論 文 内 容 要 旨

Sarcopenia is closely associated with pancreatic exocrine insufficiency in patients with pancreatic disease

（サルコペニアと膵外分泌機能との関連性）

Pancreatology, 2016, in press.

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Background/Objectives: Frailty has been proposed as a global metric of patient physiological reserve and overall health status. Sarcopenia has been reported to be an accurate and quantitative marker of frailty. Sarcopenia is defined as depletion of skeletal muscle mass with a risk of adverse outcomes, such as physical disability, poor quality of life, and death. Prognosis is multifactorial and related not only to tumor specific factors but also to individual patient characteristics, such as frailty. The current literature suggests that decreased skeletal muscle (SM) mass (sarcopenia), sarcopenic obesity (obesity with depleted muscle mass), and loss of visceral adipose tissue (VAT) are associated with a poor prognosis in patients with pancreatic cancer. It has been reported that pancreatic exocrine insufficiency (PEI) in patients with chronic pancreatitis is associated with low body fat mass and with low serum nutritional markers such as albumin, prealbumin, retinol binding protein, and magnesium. However, there has been no report about the relationship between sarcopenia and PEI. We wondered whether body components such as SM mass, VAT, subcutaneous adipose tissue (SAT), intramuscular adipose tissue content (IMAC) and serum nutritional markers are associated with pancreatic exocrine function The aim of this study is to determine whether body composition, including SM, subcutaneous adipose tissue (SAT), VAT, intramuscular adipose tissue content (IMAC), and serum nutritional markers are associated with pancreatic exocrine function in patients with pancreatic disease.

Methods: This was a prospective review of the medical records of patients with pancreatic disease who underwent pancreatic surgery in the authors' institution between 2010 and 2013. Data were collected prospectively on 132 patients with pancreatic disease. SM, SAT, VAT and IMAC were assessed by computed tomography. Patients underwent a ^{13}C-labeled mixed triglyceride breath test to measure pancreatic exocrine function. Serum nutritional markers were measured at the same time of ^{13}C-labeled mixed triglyceride breath test. The following nutritional markers were used: serum cholesterol (mg/dl), peripheral blood lymphocyte count (cells per µl), serum albumin (g/dl), serum total protein (g/dl), serum triglycerides (mg/dl) and serum amylase (U/l). Patients were also stratified by quartiles according to SM are, SAT area and VAT area, and for each the lowest group was defined in the categorical analyses as the lowest quartile for men and women separately. The lowest group for SM was defined as sarcopenia. Patients were also stratified by quartiles according

to IMAC; each highest group was defined as the highest quartile for men and women separately. PEI was defined as a percentage $^{13}CO_2$ cumulative dose at 7 h below 5%.

Results: A total of 221 patients with pancreatic disease underwent pancreatic surgery at our institution between 2010 and 2013. A total of 132 patients who underwent the ^{13}C - labeled mixed triglyceride breath test, CT and the blood test for serum nutritional markers before the pancreatic surgery were enrolled in this study. Of 221 patients, 89 (40%) were excluded because 64 patients (29%) refused to participate and 25 patients (11%) were not able to tolerate a normal solid diets before the surgery. There was no significant relationship between clinical factors and PEI. When stratified by gender, the median adjusted L3 muscle mass index was lower in women than in men (36.3 vs 43.5 cm^2/m^2, P <0.001). The lowest quartile of the L3 muscle mass index threshold in men was 39.1 compared with 30.4 cm^2/m^2 in women. The median adjusted SAT area (cm^2) was greater in women than in men (139.2 vs 88.9 cm, P<0.001). The lowest quartile SAT threshold in men was 63.0 vs 93.7 cm^2 in women. The median adjusted VAT area (cm^2) was lower in women than in men (75.7 vs 95.4 cm^2, P =0.01). The lowest VAT threshold in men was 57.4 vs 50.9 cm^2 in women. The median adjusted MMF/R was greater in women than in men (- 0.005 vs - 0.273, P<0.001). The highest MMF/R threshold in men was -0.148 vs 0.049 in women. On univariate analyses, the presence of sarcopenia (lowest vs highest quartile of L3 muscle mass index) was associated with PEI in both men (P<0.001) and women (P=0.012). Other measures of body composition were not associated with PEI. Serum albumin was associated with PEI in men only (P=0.005). Other serum markers were not associated with PEI. On univariate analysis of the total sample, sarcopenia (P=0.001) and serum albumin (P=0.058) were associated with PEI. On multivariate analysis, sarcopenia remained independently associated with pancreatic exocrine insufficiency (lowest vs highest SM quartile, Odds ratio=7.39; 95% CI 3.013-19.83; P<0.001)

Conclusions: We have observed a clear correlation between PEI and sarcopenia, but not with other body components or serum nutritional markers. It is assumed that PEI would be involved in the pathogenesis of sarcopenia.