ORIGINAL ARTICLE

Significance of osteopenia in elderly patients undergoing emergency gastrointestinal surgery

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Abstract

Aim: Frailty assessment in elderly patients is crucial to predict the postoperative course, considering that frailty is highly associated with postoperative complications and mortality. The aim of this study was to evaluate the value of osteopenia as a risk factor for severe postoperative complications in elderly patients who underwent emergency gastrointestinal surgery.

Methods: This study comprised 103 elderly patients who underwent emergency gastrointestinal surgery. Osteopenia was diagnosed by measuring bone mineral density, which was calculated as the average pixel density in the midvertebral core at the 11th thoracic vertebra on the preoperative plain computed tomography image. We retrospectively investigated the relationship between preoperative osteopenia and severe postoperative complications (Clavien–Dindo classification ≥III). Univariate and multivariate analyses were performed to evaluate the risk factors for severe postoperative complications.

Results: Twenty-three patients (22.3%) developed severe postoperative complications. The optimal cutoff value of bone mineral density for severe postoperative complications was 119.5 Hounsfield unit (HU) and 39 patients (37.9%) were diagnosed with osteopenia. The univariate analysis revealed that the American Society of Anesthesiologists Physical Status of ≥3 ($P = .0084$), hemoglobin levels ($P = .0026$), albumin levels ($P < .001$), sarcopenia ($P = .015$), and osteopenia ($P < .001$) were significantly associated with severe postoperative complications. The multivariate analysis showed that osteopenia ($P = .014$) was an independent risk factor for severe postoperative complications.

Conclusion: Osteopenia may be a risk factor for severe postoperative complications in elderly patients after emergency gastrointestinal surgery.

KEYWORDS
bone mineral density, elderly, emergency surgery, osteopenia, sarcopenia

1 | INTRODUCTION

As a result of the increase in life expectancy, more elderly patients are presenting the high-risk emergency surgery.[1,2] Elderly patients are likely to develop postoperative complications due to comorbidities and malnutrition.[3,4] Furthermore, frail elderly patients are at an increased risk for postoperative complications and mortality.[5-7] In emergency surgery, frail elderly patients have higher postoperative complications and mortality rate than non-frail, which occur in 40–60% and 20–40%, respectively.[6,7] Therefore, frailty assessment is required to perform perioperative management of the elderly patients undergoing emergency surgery.

Sarcopenia and osteopenia, which are features of aging, have been proposed as risk factors for falls, fractures, and frailty in the elderly.[8] Sarcopenia is characterized by progressive and generalized loss of skeletal muscle mass and strength.[9] Several studies have shown that sarcopenia is associated with the postoperative complications and in-hospital mortality in emergency surgery.[10,11] Meanwhile, osteopenia, which exhibits a low bone mineral density (BMD), has been reported to be associated with sarcopenia.[12] Recently, BMD was evaluated by calculating the average pixel density within a circle of the 11th thoracic vertebra (Th11), using preoperative computed tomography (CT), to show the association between osteopenia and poor prognosis in patients with several cancers.[12-14] However, the association between osteopenia and postoperative complications or mortality in emergency surgery has not been well investigated by measuring BMD.

The aim of this study was to evaluate the significance of preoperative osteopenia as a risk factor for severe postoperative complications in elderly patients after emergency gastrointestinal surgery.

2 | METHODS

2.1 | Patient selection

Between March 2014 and August 2021, 180 elderly patients (aged 65–97 years) underwent emergency gastrointestinal surgery at a single institution (Tokyo General Hospital, Nakano-ku, Japan). Of these, 77 patients were excluded (63 patients for moderate severity including acute appendicitis, incarcerated hernia without bowel resection or acute cholecystitis, and 14 for reoperations), thus, the remaining 103 patients who underwent emergency major gastrointestinal surgery for this study.[15]

The patient data included age, sex, body mass index (BMI), comorbidities (diabetes mellitus or cardiac disease), antithrombotic agent status, sarcopenia, BMD, blood cell counts, and biochemical blood tests. Blood test data were collected within 48 hours before surgery. The physical status (PS) score was defined according to the American Society of Anesthesiologists (ASA).[16] Postoperative complications, which were graded II or III–V using the Clavien–Dindo classification and occurred within 90 days postsurgery were defined as mild or severe complications.[17] Predictive risk factors were examined with respect to severe complications and mortality. This study was approved by the Ethics Committee of Tokyo General Hospital (No. 21-18) and was conducted in compliance with the Declaration of Helsinki.

