



Development of a nutritional index to evaluate the effectiveness of total parenteral nutrition during the early postoperative period after pancreaticoduodenectomy

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Background: Malnutrition leads to adverse effects on the short- and long-term prognosis in patients with periampullary diseases who underwent surgery. Nutritional risk indicators based on albumin and body weight have been developed to evaluate nutritional status and nutritional therapy efficacy, but no standard objective measurement has been devised to evaluate nutritional status during the early period after pancreaticoduodenectomy (PD). Therefore, this study aimed to assess the efficacy of total parenteral nutrition (TPN) during the early postoperative period after PD.

Methods: We analyzed 28 patients with a periampullary disease—common bile duct cancer, ampulla of Vater cancer, pancreatic head cancer, neuroendocrine tumor, chronic pancreatitis—who have undergone PD from Jan. 1, 2012 to Dec. 31, 2016. For all the patients, TPN was administered from postoperative day (POD) 1 at 25 Kcal/kg ideal body weight. Various nutritional indicators were measured such as Body mass index, nutritional risk index, protein, albumin, prealbumin, C-reactive protein. The volume of skeletal muscle area, muscle density, visceral and subcutaneous fat areas were assessed two times, preoperatively and on POD 7 by CT scan at the 3rd lumbar spine (L3) level.

Results: Average age of the 28 study subjects (18 males and 10 females) was 63.5±9.7 years. Although there is no difference in BMI between preoperative result and POD 7, protein, albumin, and prealbumin levels were significantly lower POD 7 the preoperative ($P<0.001$), but CRP was higher ($P<0.001$), and prealbumin and CRP levels were negatively correlated ($R=-0.682$, $P<0.01$). Muscle mass increased postoperatively ($P=0.02$), but the amount of visceral fat decreased ($P=0.00$). Based on CRP, and muscle density results, muscle, visceral and subcutaneous fat masses did not change after PD.

Conclusions: In order to evaluate the nutritional status accurately after the hepato-biliary radical surgery, we suggest the muscle and fat mass measurement that can adjust the degree of inflammation during the early postoperative period.

Keywords: Pancreaticoduodenectomy (PD); total parenteral nutrition (TPN); nutritional assessment; sarcopenia

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Introduction

Since its introduction by Whipple in 1935 (1), pancreaticoduodenectomy (PD) remains the treatment of choice for periampullary carcinomas, including such as those of the pancreas head, ampulla of Vater, duodenum, and distal common bile duct, and some benign lesions. After PD, patients are at high risk of malnutrition, because of gastrointestinal tract changes that cause poor oral intake, and loss of duodenum, which is required for nutrient breakdown and absorption (2,3).

Malnutrition is an independent predictor of poor outcomes in patients who have undergone radical surgery for malignant hepatobiliary disease and increases morbidity, mortality, length of stay, and financial burden (4,5). To overcome this physiologic condition, which is the hallmark of the postsurgical state, the administration of high caloric intake during the immediate postoperative period is necessary. Furthermore, the early detection of nutritional risk facilitates early intervention and prevents later complications, but no single gold standard objective measurement has been devised for the evaluation of nutritional status during the early period after radical surgery.

Nutritional support is performed routinely via the oral route, but when this is problematic, alternative sources of nutritional supplementation such as intravenous total parenteral nutrition (TPN) are essential (6). Nutritional support strategies have evolved considerably over the past decades and commonly TPN has been used postoperatively (7).

Although TPN is an effective method of nutritional support, its use is associated with risks of complications such as central line-associated bloodstream infection, hyperglycemia, liver function abnormalities, and electrolyte imbalance (8). Despite these shortcomings, TPN still plays a key role in the rescue of patients from severe postoperative complications and the risk of postoperative malnutrition. Notably, patients who have not received sufficient nutritional support for more than 14 days have remarkably elevated complications and mortality rates (9), and furthermore, malnutrition can result in sarcopenia. Thus, it is positively necessary to identify appropriate indications for early nutritional supplementation to avoid these poor outcomes.

