

## Effect of Long-term Peritoneal Dialysis on Change in Visceral Fat Area: A Single-Center Experience

### Abstract

**Introduction:** Visceral fat area (VFA) is known to increase after initiation of peritoneal dialysis (PD). However, the factors contributing to the increase in VFA in long-term PD patients have not been sufficiently elucidated. The present study investigated factors that affect VFA in patients who continue PD for  $\geq 3$  years. **Methods:** Twenty patients ( $63.1 \pm 10.3$  years, 9 men, 11 diabetic patients) between January 2008 and January 2015 were included. VFA, subcutaneous fat area (SFA) and waist circumference at initiation and follow-up were measured at the level of the umbilicus by computed tomography using an image analysis system. Change in VFA was defined as the value obtained by dividing VFA at the final follow-up by that at the initiation. The correlations between clinical parameters at initiation and changes in VFA were analyzed. **Results:** There was no significant change in body weight ( $57.6 \pm 10.4$  vs  $58.3 \pm 7.8$  kg,  $P = 0.296$ ) during the mean final follow-up period of  $55 \pm 13$  months, although VFA increased significantly ( $103.6 \pm 39.2$  vs  $122.6 \pm 38.3$  cm<sup>2</sup>,  $P = 0.030$ ). Although subcutaneous fat area (SFA) did not change ( $124.7 \pm 52.3$  vs  $124.5 \pm 49.2$  cm<sup>2</sup>,  $P = 0.989$ ), waist circumference increased significantly ( $79.4 \pm 8.4$  vs  $83.7 \pm 6.9$  cm,  $P = 0.010$ ). SFA ( $r = -0.735$ ,  $P < 0.001$ ), waist circumference ( $r = -0.644$ ,  $P = 0.002$ ), high-density lipoprotein cholesterol (HDL-C) ( $r = 0.487$ ,  $P = 0.029$ ), and age ( $r = 0.507$ ,  $P = 0.023$ ) correlated significantly with changes in VFA. **Conclusions:** VFA might increase with long-term PD in patients with end-stage kidney disease who have high HDL-C, small SFA, and small waist circumference at initiation.

**Keywords:** High-density lipoprotein cholesterol, peritoneal dialysis, subcutaneous fat area, visceral fat area, waist circumference

### Introduction

Visceral fat is reportedly strongly related to cardio-metabolic risk factors and insulin resistance and is a strong independent predictor of all-cause mortality in the general population.<sup>[1,2]</sup> In recent years, it has been revealed that an increase in visceral fat area (VFA) in Japanese hemodialysis patients is a strong risk factor for cardiovascular death.<sup>[3]</sup> Whereas the relationship between VFA and cardiovascular risk factors or diseases is recognized in Chinese peritoneal dialysis (PD) patients,<sup>[4]</sup> visceral obesity in PD patients is reportedly not a predictor of poor prognosis in Korean patients<sup>[5]</sup> and these relationships are not elucidated in Japanese PD patients. Thus, it is controversial as to whether visceral fat affects prognosis in Asian PD patients. In addition, the visceral fat increase in PD patients after initiation of therapy has been clarified in several studies,<sup>[6-8]</sup>

however, the observation period in these studies was as short as 3 years or less, and the factors contributing to the increase in VFA in long-term PD patients have not been sufficiently elucidated. Therefore, the present study investigated factors that affect the change in VFA of patients who continue PD for 3 or more years.

### Methods

Inclusion criteria of the study subjects were those who initiated PD at St. Marianna University School of Medicine Hospital, used glucose-based dialysis solutions or icodextrin, continued PD for  $\geq 3$  years, and underwent abdominal computed tomography (CT) (Aquilion 64, Prime, One vision edition; Toshiba Medical Systems, Tokyo, Japan). The CT tube voltage was 120 kV, and the tube current was adjusted by automatic exposure control, with a relative pitch of 0.813–0.828, rotation time of 0.5 s, and slice thickness of 0.5–7.0 mm. VFA, subcutaneous fat area (SFA), and

**Mari Ikeda,  
Kiyomi Osako,  
Shigeki Kojima,  
Kenichiro  
Koitabashi,  
Naohiko Imai,  
Yugo Shibagaki,  
Tsutomu Sakurada**

*Division of Nephrology and Hypertension, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan*

**Received:** 02-09-2019

**Revised:** 02-11-2019

**Accepted:** 23-12-2019

**Published:** 11-11-2020

### Address for correspondence:

*Dr. Mari Ikeda,  
Division of Nephrology and Hypertension, Department of Internal Medicine, St. Marianna University School of Medicine, 2-16-1 Sugao Miyamae-ku, Kawasaki, Kanagawa 216-8511, Japan.  
E-mail: mari\_602\_sunflower@yahoo.co.jp*

