

# Generalized Muscle Quality Loss as a Risk Factor for Pelvic Organ Prolapse: A Single-Center, Observational Study

**Yoko Chino**

Tannan Regional Medical Center

**Daisuke Inoue**

University of Fukui Hospital

**Makoto Yamamoto**

University of Fukui Hospital

**Toshimichi Onuma**

University of Fukui Hospital

**Yoshio Yoshida** (✉ [yyoshida@u-fukui.ac.jp](mailto:yyoshida@u-fukui.ac.jp))

University of Fukui Hospital

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## Research Article

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# Abstract

Among the physiological changes associated with aging, myopenia due to increased amounts of fatty tissue in muscles and loss of muscle mass have recently gained attention. This study retrospectively examined the relationship between generalized muscle quality and pelvic organ prolapse (POP). Participants comprised 25 patients between 40 and 79 years old showing a Pelvic Organ Prolapse Quantification system stage of 3 or higher who underwent surgery between 2017 and 2019. Control cases comprised 23 patients with benign gynecological diseases who underwent surgery without POP. CT performed within 3 months before surgery was used to measure muscle mass. Smooth muscle index (SMI) was significantly higher in the POP group than in the non-POP group ( $p = 0.017$ ), and muscle mass was rather large in the POP group. Comparing the POP and non-POP groups, both subcutaneous and visceral fat accumulation were significantly higher in the POP group ( $p = 0.03$ ,  $p = 0.002$  respectively). Conversely, intramuscular adipose tissue content (IMAC), indicating lower muscle quality, was significantly higher in the POP group ( $p = 0.024$ ). Multivariate analysis revealed BMI and number of deliveries, but not IMAC, as significant independent risk factors of POP. Although not an independent risk factor, decreased muscle quality was involved in the pathophysiology of POP.

## Introduction

Pelvic organ prolapse (POP) is a condition in which pelvic organs such as the uterus, bladder, and rectum prolapse through the vaginal canal. The lifetime risk of developing POP-related diseases in women is estimated to be 11.1% by 80 years old, and this disease markedly reduces quality of life [1]. POP arises under conditions of pelvic floor muscle weakness. The risk factors for weakness of the pelvic floor muscles are number of vaginal deliveries, body mass index (BMI), and aging. Approximately 50% of women who have had a vaginal delivery reportedly experience symptoms of POP, and 37% of patients with POP symptoms have symptoms of urinary incontinence. Postpartum weight control has also been pointed out as an important factor in the development of POP. Declines in estrogen levels with aging have been suggested to initiate irreversible muscle loss in the pelvic floor, resulting in symptoms of POP in 30% of women between 20 and 59 years old, and in about 55% of women in their 50s [2–4]. Among the physiological changes associated with aging, myopenia due to increased fatty tissue in muscles and decreased bone and muscle mass have gained attention. Research into POP has so far only focused on local pelvic floor muscle groups, and potential relationships with myopenia as a physiological change affecting the whole body have not been investigated. This study retrospectively therefore examined whether a relationship exists between generalized muscle quality and POP.

## Patients And Methods

### Patients

The POP group comprised 25 patients between 40 and 79 years old with a Pelvic Organ Prolapse Quantification (POP-Q) system score of stage 3 or higher [5, 6] who underwent surgery at the University of

Fukui Hospital between January 1, 2017, and December 31, 2019, and for whom preoperative CT was performed. The Non-POP group comprised 23 patients with benign gynecological diseases who underwent surgery without POP (uterine fibroids, benign ovarian tumors) for whom preoperative CT was performed. Patients were excluded from the study if they had previously undergone surgery for POP, had a history of malignancy, or had a history of chronic pancreatitis.

