

## A Radiological Encomium Depicting Pancreatic Fibrosis and Sarcopenia: A Research Perspective

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### Abstract

**Aims and Objectives:** In this study we compared DW MRI findings with the results of histological examination and CT findings in patients with chronic pancreatitis and pancreatic cancer, to confirm a non-invasive diagnostic method, determining pancreatic fibrosis. Moreover, we looked for correlation between histologically determined PF and sarcopenia, since this pathology is highly suspected in patients of our research.

**Materials and Methods:** We collected a group of 9 patients, who underwent surgical resection of the pancreas due to pancreatic cancer or chronic pancreatitis. All patients were treated at the Department of Gastroenterology and Surgery of P.B.M hospital, Bikaner, Rajasthan after being approved by the ethical committee of the associated Sardar Patel Medical College, Bikaner. All examinations and surgeries were performed in 2017.

**Conclusion:** We found that ADC value in histologically determined fibrotic pancreatic tissue is significant lower. Since DW MRI can be performed relatively quickly, does not require administration of gadolinium-based contrast agents and enables qualitative and quantitative assessment of tissue diffusivity, it can be routinely implemented in clinical protocols.

**Keywords:** Fibrosis; Computed tomography; Magnetic resonance imaging; Protocol

### Introduction

Pancreatic fibrosis is a histological feature of chronic pancreatitis. Moreover, it develops during the course of pancreatic cancer. The only method that can be used to determine the level of PF accurately is histological examination of pancreatic tissue. However, it remains a challenge to determine exact level of PF noninvasively. Non-invasive diagnostic methods, such as diffusion weighted magnetic resonance imaging (DW MRI) and computed tomography (CT) scan could help evaluate the levels of fibrosis in the pancreatic tissue and confirm clinically suspected morphological changes of pancreas. Therefore, by using a complex treatment we can prevent PF further development [1-3].

Patients with chronic pancreatitis and pancreatic cancer often develop the most severe degrees of cachexia. Traditional understanding of cachexia has focused on loss of body weight. However, skeletal muscle and adipose tissue may behave independently during weight loss [4]. The loss of skeletal muscle mass (sarcopenia) is a serious condition, associated not just with reduced muscle strength, but also with impaired glucose regulation, hormone production and other cellular mechanisms [5]. In addition, skeletal muscle has been identified as an endocrine organ due to its capacity to produce and secrete myokines and other proteins. Metabolic disorders, like sarcopenia, are important factors in patient's long-term prognosis and should be considered in combined treatment of pancreas diseases [6].

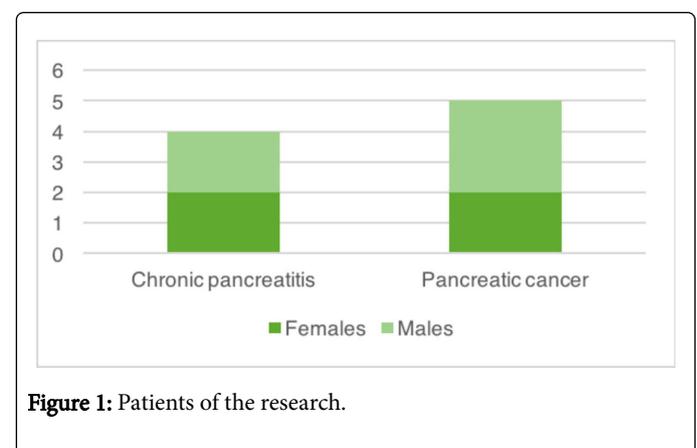
In this study we compared DW MRI findings with the results of histological examination and CT findings in patients with chronic

pancreatitis and pancreatic cancer, to confirm a non-invasive diagnostic method, determining PF. Moreover, we looked for correlation between histologically determined PF and sarcopenia, since this pathology is highly suspected in patients of our research [7-9].

### Materials and Methods

#### Patients

We collected a group of 9 patients, who underwent surgical resection of the pancreas due to pancreatic cancer or chronic pancreatitis. All patients were treated at the Department of Gastroenterology and Surgery of P.B.M hospital, Bikaner, Rajasthan. All examinations and surgeries were performed in 2017.