Several types of serologic markers (e.g., albumin, transferrin, prealbumin) have been widely used to evaluate nutritional status, and shown to be associated with the prognoses of malnourished patients (10,11). Malnutrition

can cause sarcopenia which is the degenerative loss of skeletal muscle mass, quality, and strength. Several techniques, such as anthropometry, bioelectrical impedance analysis (BIA), dual-energy X-ray absorptiometry (DEXA), and CT/MRI, are available to measure muscle mass. Of these tools, a CT scan provides the most valid and precise means of measuring muscle mass and fat and can measure the most exact physical properties of muscle mass (12).

However, no tool has been developed to determine the efficacy of TPN administered to patients during the early postoperative period. We aimed to assess the effectiveness of TPN for the patients who are in the early postoperative period after PD.

We present the following article in accordance with the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/gs-20-390>).

Methods

This retrospective study was conducted at a single university hospital. We analyzed 28 patients with a periampullary disease, that underwent PD from January 1, 2012 to December 31, 2016. All patients were operated upon by a single surgeon using the same procedures, which included (I) single-loop pancreatic and biliary reconstruction; (II) pancreaticojejunostomy; (III) duct-to-mucosa anastomosis; (IV) internal pancreatic duct silicone stent placement, and (V) continuous suturing of pancreatic parenchyma to jejunal serosa with prolene.

For all the patients, TPN was administered from postoperative day (POD) 1. The total required calorie was calculated at 25 Kcal/kg ideal body weight as this calorie furnishes an approximate estimate of daily energy expenditure and requirements (13). The initial target calorie that TPN provides on POD 1 was to supply 60% of the total required calories. Then, the target calorie gradually increased daily; 80% on POD 2, and 100% on POD 3.

CT scan was taken in all the patients on POD 7. And enteral feeding began when the CT scan showed no evidence of complications. The amount of TPN administration was gradually decreased depending on the amount of oral intake. If the patients are tolerable with 20% amount of usual oral intake, the total calorie of TPN was decreased to 80% of required calorie. This gradual increase and decrease method of TPN administration was determined by our team.

Several nutritional indicators—body mass index (BMI), nutritional risk index (NRI), protein, albumin, prealbumin,

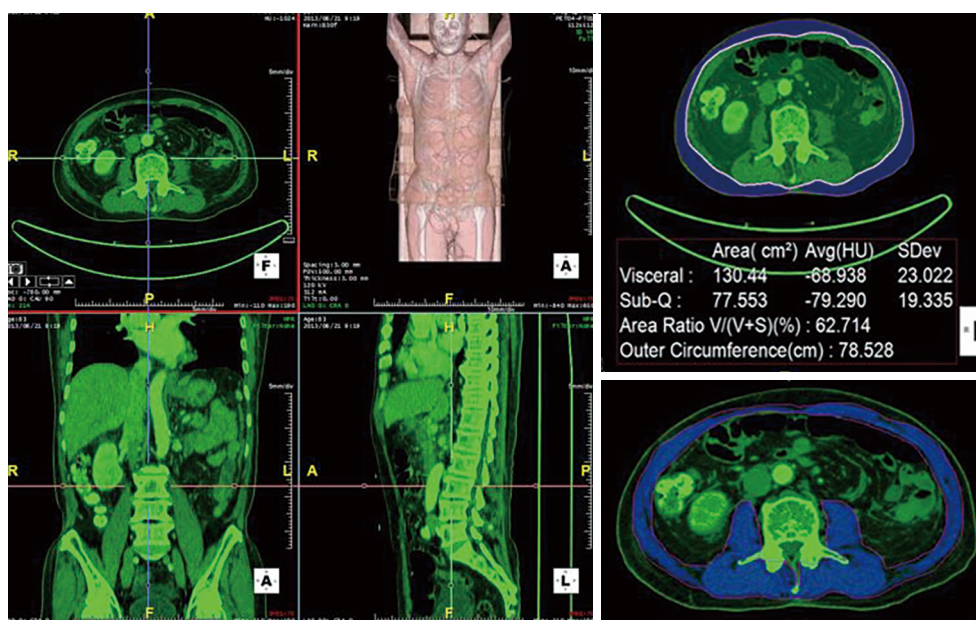


Figure 1 Muscle and fat mass measurement in PD patients. PD, pancreaticoduodenectomy.