### **Measurements of muscle mass**

In POP, images from CT performed within 3 months before surgery were used to measure muscle mass. CT measurements were made from horizontal-section CT at the L3 level with a 3-mm slice. Areas were calculated using OsiriX version 11.0 analysis software (Newton Graphics, Sapporo, Japan). For the measurement of muscle area, the CT attenuation threshold was set at -29 Hounsfield units or higher. Psoas muscle area, total muscle area, subcutaneous fat area, visceral fat area, and fat within the erector spinae muscle were measured (Fig. 1). Muscle mass was corrected for height ( $m^2$ ), and psoas muscle index (PMI) (psoas muscle area corrected for height), smooth muscle index (SMI) (L3 total muscle area corrected for height), subcutaneous fat index (subcutaneous fat area corrected for height), visceral fat index (visceral fat area corrected for height), and intramuscular adipose tissue content (IMAC) were calculated. SMI was calculated by dividing the total area of muscles (rectus abdominis, internal and external oblique abdominis, transversus abdominis, psoas major, and erector spinae muscles) from horizontal-section CT at the L3 level by the square of the height in meters. IMAC is the CT attenuation value of the multifidus muscle (erector spinae muscle) divided by the CT attenuation value of the subcutaneous fat of the back, yielding a negative value. [7–10]. All CT images were reviewed by a physician specializing in obstetrics and gynecology and a radiologist.

### **Statistical analysis**

BMI, history of vaginal deliveries, underlying diseases (hypertension, diabetes, dyslipidemia), subcutaneous fat, visceral fat, muscle area, and erector spinae fat were compared between the POP group and the non-POP group with benign gynecological tumor. The Mann-Whitney U test, a non-parametric test, was used to analyze the results. In the multiple regression model using the forward selection method, three independent variables (number of deliveries, BMI, and IMAC) and POP or non-POP status were used as dependent variables. The coefficient of determination ( $R^2$ ) represents the explanatory power of the variables. All statistical analyses were performed using SPSS v. 18.0 software (SPSS Inc., Chicago, IL, USA), with an alpha value of 0.05.

### **Ethics approval**

This study was approved by the Research Ethics Committee of the University of Fukui (No. 20180033) and waived the need for informed consent for our retrospective study. The study was complied with all tenets of the Declaration of Helsinki.

## **Results**

Table 1 summarizes the age, BMI, history of vaginal deliveries, and underlying diseases (hypertension, diabetes mellitus, or dyslipidemia) of the 25 women in the POP group and 23 women in the Non-POP group. BMI was higher ( $p = 0.006$ ) and history of vaginal deliveries was more frequent ( $p = 0.001$ ) in the POP group. Significant differences in the prevalence of hypertension ( $p = 0.023$ ) and dyslipidemia ( $p = 0.034$ ) were seen between POP and non-POP groups. On the other hand, no significant difference in the prevalence of diabetes mellitus was evident between groups.

Table 1  
 Characteristics of patients in POP and non-POP groups

	POP, n = 25	Non-POP, n = 23	p
Age (y), mean (SD)	60.32 (7.69)	57.87 (8.87)	0.311
< 45	0	2	
45–49	3	2	
50–54	2	4	
55–59	9	6	
60–64	2	2	
65–69	7	5	
70–74	1	2	
> 74	1	0	
BMI (kg/m <sup>2</sup> ), mean (SD)	24.46 (3.50)	21.95 (2.41)	0.006
< 18.5	0	2	
18.5–24.9	14	20	
25–29.9	9	1	
30–34.9	2	0	
> 34.9	0	0	
History of vaginal deliveries (SD)	2.44 (0.96)	1.48 (0.85)	0.001
0	1	4	
1	2	5	
2	10	13	
3	9	1	
> 3	2	0	
Hypertension			
Yes	12	4	0.023
No	13	19	
DM			

POP, pelvic organ prolapse; BMI, body mass index; DM, diabetes mellitus.

	POP, n = 25	Non-POP, n = 23	p
Yes	3	2	0.715
No	22	21	
Dyslipidemia			
Yes	10	3	0.034
No	15	20	
POP, pelvic organ prolapse; BMI, body mass index; DM, diabetes mellitus.			

In the present study, SMI was significantly higher in the POP group than in the non-POP group (Fig. 2a,  $p = 0.017$ ), and the muscle mass was significantly larger in the POP group ( $p = 0.023$ ). Comparing the POP and non-POP groups, both subcutaneous and visceral fat accumulation were significantly higher in the POP group. ( $p = 0.03$ ,  $p = 0.002$ , respectively) (Fig. 2b,c). On the other hand, IMAC, which indicates muscle quality, was significantly higher ( $p = 0.024$ ) in the POP group than in the Non-POP group, suggesting a decrease in muscle quality (Fig. 2d).