There were 4 patients with chronic pancreatitis (2 females and 2 males, age range 34-52) and 5 patients with pancreatic cancer (2 females and 3 males, age range 63-80) (Figure 1). Diagnoses were confirmed by histological examination of resection margin, as well as preoperative abdominal CT scan and DW MRI. Radiological examinations were evaluated by radiologist, with 10 years' experience.

### MRI examination

All MRI examinations were performed by means of 1.5 - Tesla. Pancreatic tissue was identified on the T1 Dixon, T2 and DWI sequences. Patients were examined the day before surgery. ADC values were measured at the anticipated resection margin, using the largest possible region of interest (ROI) for each patient. The ADC measurements were repeated three times with different ROI's placed in a different part of the segment (Figures 2-4). The average of the three measurements was accepted as the final ADC value of the segment. All ADC values were measured directly from the ADC map data on an independent workstation console.

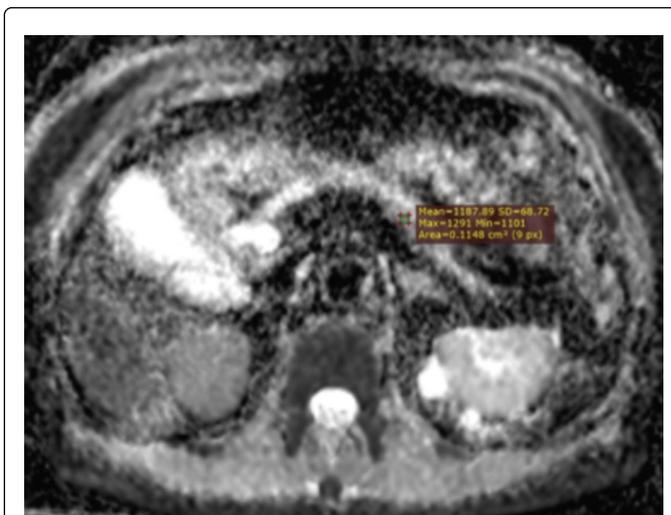


Figure 4: ADC value in pancreas tail.

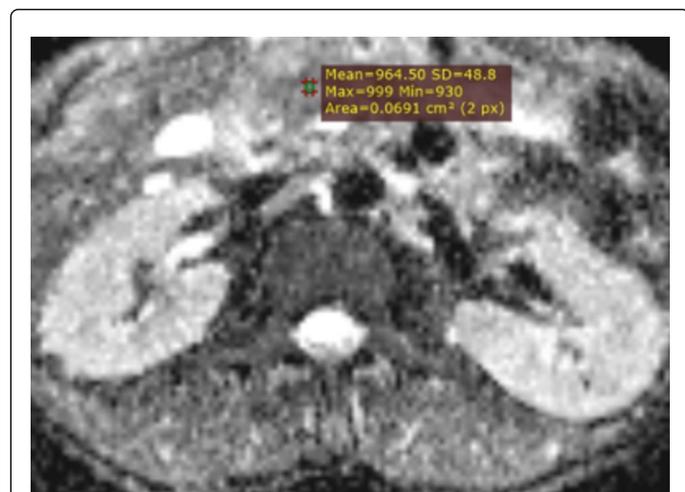


Figure 2: ADC value in pancreas head.



Figure 3: ADC value in pancreas body.

### Histological examination

The pancreatic tissue was processed with Mason's trichrome staining for accurate estimation of fibrosis. Digital images of each slide were analyzed by an experienced pathologist, using microscope (BP72 camera, 1 × 1 cm area, x40 increase). Images were processed using the program CellSens Dimension. Pancreatic fibrosis was rated as mild, when there was 1-33%, medium - 34-66% and severe - 67-100% of fibrotic tissue in the pancreatic tissue (Figure 5 and 6).