and C-reactive protein (CRP)—were measured at the preoperative period and on POD 7. All the indicators in the preoperative period were examined one day before surgery. NRI was calculated as follows; $NRI = (1.519 \times \text{serum albumin, g/dL}) + [41.7 \times \text{present weight (kg)/ideal body weight (kg)}]$. Muscle density and muscle, visceral fat, and subcutaneous fat masses were determined using a CT scan (12) before surgery and POD 7 at the 3rd lumbar spine (L3) level (Figure 1). The preoperative CT scan was taken at the out-patient clinic, and the average period from the day when the CT scan was taken to surgery was 16.25 ± 5.78 days. The CT scan was obtained using a 16- or 64-section scanner (Somatom Sensation 16 or 64; Siemens Medical Solutions, Forchheim, Germany) and a section thickness 3 mm (14).

To see whether they are affected by the inflammation, we analyzed the correlation between albumin and prealbumin, CRP and prealbumin. And the comparison of prealbumin to CRP ratio between preoperative period and POD 7 was conducted.

The difference of serum CRP level between the perioperative period and POD 7 was divided into three groups: (I) less than zero square of ten ($<10^0$), (II) from greater than or equal to a square of ten up to less than two square of ten ($\leq 10^1 - <10^2$), (III) greater or equal to two square of ten ($\geq 10^2$). For each group, we analyzed the correlation with prealbumin, muscle mass, muscle density, visceral and subcutaneous fat.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional of CR321018 and informed consent was taken from all the patients

Statistical analysis

The statistical analysis was performed using SPSS version 23, and correlation analysis using the Pearson test. The paired *t*-test and ANOVA were used for group comparisons. Results are presented as means \pm SDs and statistical significance was accepted for *P* values <0.05 .

Results

The study subjects were 18 males and 10 females of overall average age 63.5 ± 9.7 years, and BMI 22.89 ± 3.11 kg/m². Of the 28 patients, common bile duct cancer was the most common diagnosis (46.4%) following in decreasing order by ampulla of Vater cancer, pancreatic head cancer, chronic pancreatitis, and neuroendocrine tumor (Table 1).

NRI, protein, albumin, and prealbumin were significantly lower ($P < 0.001$), but CRP was significantly higher ($P < 0.001$) at POD 7 than preoperative period (Table 2).

Prealbumin and albumin levels were positively correlated ($P = 0.006$) (Figure 2). But on the contrary prealbumin and CRP levels were negatively correlated ($P < 0.001$) (Figure 3),

and prealbumin to CRP ratio was significantly lower on POD 7 ($P=0.003$) (*Figure 4*). There was a significant difference in comparison the group divided by CRP change with prealbumin between the preoperative period and POD 7 ($P<0.001$) (*Figure 5*).

Muscle mass was higher ($P=0.02$) and visceral fat was lower ($P<0.001$) on POD 7 than preoperative period, but muscle density and amount of subcutaneous fat were similar in both periods (*Figure 6*). There was no significant difference in comparison between the groups divided by CRP change and muscle density, muscle mass, visceral and subcutaneous fat amount (*Figure 7*).

Discussion

Hepatobiliary and pancreatic malignancy is often associated with malnutrition, which is attributed to sustained pro-

inflammatory cytokine response, poor dietary intake, and the catabolic effects of sepsis (15,16). As malnutrition has a negative effect on prognosis after radical surgery, adequate nutritional support is mandatory.

Various methods have been used to provide patients with sufficient nutrition during the postoperative period. The early recovery after surgery (ERAS) protocol reported that the initiation of early enteral feeding has shown to reduce complications and hospital stays, and promote earlier bowel function recovery and the resumption of normal activities (17,18).

