therefore, LSMI measured on preoperative abdominal CT can be a predictive indicator of PONV. Appropriate PONV prophylaxis is necessary in patients with low LSMI before PPPD.

**Keywords:** Anesthesia recovery period; General anesthesia; Lumbar skeletal muscle index; Postoperative complications; Postoperative nausea and vomiting; Retrospective studies; Sarcopenia; X-Ray computed tomography.

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## INTRODUCTION

Sarcopenia consists of loss of appendicular muscle mass, decline in muscle strength, and loss of physical performance, which are associated with increased mortality and decreased quality of life [1]. It has emerged as an important public health concern, especially among the older adult population [2,3]. Sarcopenia is associated with various comorbidities such as cardiovascular disease, diabetes, metabolic syndrome, and liver disease [4,5]. Skeletal muscle mass can be measured in various ways; however, skeletal muscle mass measured through computed tomography (CT) is likely correlated with muscle strength and physical function [6,7].

Skeletal muscle mass and strength affect the prognosis of patients after surgery. Preoperative sarcopenia is associated with extended hospital stay, post-surgical complications, and increased mortality after colorectal cancer surgery [8]. In cardiac surgery, low muscle mass increases stay in the hospital and intensive care unit (ICU), and the rate of postoperative complications [9,10]. In patients undergoing liver transplantation, high muscle mass is associated with early tracheal extubation and a short mechanical ventilation period [11], and a rapid decrease in muscle mass before and after surgery is associated with the patient survival rates [12]. Therefore, preoperative screening for preoperative sarcopenia will significantly improve prognostic predictions after surgery.

The recently published Enhanced Recovery After Surgery protocol for pancreatoduodenectomy underscores postoperative nausea and vomiting (PONV) prophylaxis and adequate pain control to improve patient outcomes [13]. Therefore, predicting which patients are at high risk of developing PONV and severe pain would help improve recovery. Whereas the association between sarcopenia and nausea has been demonstrated in cancer patients [14-16], no studies have investigated the effects of preoperative sarcopenia on the development of PONV. If preoperative sarcopenia affects patient recovery after surgery, postoperative recovery can be improved by screening high-risk patients and providing appropriate treatment in advance. The purpose of this study was to evaluate the association between preoperative skeletal muscle mass and PONV, postoperative pain, and postoperative complication rates.

## MATERIALS AND METHODS

This study was approved by the institutional review board of Yonsei University Health System, Seoul, Korea (#4-2020-0964), and the requirement for patient consent was waived as this was a retrospective study with minimal risk. We included patients aged 19 years or older who received pylorus-preserving pancreatoduodenectomy (PPPD) under general anesthesia from September 2010 to July 2020 at a tertiary referral hospital. At this Hospital, specialized patient-controlled analgesia (PCA) management teams record postoperative pain, side effects, and PCA effects in every patient who receives postoperative PCA. These data and other electronic medical records were retrieved for this study. Patients with incomplete medical records or without preoperative abdominal CT images were excluded.

The skeletal muscle area ($cm^2$) was measured, including the psoas, erector spinae, quadratus lumborum, transverse abdominis, external oblique, internal oblique, and rectus abdominis, at the L3 level using abdominal CT images (Centricity Web PACS Viewer, version 3.0, GE Medical Systems). Lumbar skeletal muscle index (LSMI) was calculated by dividing the skeletal muscle area by the square of the patient's height (m). The primary outcome was the overall incidence of PONV on two postoperative days. The nausea and vomiting scores were defined as follows: 0 = no symptoms; 1 = mild nausea; 2 = moderate nausea; 3 = severe nausea with or without vomiting; and 4 = extreme nausea and vomiting. The postoperative period was divided into the post-anesthesia care unit (PACU), postoperative 0–6 h, 6–24 h, 24–48 h, and overall (0–48 h) periods to determine whether PONV occurred. Secondary outcomes included the highest numeric pain rating scale (NRS) by time period, number of rescue analgesic administrations, PCA duration after surgery, duration of hospital stay after surgery, PCA-related side effects (dizziness, headache, and sedation), postoperative complications during hospitalization (wound infection, wound dehiscence, deep vein thrombosis, stroke, cardiac complications, pneumonia, acute kidney injury, and delirium), ICU admission, all-cause reoperation, and all-cause mortality 1 year after surgery.