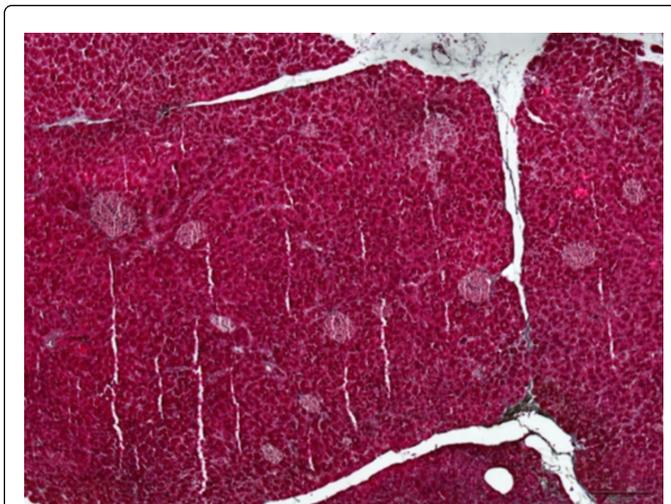
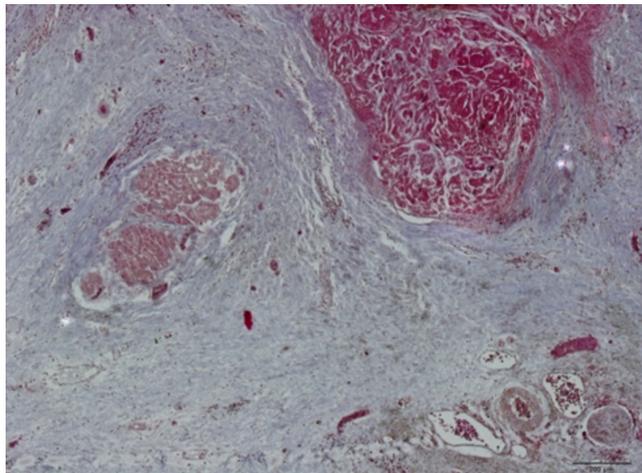


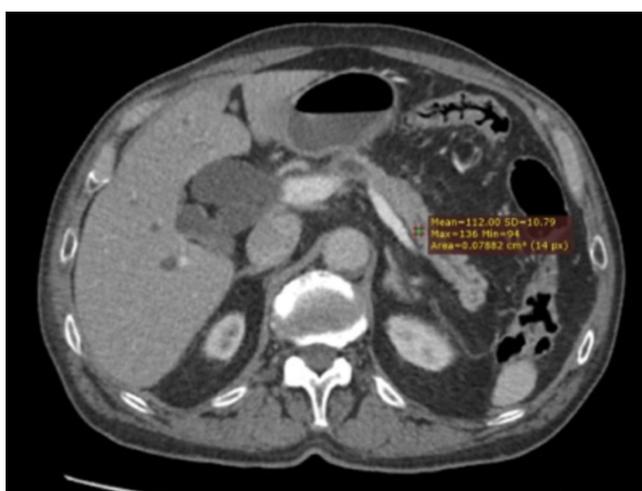
Figure 5: Pancreatic tissue processed with Mason's trichrome staining. Mild pancreatic fibrosis (2% of fibrotic tissue in the pancreatic tissue).



**Figure 6:** Pancreatic tissue processed with Mason's trichrome staining. Severe pancreatic fibrosis (82% of fibrotic tissue in the pancreatic tissue).

### CT examination

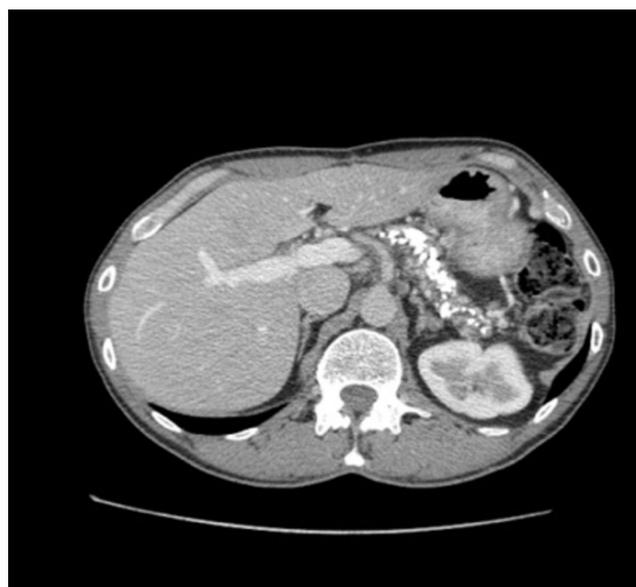
All CT examinations were performed with a 64-slice CT tomograph, with and without the intravenous injection of 100 ml water-soluble iodine contrast medium. Pancreatic tissue was referred as "atrophic" with typical enhancement (Figure 7). Atrophic, with lesser enhancing pancreatic tissue was referred as "potentially fibrotic" (Figure 8), and pancreatic tissue with no enhancement and with multiple calcifications (>10) - rated as "pancreatic fibrosis" (Figure 9).



