

**Original Article: Clinical Investigation****Excessive accumulation of visceral fat is associated with lower urinary symptoms including overactive bladder in female patients**

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**Abbreviations & Acronyms**

AC = abdominal circumference  
BMI = body mass index  
CI = confidence interval  
CT = computed tomography  
LUTS = lower urinary tract symptoms  
MetS = metabolic syndrome  
OAB = overactive bladder  
OABSS = Overactive Bladder Symptom Score  
OR = odds ratio  
PVR = post-void residual  
 $Q_{\max}$  = maximum flow rate  
QOL = quality of life  
SD = standard deviation  
SFA = subcutaneous fat area  
SFV = subcutaneous fat volume  
TAV = total abdominal fat volume  
UTI = urinary tract infection  
VFA = visceral fat area  
VFV = visceral fat volume

**Objective:** To assess the relationship between visceral fat accumulation and lower urinary tract symptoms in female patients.

**Methods:** In this single-center study, we enrolled all women who underwent screening abdominal computed tomography 3 months before the study, irrespective of whether they experienced lower urinary tract symptoms. The Overactive Bladder Symptom Score was used to assess subjective symptoms. Uroflowmetry and ultrasound assessment of post-void residual urine were carried out to assess objective signs. We analyzed the relationship between lower urinary tract symptoms and various body fat accumulation parameters, including visceral fat area, visceral fat volume and total abdominal fat volume, assessed using computed tomography scans.

**Results:** A total of 182 patients were divided into the overactive bladder ( $n = 71$ , 39.0%) and the non-overactive bladder ( $n = 111$ , 61.0%) groups. The visceral fat area, visceral fat volume and visceral fat volume/total abdominal fat volume values were all significantly higher in the overactive bladder group than in the non-overactive bladder group ( $P < 0.001$ ). Of these parameters, the visceral fat volume/total abdominal fat volume ratio showed the strongest correlation with the total Overactive Bladder Symptom Score ( $r = 0.394$ ,  $P < 0.001$ ). The maximum urine flow rate correlated negatively with the visceral fat volume/total abdominal fat volume value (visceral fat volume/total abdominal fat volume  $r = -0.289$ ,  $P < 0.001$ ). Subsequent multivariate analysis showed that a high visceral fat volume/total abdominal fat volume value, age and metabolic syndrome-related diseases were independent risk factors for the presence of overactive bladder.

**Conclusions:** Excessive accumulation of visceral fat is independently associated with overactive bladder in females.

**Key words:** lower urinary tract symptoms, overactive bladder, visceral fat.

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**Introduction**

OAB is defined as a syndrome characterized by the symptom of urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of UTI or other obvious pathology.<sup>1</sup> Worldwide, individuals diagnosed with OAB also suffer from urgency and experience other concomitant LUTS. An epidemiological survey estimated that 8.1 million people (prevalence, 12.4%) are affected by OAB in Japan.<sup>2</sup> Furthermore, it is widely known that LUTS, including OAB, can significantly impair the QOL of affected patients.

Many recent studies have shown that MetS and lifestyle-related diseases are closely associated with OAB.<sup>3–5</sup> Likewise, many researchers have also reported that obesity-related, excessive fat accumulation in the body is strongly associated with the occurrence of LUTS, including those associated with OAB.<sup>6,7</sup> Interestingly, an increase in abdominal visceral fat induces abnormal secretion of adipocytokines, promotes excessive production of various inflammatory cytokines and further leads to chronic systemic inflammation.<sup>8,9</sup> Furthermore, these factors might finally contribute to the development of MetS, which includes hypertension, hyperglycemia and dyslipidemia, associated with an excessive increase in body fat.<sup>10</sup>

Chronic and widespread systemic inflammation caused by MetS and other lifestyle-related diseases are important factors associated with OAB and other LUTS.<sup>6,7</sup>

Thus, a wide variety of available information supports the pathological significance of excessive visceral fat accumulation, which is the strongest trigger for MetS and is an essential aspect of any discussion on the pathogenesis of urinary dysfunction, including OAB and related treatment strategies. However, no studies have investigated the correlation between excessive accumulation of visceral fat and the presence and severity of OAB. Therefore, we carried out the present study with the aim to clarify the relationship between urinary disorders and visceral fat accumulation in patients with LUTS, including OAB.

## Methods

### Patient selection

In this single-center study, we enrolled women who underwent an abdominal CT scan as a screening test in a physical checkup during the 3-month period before the onset of the study, irrespective of whether or not they had been identified to have LUTS. Exclusion criteria were as follows: (i) patients with a PVR urine volume of  $\geq 100$  mL; (ii) those with a history of urinary retention; (iii) those already diagnosed with neurogenic bladder, urethral stricture, bladder stones, pelvic organ prolapse, renal insufficiency (glomerular filtration rate  $< 30$  mL/min/1.73 m<sup>2</sup>), liver impairment, urological malignancy or an active UTI; (iv) those receiving treatment with any antimuscarinic agent, a  $\beta 3$  adrenergic receptor agonist or an  $\alpha 1$  adrenal receptor antagonist; and (v) those found to be unsuitable for inclusion in the trial by the treating physicians. Furthermore, male patients were excluded, considering the confounding effect of bladder neck obstruction occurring secondarily to benign prostatic hyperplasia. The study was approved by the appropriate ethics review board of Nagasaki University Hospital, Nagasaki, Japan (No. 11120266).