We also collected data on potential confounding variables that may affect postoperative PONV, including age, sex, body mass index, American Society of Anesthesiologists physical status classification, hypertension, diabetes mellitus, heart disease, kidney disease, history of abdominal surgery, preoperative chemotherapy, smoking, history of motion weak-

ness, Apfel score for PONV [17], maintenance anesthetic agent (inhalation or total intravenous), anesthesia time, estimated blood loss, and type of PCA (intravenous or epidural). Variables were included in the multivariate model if they showed statistical significance in the univariate regression analysis.

A linear regression model was fitted to the PONV score according to the time period, and logistic regression models were used to determine whether PONV occurred in each time interval or in the overall time period. The Poisson regression model was used to estimate the relative risks of the number of rescue analgesics administered in each period. A linear regression model was fitted for NRS according to the period. Additionally, the distribution of data on the length of PACU stay and length of hospital stay was highly skewed; therefore, a log transformation was performed, and a linear regression model was fitted. A logistic regression was fitted for PCA-related complications, postoperative complications, and all-cause reoperation. For mortality, the Cox proportional hazards regression model was fitted to estimate the hazard ratios because the results comprised time-to-event data. For univariate analysis showing statistical significance, a multivariate analysis was conducted including other potential confounding variables. Statistical significance was set at $P < 0.05$. SAS (version 9.4, SAS Inc.) was used for the analysis.

## RESULTS

In total, 756 patients who underwent PPPD were identified. Baseline patient demographics are presented in Table 1. In this study population, the L3 skeletal muscle area ($cm^2$) and LSMI ($cm^2/m^2$) were 128.83 (101.30, 148.19) and 47.72 (40.74, 53.41), respectively. Table 2 shows the intraoperative and postoperative variables in this study. The median (1Q, 3Q) for maximum PONV score at two postoperative days was 0 (0, 0), and that in the subgroup with PONV occurrence

**Table 1.** Demographic Data of Patients in This Study

| Variable | Value |
|---|---|
| Age (yr) | 64 (57, 70) |
| Sex (F) | 323 (42.7) |
| Height (cm) | 163.1 (157, 169) |
| Weight (kg) | 61 (54.7, 68.2) |
| BMI ($kg/m^2$) | 23.05 (21.2, 25.0) |
| History of motion sickness | 44 (5.8) |
| Smoker | 250 (33.1) |
| ASA physical status | |
| 1/2/3/4 | 38 (5.0)/413 (54.6)/303 (40.1)/2 (0.3) |
| Apfel score | |
| 0/1/2/3/4 | 65 (8.6)/237 (31.3)/250 (33.1)/182 (24.1)/22 (2.9) |
| Comobidities and past history | |
| Hypertension | 292 (38.6) |
| Diabetes mellitus | 210 (27.8) |
| Heart disease | 24 (3.2) |
| Kidney disease | 8 (1.1) |
| History of abdominal surgery | 149 (19.7) |
| History of preoperative chemotherapy | 57 (7.5) |

Values are presented as median (1Q, 3Q) or number (%). BMI: body mass index, ASA: American Society of Anesthesiologists.

**Table 2.** Intraoperative and Postoperative Variables in This Study

| Variable | Value |
|---|---|
| Intraoperative | |
| Inhalation aneshesia/total intravenous anesthesia | 694 (91.8)/62 (8.2) |
| Anesthesia time (min) | 450 (385, 520) |
| Estimated blood loss (ml) | 300 (150, 500) |
| Intravenous PCA/Epidural PCA | 707 (93.5)/49 (6.5) |
| Intravenous PCA regimen (total volume of 100 ml) | |
| Fentanyl; μg/kg/ml | 0.33 (0.29, 0.37) |
| Non-opioid adjuvant | 248 (35.1) |
| Ramosetron | 707 (100.0) |
| Epidural PCA regimen (total volume of 250 ml) | |
| 0.15% ropivacaine | 49 (100.0) |
| Adjuvant fentanyl; μg/kg | 9.1 (7.3, 11.2) |
| Postoperative | |
| Postoperative nausea and vomiting | |
| PACU/0-6 h/6-24 h/24-48 h/overall | 42 (5.5)/54 (7.1)/120 (15.9)/46 (6.1)/234 (31.0) |
| Postoperative rescue analgesics use (number) | |
| PACU/0-6 h/6-24 h/24-48 h/overall | 1 (0, 2)/1 (1, 2)/1 (0, 3)/1 (0, 2)/5 (3, 7) |
| Numeric pain rating scale | |
| PACU/0-6 h/6-24 h/24-48 h | 5 (3, 6)/7 (5, 8)/6 (5, 7)/5 (4, 6) |
| PCA duration (day) | 3 (2, 4) |
| Duration of hospital stay (day) | 15 (12, 22) |
| PCA related complications | 149 (19.7) |
| Postoperative complications | 54 (7.1) |
| All cause reoperation | 9 (1.2) |
| One year mortality | 59 (7.8) |