**Figure 7:** Atrophic pancreatic tissue, enhancing with contrast medium (portal phase ~112 HU).

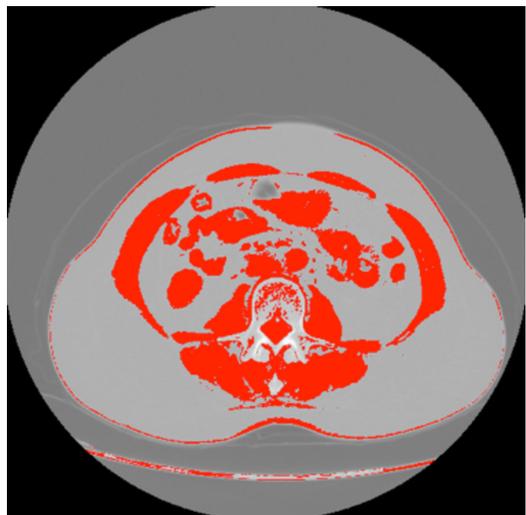


**Figure 8:** Atrophic pancreatic tissue, with lesser enhancing (portal phase ~77 HU).



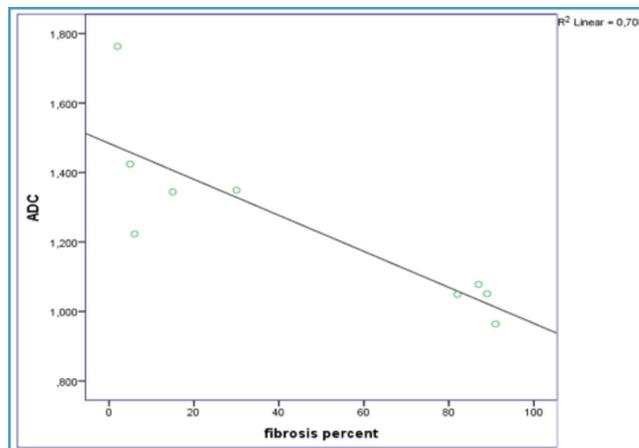
**Figure 9:** Pancreatic fibrosis, multiple calcifications.

A single axial CT-image at the level of the third lumbar vertebrae was assessed to measure cross-sectional areas of skeletal muscle (m. psoas major, m. erector spinae, m. quadratus lumborum, m. obliquus externus abdominis, m. obliquus internus abdominis, m. transversus abdominis, m. rectus abdominis). The tissue cross-sectional area at this level correlates with total body skeletal muscle and adipose tissue mass distribution. Images were analyzed using Image J (1.50i) software, which allows quantifying the tissue composition, by using Hounsfield units (HU). HU threshold for skeletal muscle was 150 to -29 and by using special formulas skeletal muscle area was counted (cm<sup>2</sup>) (Figure 10). The values were normalized for the height of the patient to get the lumbar skeletal muscle index (L3 SMI) in cm<sup>2</sup>/m<sup>2</sup>. Sarcopenia for women was determined when SMI was lower than 38, 9 cm<sup>2</sup>/m<sup>2</sup>, for men - SMI below 55, 4 cm<sup>2</sup>/m<sup>2</sup> [10].



**Figure 10:** Red - skeletal muscle at the level of L3 vertebrae, grey - adipose tissue.

There was no correlation between histological pancreatic fibrosis degree and sarcopenia ( $p=0.55$ ).



**Figure 11:** Significantly negative correlation between ADC mean and histologically determined pancreatic fibrosis ( $r=-0.84$ ,  $p=0.004$ ).

### Statistical Analysis

Statistical analysis was performed using SPSS 22.0 (SPSS, Inc., Chicago, IL, USA) software. Quantitative parameters between independent groups were compared using independent sample t test, Pearson and Spearman correlation. Associations were considered significant if P values were  $<0.05$  or less.

### Results

We found significantly negative correlation between ADC mean and histologically determined pancreatic fibrosis ( $r=-0.84$ ,  $p=0.004$ ) (Figure 11), as well as contrast agent accumulation in the resection margin on CT scan ( $r=0.76$ ,  $p=0.016$ ). 5 patients had histologically determined mild pancreatic fibrosis and 4 patients - severe pancreatic fibrosis. There were no patients with medium pancreatic fibrosis (Figure 12).