Figures 3 and 4 present two cases with the same patient background, one with POP (a) and the other with non-POP (b). Both patients were of similar height and weight, had normal BMI, had experienced two vaginal deliveries, and had no hypertension, diabetes, or dyslipidemia as underlying medical conditions. SMI for muscle mass was normal (i.e., muscle mass was maintained), but the IMAC value for muscle quality was high (i.e., muscle quality was decreased) in POP.

In multivariate analysis examining BMI, number of deliveries, and IMAC, both BMI and number of deliveries were independent risk factors, while IMAC was not (Table 2).

Table 2  
Multiple linear regression results

Independent variables	Unstandardized coefficients		Standardized coefficients	t	P value
	B	Std. error	$\beta$		
Constant	-1.009	0.678		-1.487	0.144
BMI	0.054	0.020	0.347	2.644	0.011
Number of vaginal deliveries	0.222	0.061	0.448	3.627	0.001
IMAC	0.111	0.199	0.076	0.560	0.578

BMI, body mass index; IMAC, intramuscular adipose tissue content.

## Discussion

Patients with POP showed no decrease in muscle mass, but a significant decrease in muscle quality compared to patients without POP. However, decrease in muscle quality was not an independent risk factor.

Age-related declines in muscle mass and quality are among the most widespread changes associated with aging. The term sarcopenia was coined by Rosenberg to describe pathological declines in skeletal muscle mass, strength and function associated with aging [11]. After 35 years old, healthy individuals lose muscle mass at a rate of 1–2% per year and muscle strength at a rate of 1.5% per year, accelerating to about 3% per year after 60 years old [12]. As a result, muscle cross-sectional area of the thigh decreases by about 40% between 20 and 60 years old. The magnitude of the decrease in fat-free mass is amplified in sedentary individuals compared to physically active individuals [12, 13]. The average adult can expect to gain about 0.45 kg [14] of fat per year between 30 and 60 years old [15], in addition to losing muscle mass. Such changes in body composition are often masked because of the relative stability of body weight, in a condition referred to as sarcopenic obesity, which further increases the risks of disability and morbidity. Although losses of muscle mass and strength with aging have long been known, sarcopenia has recently become a hot topic in gerontology. Several processes and mechanisms have been proposed for the multifaceted etiology of sarcopenia, including lifestyle, systemic factors (such as inflammatory cytokines), changes in the local environment (e.g., vascular disorders), changes in the neuromuscular system, and changes in specific processes within muscles [16]. All these factors ultimately disrupt the balance between anabolic and contractile effects, leading to muscle protein degradation, muscle cell loss, and changes in specific processes within the muscle.

The three most common risk factors for POP are the number of vaginal deliveries, postpartum weight gain, and aging. Awwad et al. found that the prevalence of POP in nulliparous women was 3.6%, compared to 6.5% in women with one delivery, 22.7% in women with two deliveries, 32.9% in women with

three deliveries, and 46.8% in women with four deliveries. The higher the number of deliveries, the higher the prevalence [17]. The effects of vaginal delivery on the pelvic floor musculature include direct injury to soft tissues and nerves [18]. The results of direct injury to soft tissues is thought to be temporary and the ptosis is likely to improve. In the case of muscle tears, irreversible changes such as vascular damage are thought to occur after birth. In addition, although the details are unknown, the nervous system may be physically damaged by the pressure of the infant's head during delivery, and this damage may accumulate with repeated deliveries, resulting in secondary damage to the pelvic floor muscle groups.

Obesity is a risk factor for POP. BMI at 1 year postpartum is reportedly associated with the occurrence of POP [18]. Weight control after the postpartum period is also an important factor in the development of POP [1–4, 17].