2.2 | Definitions of preoperative osteopenia and sarcopenia

Preoperative osteopenia and sarcopenia were evaluated using CT findings. All patients included in this study underwent preoperative plane and contrast-enhanced CT within 48 hours before surgery with a Canon (Tokyo, Japan) Aquilion ONE-slice scanner (120 kv, 30 mA). BMD was measured as the average pixel density (Hounsfield unit; HU) within a circle in the midvertebral core at the bottom of the Th11 on the preoperative plain CT image (Figure 1A).[12] The axial slice at the bottom of the Th11 was identified using the sagittal slice as a reference. Patients were scanned volumetrically and the thickness of the CT slice was reconstructed in 5-mm sections. The sizes of the regions of interest were constant in all patients (area: 300 mm^2) and were manually positioned in the midvertebral core. Preoperative osteopenia was defined as BMD below the cutoff value (119.5 HU) for severe postoperative complications. Preoperative sarcopenia was evaluated using the skeletal muscle index (SMI).[18] Cross-sectional areas (cm^2) of skeletal muscles in the third lumbar vertebra (L3) region were measured and normalized for height (cm^2/m^2) to obtain the SMI. The cutoff value for SMI was defined as ≤ 43.75 cm^2/m^2 for men and ≤ 41.10 cm^2/m^2 for women.[19] Preoperative BMD and SMI were measured by two surgeons (Y.T. and W.K.) using the Synapse image analysis system (Fujifilm Medical, Tokyo, Japan), and no significant difference in the mean values of preoperative BMD and SMI was obtained.

2.3 | Statistical analysis

Data were expressed as medians. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal cutoff values of continuous variables for severe postoperative complications and calculate the area under the curve (AUC). The Mann–Whitney U-test, the chi-squared test, and Fisher's exact test were used to compare the two groups in the univariate analysis. Multivariate logistic analysis, which incorporated the variables with $P < .05$ on univariate analysis, was performed to identify an independent risk factor for severe postoperative complications and mortality after emergency major gastrointestinal surgery. The EZR software v. 1.51 (Saitama Medical Center, Jichi Medical University, Japan) was used for all statistical analyses. Statistical significance was set at $P < .050$.

FIGURE 1 (A) BMD measured by calculating the average pixel density within a circle in the midvertebral core at the bottom of the 11th thoracic vertebra on preoperative CT. (B) The optimal cutoff value of preoperative BMD for severe postoperative complications (≥ grade III) was evaluated using receiver operating characteristic curve analysis. AUC, area under the curve; HU, Hounsfield unit

(A) 55.7 HU　　245.3 HU

(B) cutoff 119.5 HU, sensitivity=73.9%, specificity=72.5%, AUC=0.730
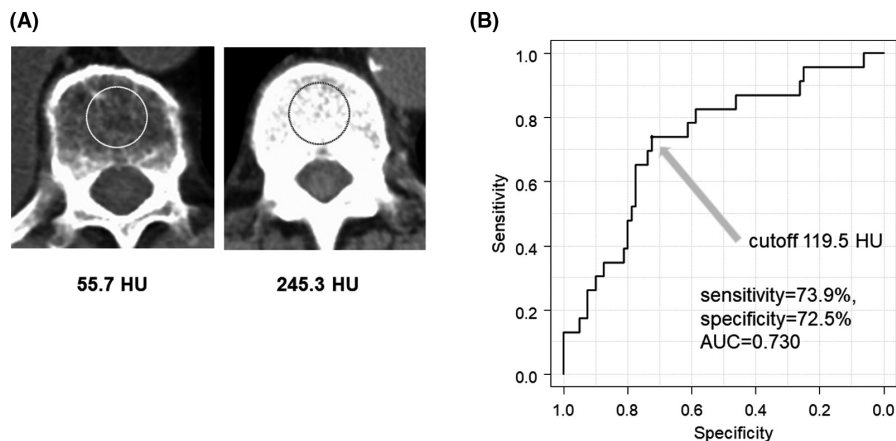
3 | RESULTS