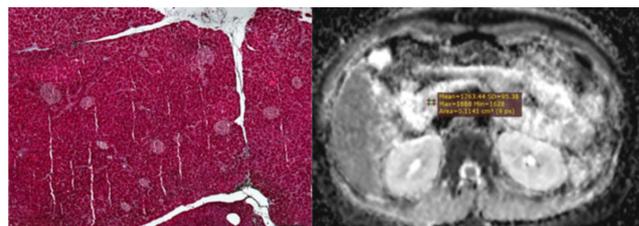
CT scan revealed 4 patients with decreased contrast agent enhancing in pancreatic tissue, rated as atrophic pancreatic tissue and 3 patients with pancreatic tissue with multiple calcifications, rated as pancreatic fibrosis. There were 2 patients with intact pancreatic tissue (Figure 13).

The average MR ADC value of all patients of pancreas resection margin was 1,249 (Figure 14).

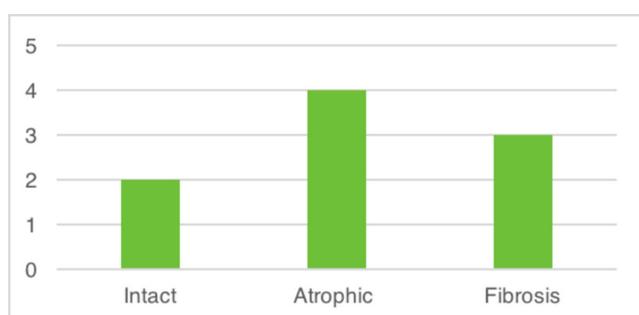
Six of 9 patients had sarcopenia, 2 females (average SMI value 32, 52  $\text{cm}^2/\text{m}^2$ ) and 4 males (average SMI value 40, 83  $\text{cm}^2/\text{m}^2$ ) (Figure 15).

Two of sarcopenic and 1 of non sarcopenic patient's had overweight ( $\text{BMI} >25$ ), 4 of sarcopenic and 2 of non sarcopenic patient's had normal weight. Average BMI value in sarcopenic patient's group was 25, 99 (23, 63-28, 36) in females and 23, 26 (18, 71-27, 68) in males. In non sarcopenic patient's group the average BMI value was 25, 39 (just one patient) in females and 22, 88 (22, 74-23, 03) in males (Figure 16).

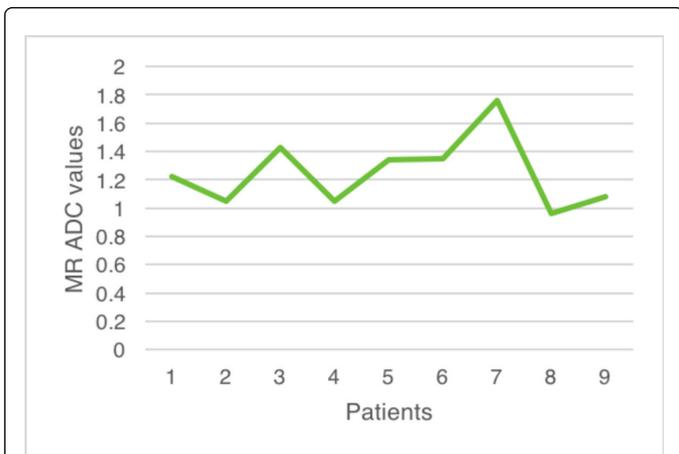
Three of 5 histologically determined mild pancreatic fibrosis and 2 of 4 severe pancreatic fibrosis patients had sarcopenia (Figure 17).