### Access this article online

**Website:** [www.indianj nephrol.org](http://www.indianj nephrol.org)

**DOI:** 10.4103/ijn.IJN\_297\_19

### Quick Response Code:



**How to cite this article:** Ikeda M, Osako K, Kojima S, Koitabashi K, Imai N, Shibagaki Y, *et al.* Effect of long-term peritoneal dialysis on change in visceral fat area: A single-center experience. *Indian J Nephrol* 2020;30:398-402.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**For reprints contact:** WKHLRPMedknow\_reprints@wolterskluwer.com

waist circumference at the time of initiation and follow-up was measured at the level of the umbilicus using an image analysis system (Ziostation2, ZIOSOFT Inc., Tokyo, Japan). The system was used at an attenuation range of -10 to -160 Hounsfield units to quantify abdominal fat area in cm<sup>2</sup>. Patients who were undergoing continuous cyclic or continuous ambulatory PD completely drained the dialysate prior to CT imaging. All patients were examined in the supine position during CT with both arms stretched above their heads. All measurements were performed by physicians who were unaware of the patients' laboratory data, identity, and demographic features. Age, sex, etiology of end-stage kidney disease, body weight, body mass index (BMI), presence of comorbidities (such as diabetes mellitus [DM], hypertension, and cardiovascular disease), and use of renin-angiotensin system (RAS) inhibitors were identified as baseline characteristics. Hemoglobin (Hb), serum albumin (Alb), serum creatinine (Cr), estimated glomerular filtration rate (eGFR), lipid profile (total cholesterol [TC], triglycerides [TG], low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C]), glycosylated hemoglobin (HbA1c), and C-reactive protein were investigated as blood biochemistry test results. eGFR was estimated using the following formula, as recommended by the JSN<sup>[9]</sup>:  $eGFR \text{ (mL/min/1.73 m}^2\text{)} = 194 \times Cr^{-1.094} \times age^{-0.287}$  ( $\times 0.739$  for women). Peritoneal equilibration tests developed by Twardowski<sup>[10]</sup> were performed 2–3 months after PD initiation. The dialysate-to-plasma creatinine concentration ratio at 4 h (D/P Cr) and the ratio of dialysate glucose concentration at 4 hours to baseline dialysate glucose concentration (D/D0 glu) were measured. Weekly Kt/V urea at initiation was calculated from a 24-hour collection of urine and dialysate as an indicator of dialysis adequacy. Normalized protein nitrogen appearance rate (nPNA) was also calculated from 24-hour dialysate and urine.<sup>[11]</sup> Change in VFA was defined as the value obtained by dividing VFA at the final follow-up by that at the initiation. The correlation between these clinical parameters at the initiation of PD and the changes in VFA were analyzed. This study was approved by the Ethics Committee of St. Marianna Medical University Hospital (approval no. 4075), with the need for informed consent waived due to its retrospective nature.

### Statistical analysis

Data were expressed as mean  $\pm$  standard deviation. Categorical variables were presented as frequencies or percentages. The Chi-square test was used for testing relationships between categorical variables. A paired t-test or Wilcoxon rank-sum test was used for comparisons of paired data, and the Spearman rank correlation test was used for correlations between continuous variables. A *P* value less than 0.05 was considered statistically significant. Statistical analyses were performed using the IBM SPSS Statistics

application for Windows (version 23.0: IBM Corp., Armonk, NY, USA).

### Results

The clinical characteristics of the study population at initiation and final follow-up of PD are shown in Table 1. The mean follow-up period by CT was  $55 \pm 13$  months. Of the 20 PD patients (mean age,  $63.1 \pm 10.3$  years) included, 45% were men and 55% had DM. Although there was no significant change in body weight ( $57.6 \pm 10.4$  vs  $58.3 \pm 7.8$  kg, *P* = 0.296), VFA increased significantly ( $103.6 \pm 39.2$  vs  $122.6 \pm 38.3$  cm<sup>2</sup>, *P* = 0.030), along with a significant increase in waist circumference ( $79.4 \pm 8.4$  vs  $83.7 \pm 6.9$  cm, *P* = 0.010), while SFA remained unchanged ( $124.7 \pm 52.3$  vs  $124.5 \pm 49.2$  cm<sup>2</sup>, *P* = 0.989). Hb, Cr, HbA1c, CRP, and nPNA were significantly elevated at the final follow-up compared to the initiation of PD. On the other hand, Alb was significantly decreased.