3.1 | Patient background and intraoperative and postoperative findings

The patients' (n = 103) demographic and preoperative characteristics are presented in Table 1. The median age was 81 years, and 46 patients were males. Thirty-nine patients (37.9%) were diagnosed with osteopenia according to the optimal BMD cutoff value (119.5 HU; sensitivity, 73.9%; specificity, 72.5%; AUC, 0.730; 95% confidence interval [CI], 0.612–0.849) (Figure 1B). Sixty-one patients (59.2%) were diagnosed with sarcopenia based on the calculated SMI values. The operative indications included strangulated small bowel obstruction (n = 40), obstructive colorectal cancer (n = 12), perforation peritonitis (n = 44; upper, 17; lower, 27), and others (n = 7; nonocclusive mesenteric ischemia, 3; superior mesenteric artery embolism, 2; gastric necrosis, 1; and ruptured liver abscess, 1). Postoperative grade II and III–V complications occurred in 40 (38.8%) and 23 (22.3%) patients, respectively. The most common grade II complication was wound infection (12.6%), which was followed by pneumonia (8.74%) and heart failure (4.85%). The most common grade III–IV complication was sepsis (9.71%), which was followed by pneumonia (3.88%), heart failure (2.91%), and anastomotic leak (2.91%). Postoperative mortality occurred in 13 patients (12.6%) (Figure S1).

3.2 | Univariate and multivariate analyses of clinicopathological variables in relation to severe postoperative complications and mortality

The clinical perioperative characteristics of elderly patients with or without severe postoperative complications are shown in Table 2. In the univariate analysis, ASA-PS ≥3 (P = .0084), preoperative serum hemoglobin levels (P = .0026), serum albumin levels (P < .001), sarcopenia (P = .015), and osteopenia (P < .001) were significantly associated with severe postoperative complications (≥ grade III). Table 3 lists the relationship between the clinical variables and severe postoperative complications. In the multivariate

TABLE 1 Patient characteristics

Characteristic	All (n = 103)
Sex	
Male	46 (44.7%)
Female	57 (55.3%)
Age (y)	81 (65–97)
BMI (kg/m^2)	20.4 (11.4–31.2)
Comorbidity	
Diabetes mellitus	22 (21.4%)
Cardiac disease	33 (32.0%)
Antithrombotic medication	21 (20.4%)
ASA-PS ≥3	29 (28.2%)
Sarcopenia	61 (59.2%)
BMD (HU)	134.0 (55.7–245.3)
Operative indications	
Strangulated small bowel obstruction	40 (38.8%)
Obstructive colorectal cancer	12 (11.7%)
Perforation peritonitis (upper GI)	17 (16.5%)
Perforation peritonitis (lower GI)	27 (26.2%)
Others	7 (6.8%)
Intestinal resection rate	63 (61.2%)
Postoperative complications (C-D classification)	
Grade II	40 (38.8%)
Grade III–IV	10 (9.71%)
Grade V	13 (12.6%)

Abbreviations: ASA-PS, American Society of Anesthesiologists physical status; BMD, bone mineral density; BMI, body mass index; C-D, Clavien–Dindo; GI, gastrointestinal; HU, Hounsfield unit.

analysis, osteopenia (odds ratio [OR] 4.45; 95% CI, 1.36–14.6; P = .014) was an independent risk factor for severe postoperative complications (≥ grade III).

The relationship between clinical variables and postoperative mortality is shown in Table S1. In the univariate analysis, age (P = .048), BMI (P = .026), ASA-PS ≥3 (P < .001), preoperative

Characteristic	Postoperative complications (≥ grade III)		
	Yes (n = 23)	No (n = 80)	*P*-value
Sex (male/female)	11/12	35/45	.81
Age (y)	79 (65–95)	82 (67–97)	.084
BMI (kg/m^2)	19.6 (11.4–23.4)	20.5 (13.8–31.2)	.086
Diabetes mellitus	5 (21.7%)	17 (21.3%)	1.00
Cardio disease	6 (26.1%)	27 (33.8%)	.62
Antithrombotic medication	6 (26.1%)	15 (18.8%)	.56
ASA-PS ≥ 3	12 (52.2%)	17 (21.3%)	.0084
Laboratory data			
White blood cell (/μL)	8820 (1270–42 120)	8790 (1970–31 150)	.84
Hemoglobin (g/dL)	10.8 (6.3–17.0)	12.3 (8.0–16.8)	.0026
Albumin (g/dL)	2.9 (1.5–3.7)	3.5 (1.4–4.6)	<.001
CRP (mg/L)	3.31 (0.03–44.9)	2.65 (0.01–42.0)	.27
Sarcopenia	19 (82.6%)	42 (53.0%)	.015
Osteopenia	17 (73.9%)	22 (27.5%)	<.001
Operative indications			
Strangulated small bowel obstruction	5 (21.7%)	35 (43.8%)	.088
Obstructive colorectal cancer	4 (17.4%)	8 (10.4%)	1.00
Perforation peritonitis (upper GI)	6 (26.1%)	11 (13.8%)	1.00
Perforation peritonitis (lower GI)	12 (52.2%)	15 (18.8%)	.30
Others	3 (13.0%)	4 (5.20%)	.18
Intestinal resection rate	18 (78.3%)	45 (56.3%)	.088
Operation time (min)	136 (48–298)	102 (18–318)	.14
Blood loss (mL)	50 (5–510)	20 (5–500)	.24
Length of hospital day (d)	37 (2–174)	18 (6–58)	.052