The most characteristic changes in body composition with aging are an increase in adipose tissue mass and a decrease in bone and muscle mass [1–4, 17]. Losses in muscle mass, in particular, are thought to lead to muscle weakness and POP. However, Awwad et al. reported in 2012 that the incidence of POP is particularly high among women who rarely develop new POP after menopause [17]. Nutritional and weight management guidance for these women might thus help prevent the onset of premenopausal POP and reduce the number of POP patients [17]. In addition, observation and close follow-up are appropriate for mild, asymptomatic women, and most women do not experience symptoms until the bulge protrudes beyond the vulva. Pelvic floor muscle training (e.g., Kegel exercises) allows systematic contraction of the anorectal muscles to strengthen the pelvic floor and has been proven to improve symptoms of stress urge incontinence and mixed urinary incontinence, and has also been reported as effective in women with mild POP [19].

Our study showed that poor muscle quality was an important factor in the development of POP, but not an independent risk factor. However, patients with POP occasionally have no history of vaginal delivery; the incidence of POP among patients without a history of delivery has been reported as 5% [17, 19]. In women, muscle mass has been reported to not change markedly throughout life [20], and muscle mass was maintained even in POP in the present study. The most important thing to be aware of is the loss of muscle quality, which may be a very important factor in the development of POP, as hidden sarcopenia associated with increased BMI may actually be a very important factor.

Muscle mass is an essential part of the criteria for the diagnosis of sarcopenia, and whole-body measurements with dual-energy X-ray absorptiometry have been cited as a method for this purpose [2]. To popularize the assessment of body composition, greater reliance on measures already included in the diagnosis or treatment of patients may be important. Psutka et al. [7] calculated a skeletal muscle index from images obtained at the level of the third lumbar vertebra during abdominal CT. Such legitimate, scientifically valid approaches have increasingly been used in the last few years to introduce discussions and interventions on body composition [7–11]. This is one reason why we measured muscle mass on CT in the present study.

However, some limitations to the present study must be considered. First, the number of patients was too small to obtain conclusive results. Second, strict criteria were not set for the selection of tomographic images to be measured. Third, this retrospective study was limited to patients from a single center.

The present findings suggest that rather than generalized muscle loss, muscle quality is associated with the pathophysiology of POP. Methods of preventing and addressing POP starting during pregnancy and postpartum should be implemented. Guidance for proper weight control during pregnancy and weight regain after delivery appears extremely important [18, 19].

From this point of view, the next step is pelvic floor muscle exercises. This is a non-invasive preventive method that has been shown to significantly improve symptoms after 6 months of practice and a consensus has been reached on its utility. In addition, avoiding undue pressure on the abdomen is important [18, 19]. Preventing the loss of muscle quality is also important. To maintain muscle mass, consuming at least 1 g of protein per kilogram of body weight per day is important, along with good oral health care to maintain the ability to eat well, and continued daily exercise habits from the time of sexual maturity [21].

## Conclusions

Loss of generalized muscle quality represents a risk factor for POP, which is a common disease in middle-aged and older women. It is no exaggeration to say that declines in the quality of the underlying muscles are key to extending not only POP, but also the "healthy life span" of women. Early therapeutic intervention seems extremely important for improving quality of life among individuals in an aging society.

## Declarations

## Contributions

Y.C., D.I. and Y.Y. wrote the main manuscript text and Y.C., D.I., M.Y. and T.O. prepared figures and tables. All authors reviewed the manuscript. Each author has made important scientific contributions to the study and is thoroughly familiar with the primary data. All authors listed have read the complete manuscript and have approved submission of the paper. The manuscript is truthful original work without fabrication, fraud or plagiarism. All authors declare that there are no conflicts of interest.