SFA (*r* = -0.735, *P* < 0.001) and waist circumference (*r* = -0.644, *P* = 0.002) were negatively correlated with VFA, HDL-C (*r* = 0.487, *P* = 0.029), and age (*r* = 0.507, *P* = 0.023) were positively correlated with VFA [Figure 1]. On the other hand, there were no correlations between changes in VFA and BMI, Hb, Alb, Cr, eGFR, TC, TG, LDL-C, HbA1c, D/P Cr, D/D0 glu, CRP, weekly Kt/V, and nPNA. In addition, there was no association between change in VFA and sex, presence of diabetes, cardiovascular disease, hypertension, etiology of end-stage kidney disease, and use of icodextrin or RAS inhibitors.

### Discussion

Fernström *et al.* were the first to report about the change in VFA using CT over time after initiation of PD.<sup>[6]</sup> They showed that VFA increased by 22.8% despite no change in body weight during follow-up of 7.2 months. Pellicano *et al.* also showed that VFA increased significantly after the initiation of PD during a 1-year observation period,<sup>[8]</sup> and Cho *et al.* reported that VFA increased significantly in the first year during a 3-year follow-up period.<sup>[7]</sup> However, they estimated VFA by bioelectrical impedance analysis rather than CT. In our study, although body weight did not change, VFA increased by approximately 18% at  $55 \pm 13$  months of final follow-up. Therefore, we believe that the increase in VFA is sustained in long-term PD patients.

Age, sex (male), and ethnicity (Asian population) are known unmodifiable factors that contribute to visceral adipose tissue accumulation in healthy populations.<sup>[12]</sup> In addition, DM, atherogenic dyslipidemia, cardiovascular disease, hypertension, cancer, sleep apnea syndrome, and metabolic syndrome are also associated with visceral fat accumulation, as are nutritional factors and low physical activity.<sup>[12]</sup> Continuous intraperitoneal glucose exposure with PD is said to be responsible for body fat accumulation.<sup>[13]</sup> In addition, the level of physical activity,

**Table 1: Clinical characteristics of the study population**

Variables	Baseline	Follow-up	P
Age (years)	63.1±10.3	NA	
Male, n (%)	9 (45)	NA	
Chronic glomerulonephritis, n (%)	7 (35)		
Diabetic nephropathy, n (%)	10 (50)		
Others, n (%)	3 (15)		
Body weight (kg)	57.6±10.4	58.3±7.8	0.296
Body mass index (kg/m <sup>2</sup> )	22.4±2.6	23.2±2.9	0.156
Diabetes mellitus, n (%)	11 (55)	NA	
Hypertension, n (%)	18 (90)	NA	
Renin-angiotensin system inhibitors, n (%)	14 (70)	NA	
Cardiovascular disease, n (%)	7 (35)	NA	
Use of icodextrin, n (%)	7 (35)	NA	
Hemoglobin (g/dL)	9.7±1.5	10.7±1.1	0.041
Albumin (g/dL)	3.9±0.5	3.4±0.6	<0.001
Creatinine (mg/dL)	7.38±2.05	8.90±2.54	0.008
eGFR (mL/min/1.73 m <sup>2</sup> )	6.1±1.6	NA	
Total cholesterol (mg/dL)	185±48	183±32	0.835
Triglyceride (mg/dL)	158±109	168±88	0.597
Low-density lipoprotein cholesterol (mg/dL)	99±32	96±26	0.548
High-density lipoprotein cholesterol (mg/dL)	51±27	47±17	0.940
Glycosylated hemoglobin (%)	5.3±0.5	5.6±0.7	0.028
C-reactive protein (mg/dL)	0.36±1.12	1.65±3.24	0.017
Weekly Kt/V	1.84±0.44	2.05±0.34	0.104
D/P Cr	0.60±0.11	0.66±0.12	0.191
D/D0 Glu	0.41±0.09	0.45±0.11	0.204
nPNA (g/kg/day)	0.89±0.19	1.01±0.20	0.020

eGFR: Estimated glomerular filtration rate, D/P Cr: The dialysate-to-plasma creatinine concentration ratio at 4 h, D/D0 glu: Ratio of dialysate glucose concentration at 4 h to baseline dialysate glucose concentration, nPNA: Normalized protein nitrogen appearance rate, NA: Not applicable

evaluated as the step count, is low in PD patients,<sup>[14]</sup> which might also contribute to the increase in VFA. Age, BMI, HbA1c, use of RAS inhibitors, and serum creatinine level are independent determinants of visceral fat in non-diabetic PD patients.<sup>[15]</sup> In our study, the change in VFA showed a positive correlation with age and HDL-C, while it was negatively correlated with waist circumference and SFA. Also, there was no correlation between VFA and sex, BMI, HbA1c, serum creatinine, and RAS inhibitor usage. We believe that the lack of a correlation between VFA and HbA1c or BMI in our study was because our patients had good blood glucose and lipid control.