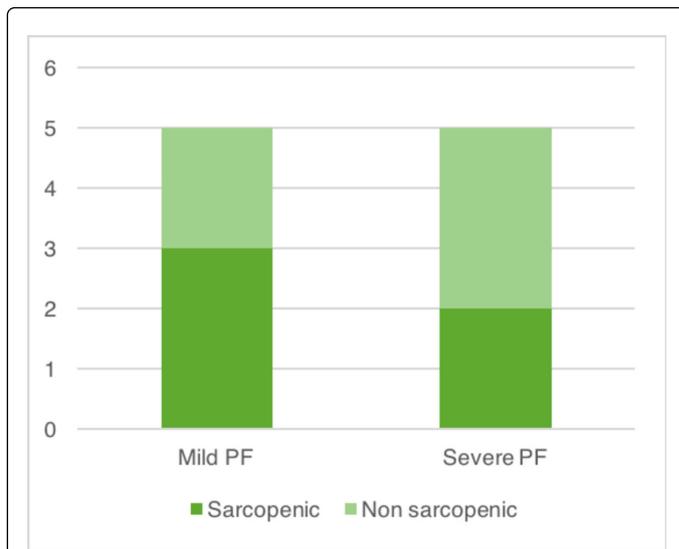
**Figure 12:** Clinical case. Patient - 22 years' female, tumor of pancreas head. On the left-pancreatic tissue processed with Mason's trichrome, 2% of fibrotic tissue. On the right-image of DW MRI, ADC value of pancreas head resection margin  $1,763 \times 10^{-3} \text{ mm}^2/\text{s}$ .



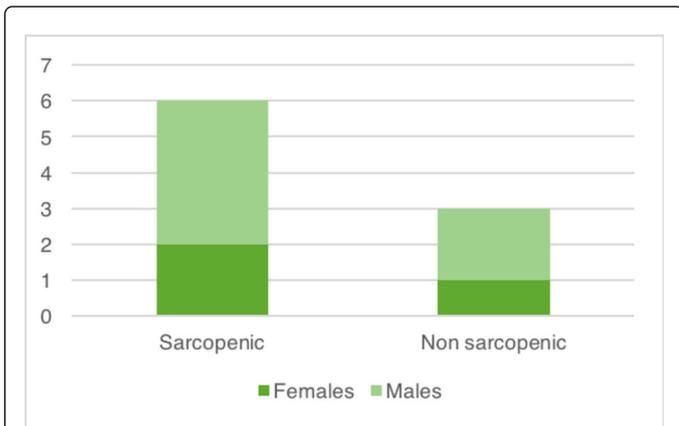
**Figure 13:** Pancreatic tissue in CT scan.



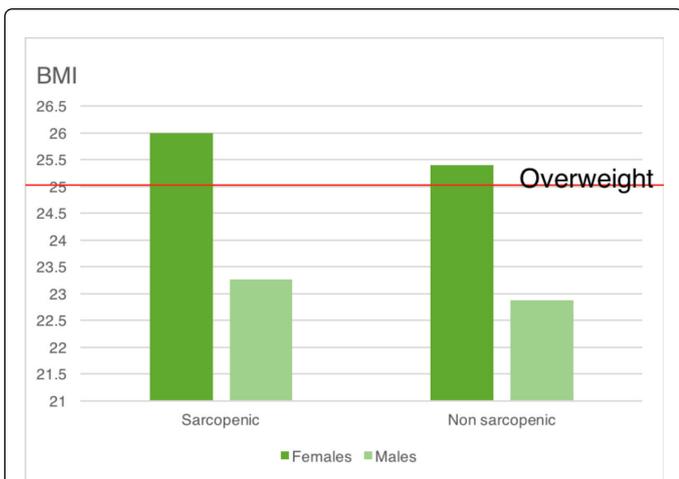
**Figure 14:** MR ADC values of all patients of pancreas resection margin.



**Figure 17:** Histologically determined pancreatic fibrosis and sarcopenia.



**Figure 15:** Sarcopenic and non sarcopenic patient's groups.



**Figure 16:** Average BMI value in sarcopenic and non sarcopenic patients.

## Conclusion

We found that ADC value in histologically determined fibrotic pancreatic tissue is significant lower. Since DW MRI can be performed relatively quickly, does not require administration of gadolinium-based contrast agents and enables qualitative and quantitative assessment of tissue diffusivity, it can be routinely implemented in clinical protocols.

Sarcopenia is highly prevalent in patients with chronic pancreatitis and pancreatic cancer. By using a single axial CT-image of L3 SMI we can evaluate sarcopenia in patients with pancreatic fibrosis during the routine care. In this research the correlation between pancreatic fibrosis degree and sarcopenia wasn't significant, probably due to too small patient group. Our study will be continued to collect as many patients as necessary to obtain reliable results.

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