Values are presented as number (%) or median (1Q, 3Q). PCA: patient-controlled analgesia, PACU: post-anesthesia care unit.

**Table 3.** Univariate and Multivariate Analyses Between Preoperative Lumbar Skeletal Muscle Index and Postoperative Nausea and Vomiting (by Score and Occurrence) at Each Postsurgical Period

| Outcomes | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | Estimate | SE | P value | Estimate | SE | P value |
| By score | | | | | | |
| PACU | −0.0020 | 0.0015 | 0.137 | | | |
| 0–6 h | −0.0040 | 0.0020 | 0.083 | | | |
| 6–24 h | −0.0099 | 0.0029 | 0.001 | −0.0085 | 0.0038 | 0.025 |
| 24–48 h | −0.0067 | 0.0018 | < 0.001 | −0.0050 | 0.0023 | 0.030 |
| Outcomes | Univariate | | | Multivariate | | |
| | OR | 95% CI | P value | OR | 95% CI | P value |
| By occurrence | | | | | | |
| PACU | 0.983 | 0.947–1.020 | 0.353 | | | |
| 0–6 h | 0.959 | 0.927–0.992 | 0.016 | 0.977 | 0.933–1.024 | 0.330 |
| 6–24 h | 0.957 | 0.934–0.980 | < 0.001 | 0.970 | 0.939–1.003 | 0.073 |
| 24–48 h | 0.941 | 0.906–0.977 | 0.002 | 0.943 | 0.891–0.997 | 0.040 |
| Overall | 0.968 | 0.950–0.986 | 0.001 | 0.971 | 0.947–0.996 | 0.022 |

SE: standard error, OR: odds ratio, CI: confidence interval, PACU: post-anesthesia care unit.

was 1 (1, 2). Intravenous PCA was infused at 2 ml/h and a 0.5 ml on-demand bolus dose was administered with a 15 min lockout time. Epidural PCA was infused at 5 ml/h and a 0.5 ml on-demand bolus dose was administered with a 15 min lockout time. Regarding PCA-related complications, dizziness occurred in 138 patients (18.3%), sedation in six patients (0.8%), and headache in 14 patients (1.9%). No patients were admitted to the ICU immediately after surgery. The incidence of postoperative complications were as follows: wound infection, 20 (2.6%); wound dehiscence, 5 (0.7%); deep vein thrombosis, 0 (0.0%); stroke, 1 (0.1%); cardiac complications, 13 (1.7%); pneumonia, 10 (1.3%); acute kidney injury, 5 (0.7%); delirium, 12 (1.6%); overall complications, 56 (7.1%); all-cause reoperation, 9 (1.2%); and all-cause 1 year mortality, 59 (7.8%).

According to the result of the multivariate regression analysis, the occurrence of PONV was inversely correlated with the preoperative LSMI at 24–48 h and in the overall time period (24–48 h, odds ratio [OR], 0.943; 95% confidence interval [CI], 0.891 to 0.997; overall, OR, 0.971; 95% CI, 0.947 to 0.996, Table 3). Preoperative LSMI and PONV scores were negatively associated 6–24 h and 24–48 h post-surgery (6–24 h, coefficient, -0.0038; P value = 0.025; 24–48 h, coefficient, -0.050; P value = 0.030).