However, the anatomical change of the gastrointestinal tract after surgery causes an insufficient oral intake, an additional nutritional supply is required such as enteral tube feeding or TPN to provide enough calorie (6). The optimal means of parenteral feeding remains controversial and though numerous studies have compared the efficacy of enteral feeding and TPN, the results vary (19-23).

Various serologic parameters have been used to estimate the nutritional statuses of patients at the postoperative period. But, these parameters are easily influenced by environmental factors, inflammatory conditions, and drugs (10). As shown in *Figures 3-5*, our results verify this phenomenon. Therefore, it appears these parameters are not suitable to assess the nutritional status at immediate postoperative period because of inflammatory process in the body.

Sarcopenia is a syndrome characterized by progressive, generalized loss of skeletal muscle mass and strength, and can be diagnosed by low muscle mass and poor muscle function. Numerous studies have reported that sarcopenia is highly associated with poor outcomes, and mortality (24-30).

Recently, sarcopenia has been identified as a poor prognostic factor for patients with pancreatic cancer, colorectal with liver metastasis, liver cirrhosis and liver

Table 1 Patient characteristics

	Value
Pancreaticoduodenectomy	
Number	28
Sex (male/female)	18/10
Age	63.54±9.72
BMI (kg/m ²)	22.89±3.11
Diagnosis	
Common bile duct cancer	13 (46.4)
Ampulla of Vater cancer	9 (32.1)
Pancreas head cancer	2 (7.2)
Chronic pancreatitis	2 (7.2)
Neuroendocrine tumor	2 (7.2)

Table 2 Postoperative nutritional marker changes

	Preoperative	Postoperative day 7	P
BMI (kg/m ²)	22.98±3.03	22.78±3.35	0.282
NRI	50.27±7.02	48.81±7.32	0.001
Protein (g/dL)	6.04±0.62	5.38±0.52	<0.001
Albumin (g/dL)	3.53±0.52	2.84±0.31	<0.001
Prealbumin (mg/L)	166.87±68.54	123.72±48.36	<0.001
CRP (mg/dL)	12.23±19.69	74.33±48.85	<0.001

BMI, body mass index; NRI, nutritional risk index; CRP, C-reactive protein.

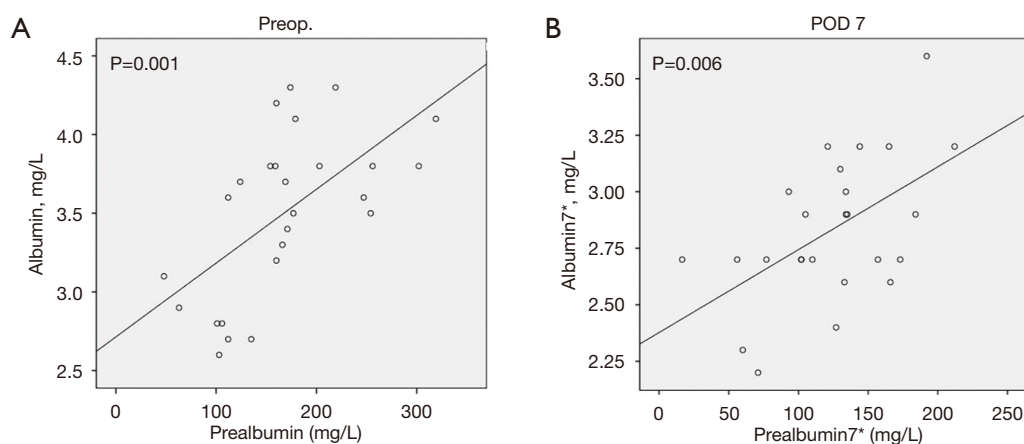


Figure 2 Correlations between prealbumin and albumin (A), and prealbumin and CRP (B) levels. *, Albumin 7 & Prealbumin 7, serum albumin and prealbumin level on POD 7; Preop, preoperative period; POD 7, postoperative day 7; CRP, C-reactive protein.