Lupattelli *et al.* reported that low HDL cholesterol is not associated with increasing VFA.<sup>[16]</sup> On the other hand, Matsuo *et al.* suggested that the change in VFA might be associated with a change in HDL-C.<sup>[17]</sup> PD patients have high TC, LDL-C and TG, and low HDL-C as compared with healthy subjects.<sup>[18]</sup> Furthermore, it has been reported that the decrease in HDL-C correlates with the rate of decline in residual kidney function in PD patients.<sup>[19]</sup> We speculated that HDL gradually declines after the initiation of PD, with a concurrent increase in VFA. Huang *et al.* showed that D/D0 glu correlated negatively with adiponectin levels in PD patients.<sup>[20]</sup> Although it has been

suggested that adiponectin is associated with visceral fat, we found no correlation between D/D0 glu and VFA.

The present study has some limitations. First, it was a retrospective observational study with small sample size. Second, the follow-up period of VFA was not consistent in all patients. Third, we did not consider treatment intervention (DM, dyslipidemia, etc.) from the initiation of PD to the follow-up period. Furthermore, we did not consider long-term continuous intraperitoneal glucose exposure by PD. To further investigate the factors related to VFA in the future, a prospective multicenter collaborative study with the registration of a large number of PD patients will be needed. Also, the primary purpose of this study was to clarify the risk factor contributing to the increase in VFAs and was not to investigate its association with clinical events. Further studies are needed to clarify its association.

## Conclusions

VFA might increase with long-term PD in elderly patients with end-stage kidney disease who have high HDL cholesterol at the time of initiation, small SFA, and small waist circumference. These patients might require diet and exercise therapy to prevent the increase in VFAs.

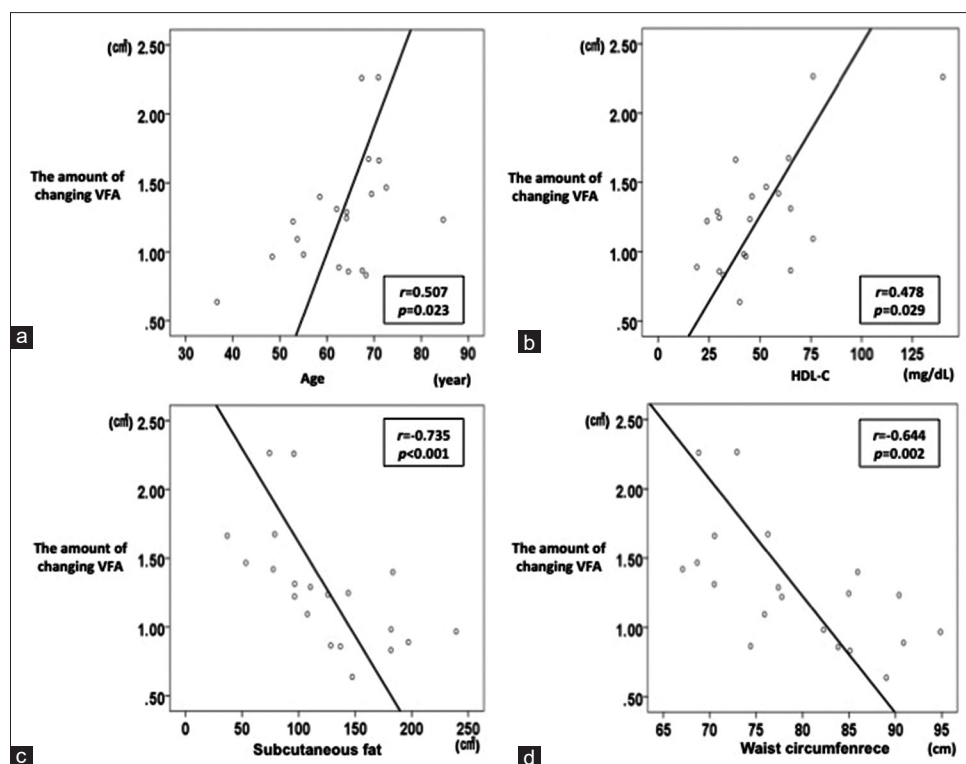


Figure 1: Correlation between visceral fat area and characteristics of patients on peritoneal dialysis. (a) Age, (b) high-density lipoprotein cholesterol, (c) subcutaneous fat area, (d) waist circumference