TABLE 2 Preoperative and intraoperative factors according to severe postoperative complications (≥ grade III)

Abbreviations: ASA-PS, American Society of Anesthesiologists physical status; BMD, bone mineral density; BMI, body mass index; C-D, Clavien–Dindo; GI, gastrointestinal.

TABLE 3 Multivariate analysis of risk factors for severe postoperative complications (≥ grade III)

Variables	Multivariate analysis		
	OR	95% CI	*P*-value
ASA-PS ≥ 3	2.40	0.76–7.58	.14
Hemoglobin (< 11.2 g/dL)	2.90	0.83–10.1	.096
Albumin (< 3.2 g/dL)	2.75	0.75–10.1	.13
Sarcopenia	3.62	0.92–14.3	.067
Osteopenia	4.45	1.36–14.6	.014

Abbreviations: ASA-PS, American Society of Anesthesiologists physical status; BMD, bone mineral density.

serum albumin levels (*P* = .012), sarcopenia (*P* = .013), and osteopenia (*P* < .001) were significantly associated with postoperative mortality. In the multivariate analysis, ASA-PS ≥3 (OR 9.07; 95%

CI, 1.47–55.8; *P* = .017) and osteopenia (OR 15.4; 95% CI, 2.44–97.3; *P* = .0037) were independent risk factors for postoperative mortality.

## 3.3 | Elderly patient characteristics with or without osteopenia

The clinical perioperative characteristics of patients with or without osteopenia are shown in Table 4. Advanced age (*P* < .001) and low serum albumin levels (*P* < .001) were significantly associated with the presence of osteopenia. Meanwhile, sarcopenia (*P* = .062) tended to be associated with osteopenia, although the difference was not statistically significant. Furthermore, the osteopenia group presented with more infectious complications, such as sepsis (23.1%) and pneumonia (17.9%), compared to those of the non-osteopenia group in the comparison of postoperative complications (grade II–V) (Figure 2).

TABLE 4 Patient characteristics according to preoperative osteopenia

Variables	Osteopenia (n = 39)	Non-osteopenia (n = 64)	P-value
Sex (male/female)	14/25	32/32	.22
Age (y)	84 (67–97)	77 (65–94)	<.001
BMI (kg/m^2)	20.1 (11.4–26.2)	20.5 (14.4–31.2)	.26
With comorbidity			
Diabetes	8 (20.5%)	14 (22.0%)	1.00
Cardio vascular disease	15 (38.5%)	18 (28.1%)	.29
Laboratory data			
Hemoglobin (g/dL)	11.2 (6.3–17.0)	12.4 (6.8–16.8)	.094
Albumin (g/dL)	3.0 (1.5–4.5)	3.4 (1.4–4.6)	.0025
Sarcopenia	28 (71.8%)	33 (51.6%)	.062
Operative indications			
Strangulated small bowel obstruction	13 (33.3%)	27 (42.1%)	.41
Obstructive colorectal cancer	4 (10.3%)	8 (12.5%)	1.00
Perforation peritonitis (upper GI)	6 (15.4%)	11 (17.2%)	1.00
Perforation peritonitis (lower GI)	13 (33.3%)	14 (22.0%)	.25
Intestinal resection rate	25 (64.1%)	38 (59.4%)	.68
Operation time (min)	120 (48–314)	106 (18–318)	.28
Blood loss (mL)	45 (5–460)	20 (5–510)	.77
Length of hospital day (d)	21 (2–97)	17 (6–174)	.20

Abbreviations: ASA-PS, American Society of Anesthesiologists physical status; BMI, body mass index; GI, gastrointestinal.