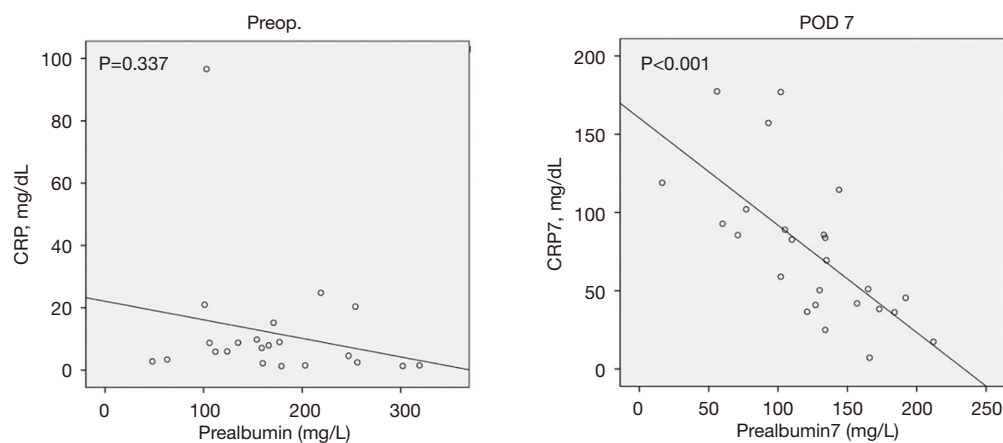


Figure 3 Postoperative changes in prealbumin-CRP ratios. CRP, C-reactive protein.

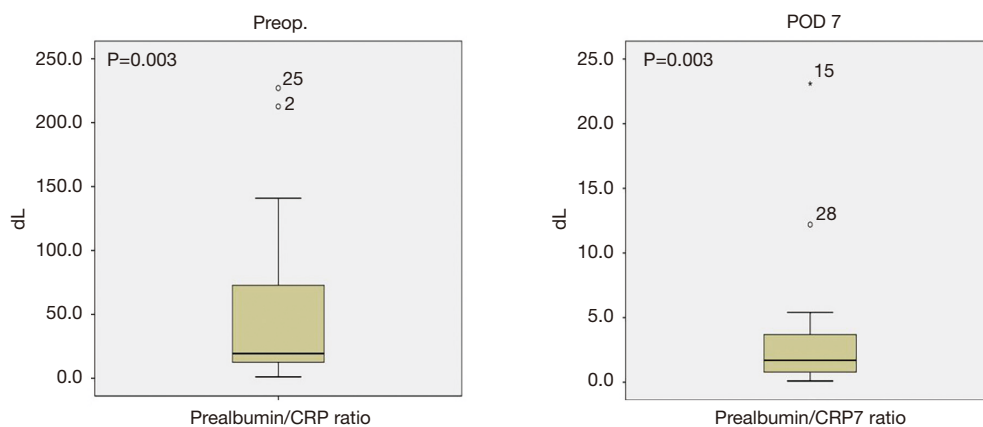


Figure 4 Comparison of prealbumin/CRP ratio. CRP, C-reactive protein.