Further studies are needed to evaluate whether VFA affects prognosis in long-term PD patients.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

### References

- Kuk JL, Katzmarzyk PT, Nichaman MZ, Church TS, Blair SN, Ross R. Visceral fat is an independent predictor of all-cause mortality in men. *Obesity (Silver Spring)* 2006;14:336-41.
- Després JP, Lemieux I. Abdominal obesity and metabolic syndrome. *Nature* 2006;444:881-7.
- Okamoto T, Morimoto S, Ikenoue T, Furumatsu Y, Ichihara A. Visceral fat level is an independent risk factor for cardiovascular mortality in hemodialysis patients. *Am J Nephrol* 2014;39:122-9.
- Lu Q, Cheng LT, Wang T, Wan J, Liao LL, Zeng J, et al. Visceral fat, arterial stiffness, and endothelial function in peritoneal dialysis patients. *J Ren Nutr* 2008;18:495-502.
- Choi SJ, Kim EJ, Park MY, Kim JK, Hwang SD. Does body fat mass define survival in patients starting peritoneal dialysis? *Perit Dial Int* 2014;34:376-82.
- Fernström A, Hylander B, Moritz A, Jacobsson H, Rössner S. Increase of intra-abdominal fat in patients treated with continuous ambulatory peritoneal dialysis. *Perit Dial Int* 1998;18:166-71.
- Cho KH, Do JY, Park JW, Yoon KW. Effect of icodextrin dialysis solution on body weight and fat accumulation over time in CAPD patients. *Nephrol Dial Transplant* 2010;25:593-9.
- Pellicano R, Strauss BJ, Polkinghorne KR, Kerr PG. Longitudinal body composition changes due to dialysis. *Clin J Am Soc Nephrol* 2011;6:1668-75.
- Matsuo S, Imai E, Horio M, Yasuda Y, Tomita K, Nitta K, et al. Revised equations for estimated GFR from serum creatinine in Japan. *Am J Kidney Dis* 2009;53:982-92.
- Twardowski ZJ, Khanna R, Nolph KD. Peritoneal equilibration test. *Perit Dial Bull* 1987;7:138-47.
- Bergström J, Heimbürger O, Lindholm B. Calculation of the protein equivalent of total nitrogen appearance from urea appearance. Which formulas should be used? *Perit Dial Int* 1998;18:467-73.
- Tchernof A, Després JP. Pathophysiology of human visceral obesity: An update. *Physiol Rev* 2013;93:359-404.
- Gokal R, Moberly J, Lindholm B, Mujais S. Metabolic and laboratory effects of icodextrin. *Kidney Int Suppl* 2002;62(Suppl 81):S62-71.
- Oishi D, Koitabashi K, Hiraki K, Imai N, Sakurada T, Konno Y, et al. Physical activity is associated with serum albumin in peritoneal dialysis patients. *Adv Perit Dial* 2012;28:148-52.
- Ho LC, Yen CJ, Chao CT, Chiang CK, Huang JW, Hung KY. Visceral fat area is associated with HbA1c but not dialysate-related glucose load in nondiabetic PD patients. *Sci Rep* 2015;5:12811.

16. Lupattelli G, Pirro M, Mannarino MR, Siepi D, Roscini AR, Schillaci G, *et al.* Visceral fat positively correlates with cholesterol synthesis in dyslipidaemic patients. *Eur J Clin Invest* 2012;42:164-70.
17. Matsuo T, Kato Y, Murotake Y, Kim MK, Unno H, Tanaka K. An increase in high-density lipoprotein cholesterol after weight loss intervention is associated with long-term maintenance of reduced visceral abdominal fat. *Int J Obes (Lond)* 2010;34:1742-51.
18. Johansson AC, Samuelsson O, Attman PO, Haraldsson B, Moberly J, Knight-Gibson C, *et al.* Dyslipidemia in peritoneal dialysis--relation to dialytic variables. *Perit Dial Int* 2000;20:306-14.
19. Chen HY, Kao TW, Huang JW, Tsai TJ, Wu KD. Association between dyslipidemia and residual renal function in patients on chronic peritoneal dialysis. *Clin Nephrol* 2008;70:233-9.
20. Huang JW, Yen CJ, Chiang HW, Hung KY, Tsai TJ, Wu KD. Adiponectin in peritoneal dialysis patients: A comparison with hemodialysis patients and subjects with normal renal function. *Am J Kidney Dis* 2004;43:1047-55.