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## Figures

Figure 1

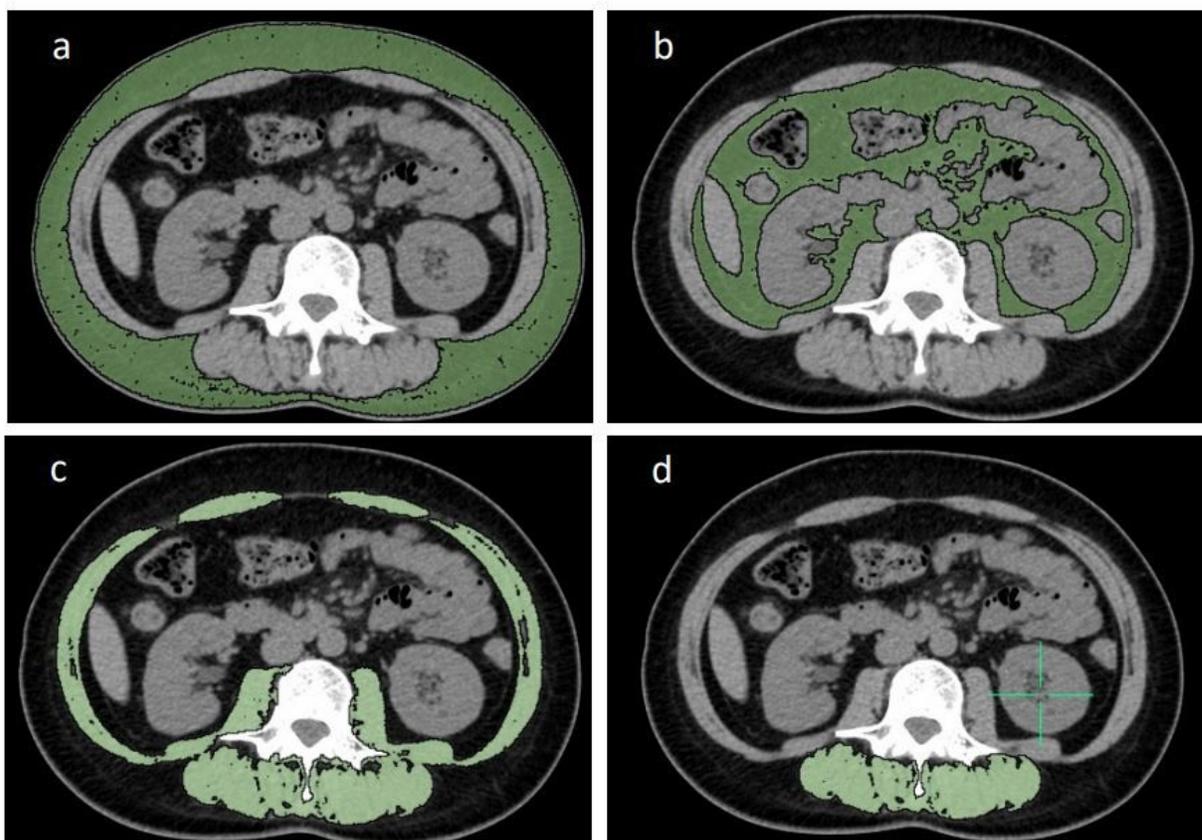
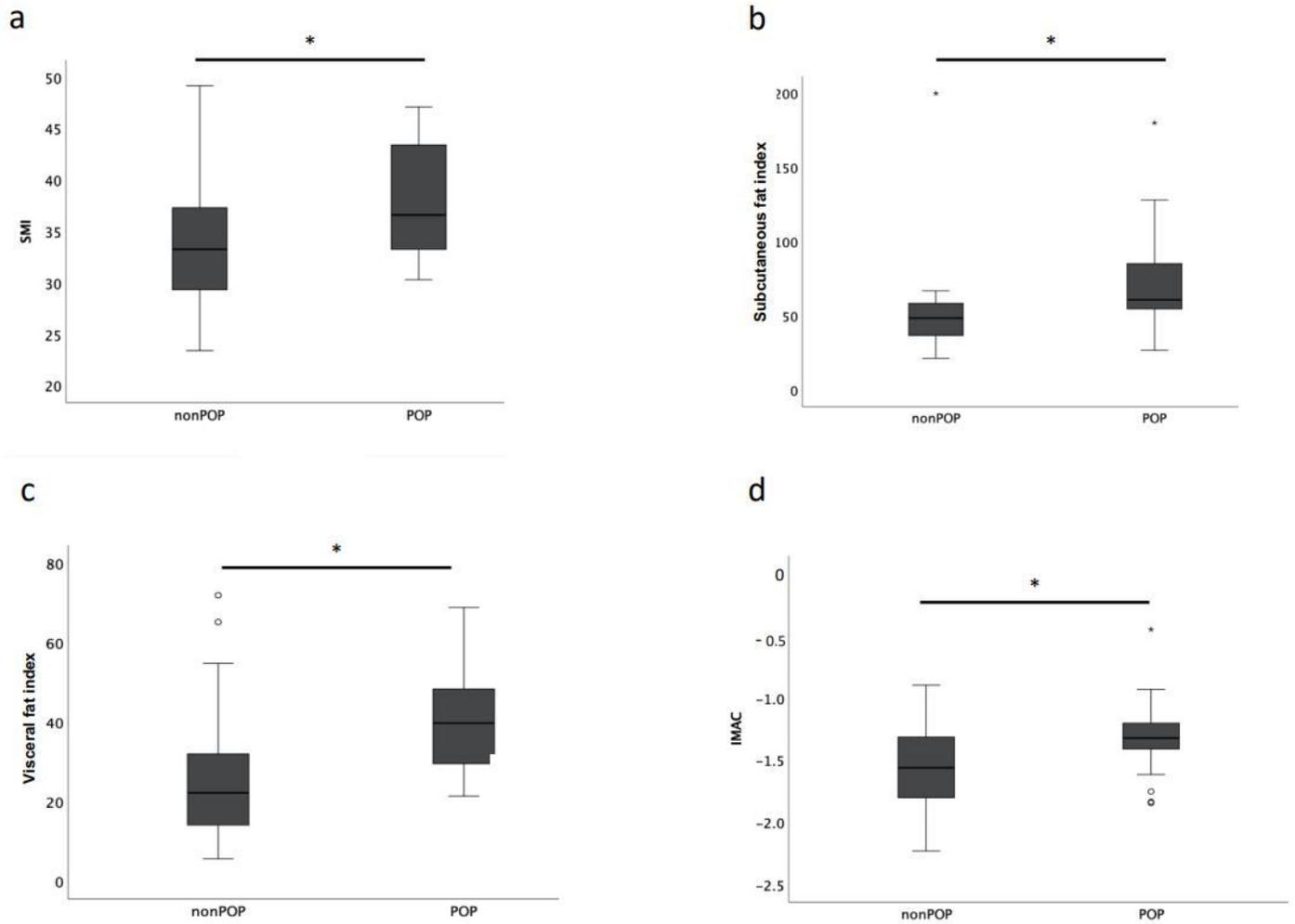