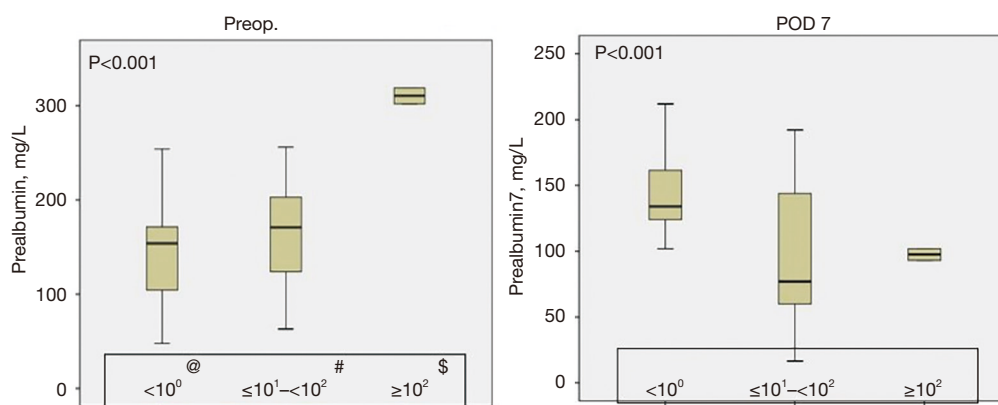


Figure 5 Variation of Prealbumin level according to the changes of CRP. @, less than zero square of ten; #, from greater than or equal to a square of ten up to less than two square of ten; \$, greater or equal to two square of ten. CRP, C-reactive protein.

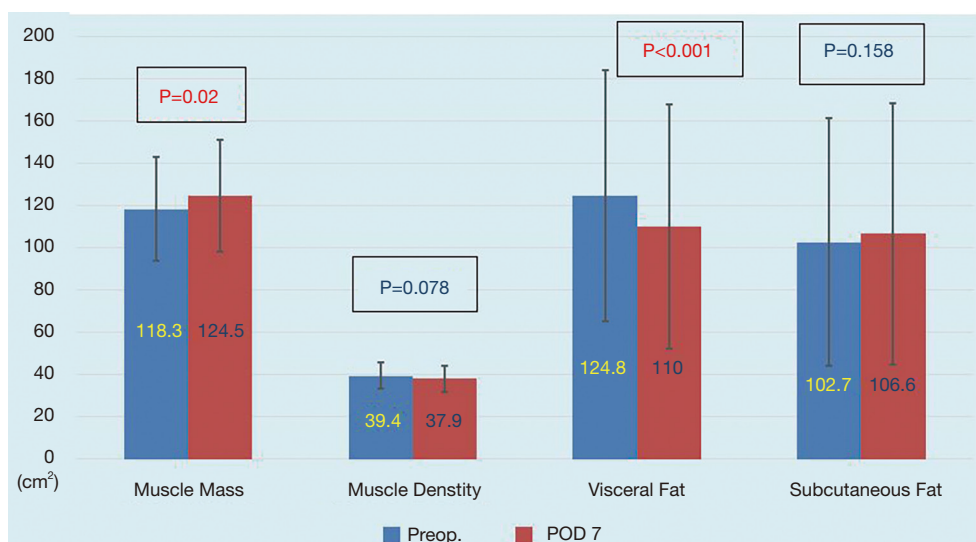


Figure 6 Comparison of anthropometric parameters. Muscle mass and density, visceral and subcutaneous fat amounts were evaluated by CT scan at L3 level, and compared between preoperative period and POD 7. POD7, postoperative day 7.

transplantation (31-34). Besides, sarcopenia is known to have negative impacts on postoperative morbidity and prognosis undergoing PD, and also it is the risk factor for postoperative pancreatic fistula which is the most fatal complication after PD (34-36). Therefore, prevention of sarcopenia after surgery is important.

Several methods can be used to assess muscle mass, but all have advantages and disadvantages. Although CT scan measures of muscle mass provide the most reliable and accurate information, the technique is hospital-based, expensive, and time-consuming as compared with other modalities. But, as all the patients who underwent

PD routinely take CT scan postoperatively to check complications, the anthropometric data can be collected without an additional charge.

To determine the effectiveness of TPN, we compared muscle mass, muscle density, and visceral and subcutaneous fat amounts measured preoperatively and on POD 7. Our important finding was that although visceral fat amounts were reduced on POD 7, muscle mass was unaffected or even tended to increase, which can be explained that the protein sparing effect of TPN administration prevented muscle degradation. Furthermore, the maintenance or increase of muscle mass can prevent sarcopenia by