No significant association was noted between preoperative LSMI, postoperative NRS, and the number of rescue analgesics administered (Table 4). Furthermore, no association was present between preoperative LSMI and the duration of PCA administration, hospital stay, postoperative complications, and mortality (Table 5).

**Table 4.** Univariate Analyses Between Preoperative Lumbar Skeletal Muscle Index and Numeric Pain Rating Scale and the Number of Rescue Analgesics Administration Postoperatively at Each Postsurgical Period

| Outcomes | Estimate | SE | P value |
|---|---|---|---|
| Numeric pain rating scale | | | |
| PACU | 0.0104 | 0.0077 | 0.177 |
| 0–6 h | −0.0022 | 0.0094 | 0.814 |
| 6–24 h | −0.0123 | 0.0081 | 0.130 |
| 24–48 h | 0.0099 | 0.0079 | 0.215 |
| Outcomes | RR | 95% CI | P value |
| Rescue analgesics administration | | | |
| PACU | 1.002 | 0.994–1.010 | 0.619 |
| 0–6 h | 1.002 | 0.994–1.010 | 0.615 |
| 6–24 h | 0.997 | 0.990–1.004 | 0.411 |
| 24–48 h | 1.006 | 0.997–1.015 | 0.188 |
| Overall | 1.001 | 0.996–1.007 | 0.587 |

SE: standard error, RR: relative risk, CI: confidence interval, PACU: post-anesthesia care unit.

## DISCUSSION

This study demonstrated that low preoperative LSMI was independently correlated with PONV scores 6–48 h post-surgery and PONV occurrence 2 days post-surgery. In contrast, a correlation between sarcopenia and postoperative pain

**Table 5.** Univariate Analyses Between Preoperative Lumbar Skeletal Muscle Index and Complications, duration of PCA Administration and Hospital Stay, and Mortality

| Outcomes | OR | 95% CI | P value |
|---|---|---|---|
| PCA related complications | 0.988 | 0.97–1.009 | 0.250 |
| Postoperative complications | 1.008 | 0.975–1.041 | 0.650 |
| All cause reoperation | 1.056 | 0.978–1.140 | 0.162 |
| Outcomes | Estimate | SE | P value |
| PCA duration (day) | 0.0007 | 0.002 | 0.721 |
| Hospital stay duration (day) | 0.0009 | 0.0019 | 0.628 |
| Outcomes | HR | 95% CI | P value |
| Mortality | 1.005 | 0.975–1.035 | 0.757 |

OR: odds ratio, CI: confidence interval, SE: standard error, HR: hazard ratio, PACU: post-anesthesia care unit, PCA: patient-controlled analgesia.

was not observed. In our study population, preoperative LSMI was not associated with postoperative complications, length of hospital stay, or the 1-year mortality rate.

PONV is very common after surgery, although its importance has long been overlooked [18,19]. Furthermore, patient discomfort can be significant and was called the "Big little problem [20]." PONV reduces patient satisfaction, increases morbidity, and occasionally causes serious complications such as aspiration pneumonia, dehydration, and electrolyte imbalance because of vomiting, as well as delayed mobilization and increased length of hospital stay [21]. Several risk factors have been identified for PONV, such as Apfel score, type of surgery including laparoscopy, and anesthetic agents (inhalation, opioid) [17,22]. However, the exact mechanism by which risk factors predispose patients to PONV is poorly understood. Therefore, efforts to identify the risk factors for PONV remain meaningful. To the best of our knowledge, the current study is the first to show a correlation between preoperative sarcopenia and postoperative PONV.

Nausea and vomiting occur when various pathways affecting the vomiting center in the brainstem are stimulated by stresses such as motion, pain, or anesthetic agents including inhalational agents or opioids [23,24]. The gut–brain interaction also induces PONV, and mechanical stimulation of the gastrointestinal tract or gastric distension can cause secretion of emetic neurotransmitters [25,26]. Anesthetic methods can also affect gastrointestinal function. In particular, inhalational agents can stimulate the vagal afferent pathway, which induces emetic reflux [27], opioid-induced bowel dysfunction, and gastric distention [28]. Accordingly, laparoscopic surgery, general anesthesia, and postoperative opioid use are risk factors for PONV. Postoperative ileus is a common complication. Previous studies have demonstrated a relationship between sarcopenia and delayed gastric emptying in patients undergoing PPPD [29,30], which could be one possible reason for increased risk of PONV in sarcopenic patients in current study. An association between sarcopenia and nausea has been reported in patients with cancer undergoing chemotherapy. Chemotherapy causes nausea and sarcopenia, and sarcopenia alone also increases the risk of chemotherapy-induced toxicity such as nausea and anorexia in patients with gastrointestinal cancer [14,15]. In a recent study including patients with locally advanced pancreatic cancer, a low total psoas area measured with lumbar CT images was a predictor of complications such as pain and nausea [16]. Therefore, our data showing the association between sarcopenia and PONV are consistent with those of previous studies.