Figure 1

A 45-year-old woman: height, 150.5 cm; weight, 51.7 kg; BMI, 22.8 kg/m<sup>2</sup>. Subcutaneous fat (a), visceral fat (b), muscle area (c), and intramuscular fat (IMAC) (d) at the L3 level. ROI of multifidus muscle (HU)/mean CT value of ROI of subcutaneous fat (HU).

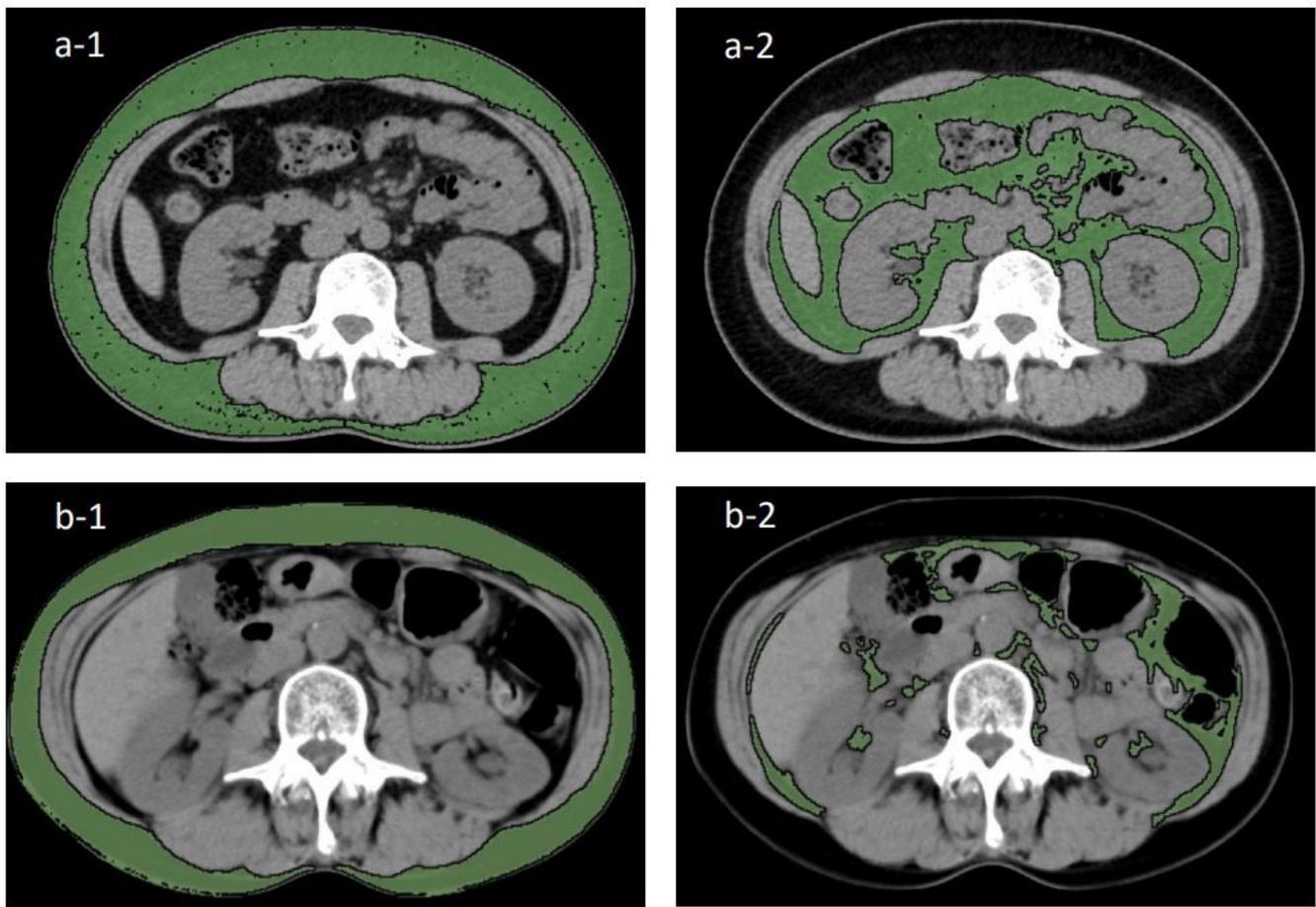
**Figure 2**



**Figure 2**

Differences in smooth muscle index (SMI) (a), subcutaneous fat index (b), visceral fat index (c), and intramuscular adipose tissue content (IMAC) (d) between POP and non-POP groups. Statistical significance was determined by the nonparametric t test with Mann-Whitney rank comparison. \*p < 0.05.