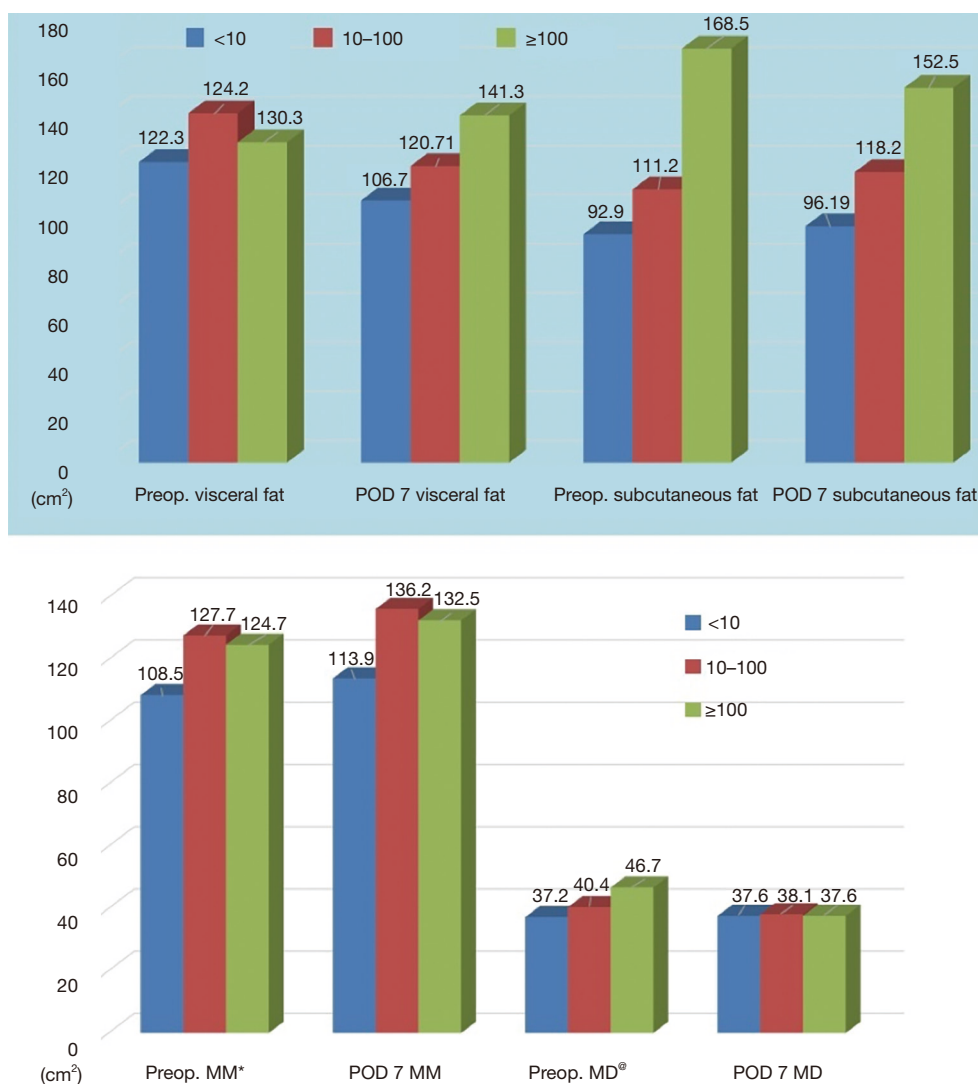


Figure 7 Changes in muscle mass, muscle density, visceral and subcutaneous fat amounts with respect to CRP. *, muscle mass; @, muscle density; CRP, C-reactive protein.

appropriate TPN administration.

In order to evaluate the nutrition status accurately after PD, we suggest that CT scan-based measurement of muscle and fat mass measurements at the postoperative period. Also we suggest a prospective study to compare nutritional statuses in enteral feeding and TPN groups after PD and to investigate the effects of oral intake amounts and the timing of supplementation.

The limitations of this study include a small number of patient populations and the lack of similar research related to the effectiveness of TPN at early postoperative period after major surgery.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://dx.doi.org/10.21037/gs-20-390>

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://dx.doi.org/10.21037/gs-20-390>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional review board of CR321018 and informed consent was taken from all the patients.

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