Several studies have investigated the effects of preoperative sarcopenia on the risk of postoperative complications. In previous meta-analyses evaluating gastrointestinal cancer surgeries [31] and urologic cancer surgeries [32], preoperative sarcopenia increased the risk of major complications and was an independent prognostic factor for short survival and increased mortality after surgery. In a previous study evaluating hepatic resection for Klatskin tumors conducted at our institution [33], preoperative sarcopenia was associated with postoperative ICU admission, length of ICU stay, postoperative complication rate, and in-hospital mortality. In contrast, we found no association between preoperative sarcopenia and postoperative complications or mortality. The relatively low disease severity in our study population could explain this discrepancy with previous studies. While 61.8% of the patients were admitted to the ICU immediately after hepatic resection in a previous study [33], none were admitted to the ICU immediately after PPPD in our study.

Evidence suggests that sarcopenia is related to chronic pain [34-36]. Nonetheless, in this study, no correlation was noted between preoperative sarcopenia and acute postoperative pain in terms of pain scores or the number of rescue analgesic administrations. Pain control with intravenous PCA could explain these results; however, data on the PCA volume administered were insufficient in this retrospective study.

This study had several limitations. First, the study was performed by retrospectively reviewing electronic medical records, which may carry an inherent bias. However, we calibrated the results by incorporating as many potential con-

founding variables as possible to minimize the risk of bias. Second, the data in this study were obtained from a patient cohort undergoing a single operation at a single hospital. Therefore, the generalizability of these results is limited, and future research should be conducted to verify the conclusions in other populations. Third, the LSMI is an indicator of decreased muscle mass as a component of sarcopenia. Therefore, it is not an ideal representation of sarcopenia, which includes not only decreased muscle mass, but also decreased muscle strength and physical performance. However, many studies have focused on sarcopenia based on muscle area and some have shown a strong association between muscle area and sarcopenia [37-40].

Preoperative LSMI was associated with the occurrence and severity of PONV in patients undergoing PPPD. Nonetheless, no association was observed between preoperative LSMI and postoperative pain, postoperative complication rates, length of hospital stay, or mortality. In conclusion, LSMI measured using preoperative abdominal CT can be a predictive indicator of PONV, and appropriate PONV prophylaxis in patients with low LSMI before PPPD should be implemented.

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## CONFLICTS OF INTEREST

Seung Hyun Kim is the current editor of *Anesthesia and Pain Medicine*. However, he was not involved in the peer reviewer selection, evaluation, or decision process of this article.

## DATA AVAILABILITY STATEMENT

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

## AUTHOR CONTRIBUTIONS

Writing – original draft: Hyun Il Kim, Seung Hyun Kim. Writing -review & editing: Hyun Il Kim, Ki Jun Kim, Sangil Kim, Hae Dong Kim, Seung Hyun Kim. Conceptualization: Seung Hyun Kim. Data curation: Hyun Il Kim, Ki Jun Kim, Sangil Kim, Hae Dong Kim, Seung Hyun Kim. Formal analysis: Hyun Il Kim, Ki Jun Kim, Sangil Kim, Hae Dong Kim, Seung Hyun Kim. Methodology: Hyun Il Kim, Seung Hyun Kim. Project administration: Hyun Il Kim, Ki Jun Kim, Sangil Kim, Hae Dong Kim, Seung Hyun Kim. Funding acquisition: Seung Hyun Kim. Investigation: Hyun Il Kim, Ki Jun Kim, Seung Hyun Kim. Resources: Seung Hyun Kim. Supervision: Ki Jun Kim.

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