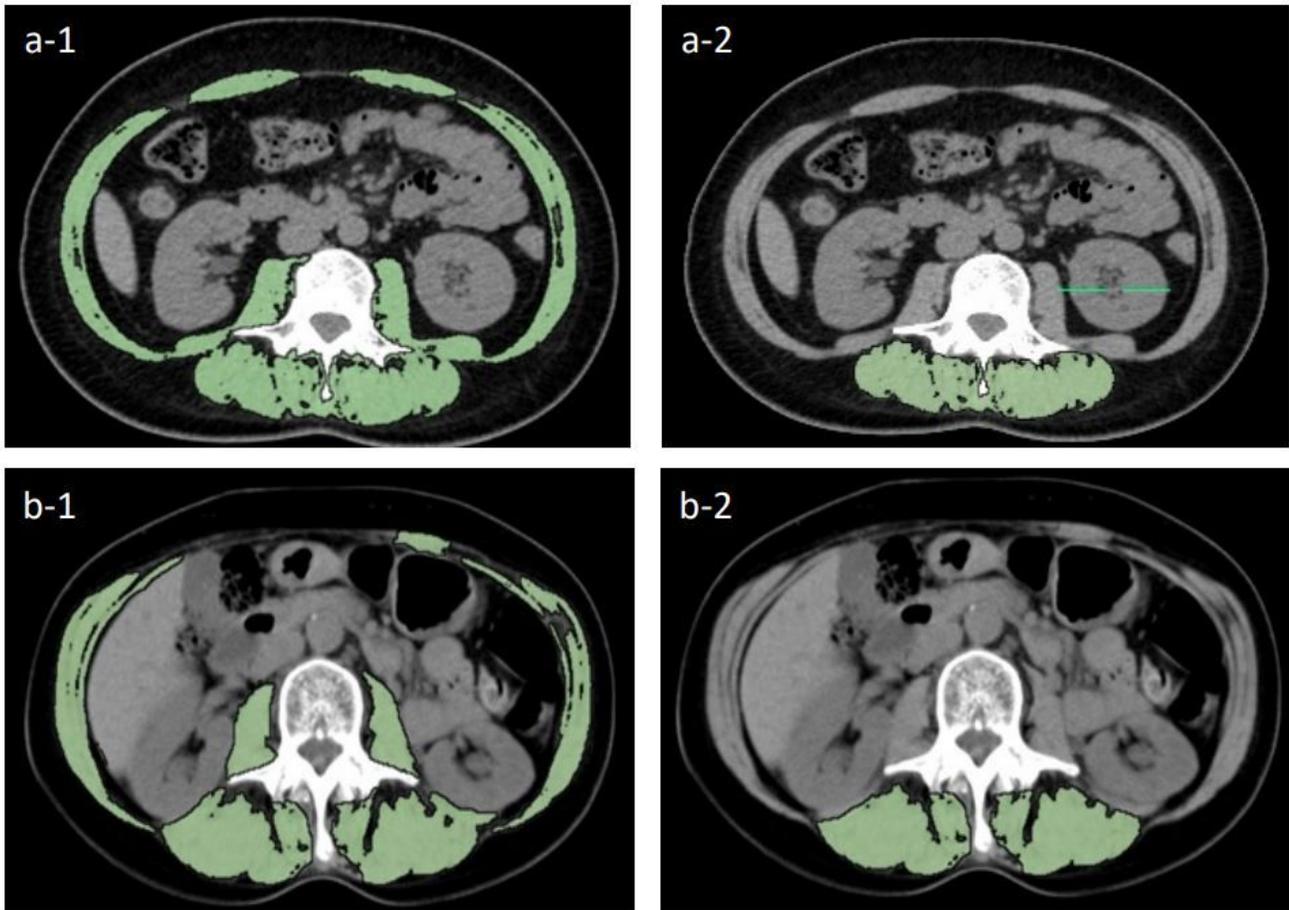
**Figure 3**



**Figure 3**

Indexes of fat in comparable representative cases from POP and Non-POP groups a) A 45-year-old woman from the POP group: height, 150.5 cm; weight, 51.7 kg; BMI, 22.8 kg/m<sup>2</sup>; 2 vaginal deliveries; no underlying disease. Subcutaneous fat index: 55.1 cm<sup>2</sup>/m<sup>2</sup> (a-1); visceral fat index: 39.8 cm<sup>2</sup>/m<sup>2</sup> (a-2). b) A 58-year-old woman from the Non-POP group: height, 149 cm; weight, 50.2 kg; BMI, 22.6 kg/m<sup>2</sup>; 2 previous vaginal deliveries; no underlying disease. Subcutaneous fat index: 39.3 cm<sup>2</sup>/m<sup>2</sup> (b-1); visceral fat index: 10.8 cm<sup>2</sup>/m<sup>2</sup> (b-2).

**Figure 4**



**Figure 4**

Indexes of muscle in comparable representative cases from POP and Non-POP groups a) A 45-year-old woman from the POP group: height, 150.5 cm; weight, 51.7 kg; BMI, 22.8 kg/m<sup>2</sup>; 2 vaginal deliveries; no underlying disease. Smooth muscle index (SMI): 36.5 cm<sup>2</sup>/m<sup>2</sup> (a), Intramuscular adipose tissue content (IMAC): -0.93 (b). b) A 58-year-old woman from the Non-POP group: height, 149 cm; weight, 50.2 kg; BMI, 22.6 kg/m<sup>2</sup>; 2 previous vaginal deliveries; no underlying disease. SMI: 32.6 cm<sup>2</sup>/m<sup>2</sup> (c), IMAC: -1.52 (d).