FIGURE 2 Comparison of each complication (grade II–V) between the osteopenia and non-osteopenia groups among elderly patients who underwent emergency gastrointestinal surgery
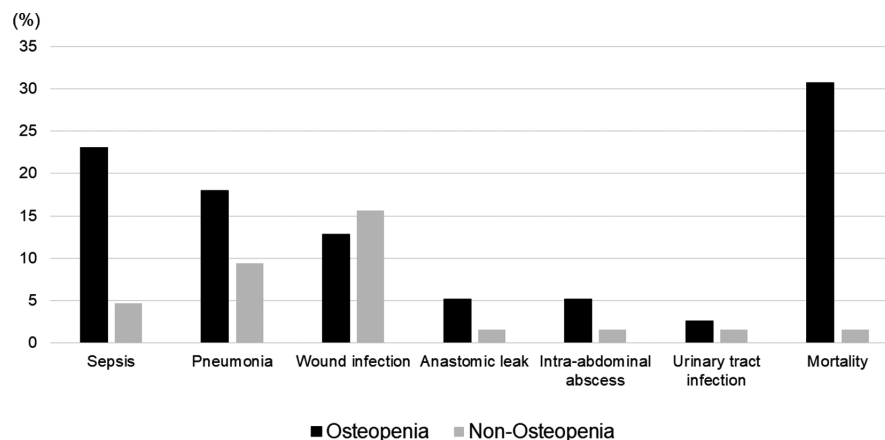
4 | DISCUSSION

We showed a significant association between preoperative osteopenia and severe postoperative complications in elderly patients who underwent emergency major gastrointestinal surgery. Multivariate analysis revealed that osteopenia was an independent risk factor for severe postoperative complications. These findings suggest that preoperative osteopenia, which exhibits a low BMD on preoperative CT image, can be a risk factor for postoperative poor outcome in elderly patients after emergency surgery.

Osteopenia is defined as low bone density that is not as low as osteoporosis.[19] Osteopenia and osteoporosis are generally calculated using dual-energy x-ray absorptiometry of the spine or the proximal femur,[20] while the CT-derived BMD assessment value of fracture risk has been shown by radiologists.[21] In gastroenterological surgery, the association between low BMD and poor prognosis has been shown in patients with cancer using BMD assessment of the midvertebral core at Th11.[12–14] The use of CT-derived BMD values for osteopenia diagnosis remains controversial. Therefore, we determined the BMD cutoff value using the ROC curve and

observed results that were similar to previous studies, which is that low BMD was correlated with advanced age.[13,14]

Low BMD has been reported to be associated with physical, endocrine, and metabolic factors.[20,22] Vitamin D is an immunomodulatory hormone and is often deficient in patients with osteopenia.[20,22] Several studies have previously shown that mortality among patients with sepsis has been associated with deficiency of serum 1,25-dihydroxyvitamin D [1,25(OH)(2)D] levels, the active form of vitamin D.[23,24] Deficiency of 1,25(OH)2D is implicated in the ineffective antimicrobial activities of macrophages and monocytes, which may increase the invasiveness of bacteria.[25,26] Furthermore, vitamin D deficiency reduces the production and secretion of antimicrobial peptides in the intestinal epithelial cells, Paneth cells, and intraepithelial lymphocytes, resulting in the promotion of gut bacterial translocation.[27–29] Taken together, osteopenia is presumed to be able to cause more severe infectious complications or sepsis in patients undergoing emergency gastrointestinal surgery than in those without osteopenia. In fact, the osteopeniagroup presented with an increased prevalence of sepsis and pneumonia, which could lead to mortality, compared with those of the non-osteopenia group.

Patients with low BMD, who were diagnosed with osteopenia, would be applicable for routine care such as a nutritional therapy with vitamin D supplementation or rehabilitation,[20,30] and these therapies may improve the outcomes in emergency gastrointestinal surgery. Furthermore, preoperative osteopenia would be helpful for identifying individuals at highest risk of severe postoperative complications after emergency gastrointestinal surgery. This will enable surgeons to provide their patients with an accurate assessment of their potential risks for poor outcomes, gaining informed consent and providing more appropriate perioperative management.

Although we have found an association between osteopenia and severe postoperative complications, this study had several limitations. The most important limitation was the retrospective observational of the study and the effect of residual confounding factors cannot be completely excluded. Another limitation was the small sample size, as this study was conducted at a single center, and perioperative management is dependent on the experience of our institution. In addition, a standard method that evaluates osteopenia and sarcopenia is not available, and the cutoff value of osteopenia differs in several studies. Therefore, further multicenter prospective studies with measurement of preoperative serum vitamin D levels and BMD are required to validate our results.

5 | CONCLUSION

Osteopenia was an independent risk factor for severe postoperative complications in elderly patients after emergency gastrointestinal surgery. This finding suggests that preoperative osteopenia may help to identify elderly patients who are at a higher risk of poor outcome and predict the postoperative course.

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