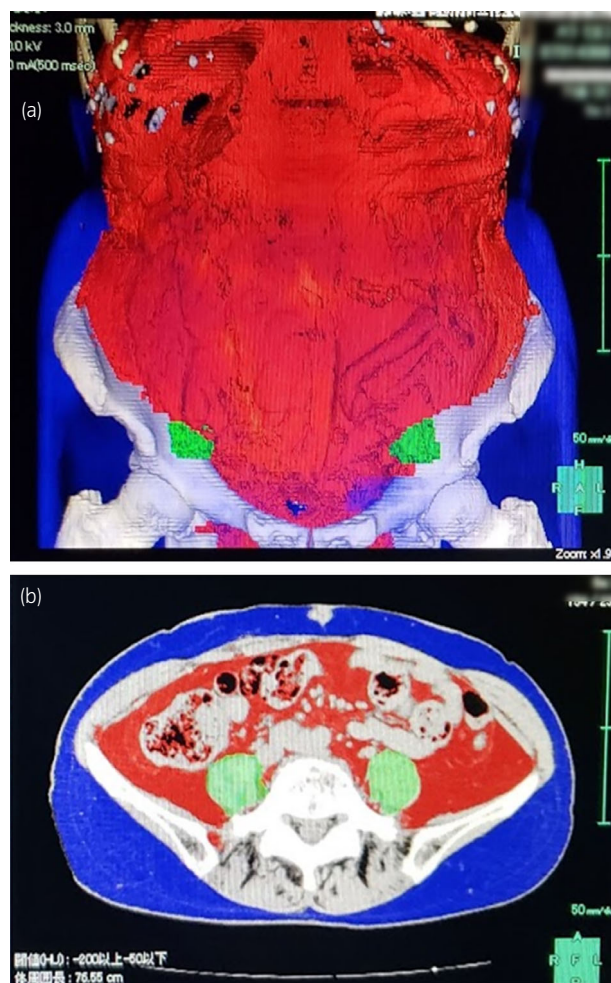
### Evaluation of urinary conditions and visceral fat status

We used the OABSS for assessment and grading of subjective symptoms. Patients were objectively assessed using uroflowmetry (Duet Logic G2 system; Mediwatch UK, Rugby, UK). The PVR was measured by ultrasound examination (Hi VISION Avius; Hitachi Medical Corporation, Tokyo, Japan). On the basis of the OABSS system, we defined participants with a urinary urgency (Question [Q] 3) score of  $\geq 2$  and those with a total score of  $\geq 3$  as having OAB. Furthermore, the relationship between LUTS and various parameters, including VFA, VFV, SFA, SFV and TAV (that is, VFV + SFV), were analyzed. Values of these parameters were estimated using abdominal CT scans. The AC, VFA and SFA were measured using scans of the umbilical section taken in the end-tidal position on an empty stomach, as described in an earlier study.<sup>11</sup> We carried out estimations of VFV and SFV from the diaphragm to the pelvic floor.<sup>12</sup> All body fat measurements were calculated using a 3-D image

analysis system (SYNAPSE VINCENT; Fujifilm, Tokyo, Japan; Fig. 1).

### Statistical analysis

Study patients were divided into two groups according to the presence or absence of OAB to comparatively evaluate the relationship between OABSS and body fat accumulation between both groups. We also studied the relationship between the existing mass of body fat in the patients and the occurrence of both subjective urinary symptoms and related objective signs. We used multivariate analysis to examine whether fat accumulation in the body could be a predictor of OAB. All data are expressed as the mean  $\pm$  SD. The Student's *t*-test and the  $\chi^2$ -test were used for comparing parametric continuous and categorical variables, respectively. Pearson's correlation and the correlation coefficient (*r*) were used to evaluate the relationship between continuous variables and determine corresponding *P*-values. Crude and adjusted effects were estimated using logistic regression



**Fig. 1** CT images used to measure body fat accumulation. The red area represents visceral fat and the blue area represents subcutaneous fat. (a) The range from diaphragm to pelvic floor: VFV and SFV. (b) Umbilical section: AC, VFA and SFA.

analysis and represented as OR with 95% CI along with *P*-values. In the present study, the statistically significant level of the *P*-value was defined as  $<0.050$ . All statistical tests were carried out using the JMP version 14 (SAS Institute, Cary, NC, USA) software. The study protocol was approved by the Clinical Study Review Board of the center at which the study was carried out. All procedures were carried out in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients who participated in the study.

## Results

A total of 182 female patients were enrolled, and they were divided into two groups: non-OAB ( $n = 111$ , 61.0%) and OAB ( $n = 71$ , 39.0%). As shown in Table 1, the mean age of the OAB group ( $65.5 \pm 12.6$  years) was significantly higher ( $P < 0.001$ ) than that of the non-OAB group ( $52.7 \pm 14.8$  years). The proportion of patients with lifestyle-related comorbidities was also significantly higher in the OAB group than in the non-OAB group (hypertension 40.9% vs 15.3%; hyperlipidemia 21.1% vs 8.1%; renal dysfunction 27.5% vs 19.8%). However, there were no significant differences between both groups with respect to BMI (non-OAB  $21.9 \pm 3.1$  kg/m<sup>2</sup>; OAB  $23.1 \pm 5.3$  kg/m<sup>2</sup>;  $P = 0.071$ ) and the prevalence of diabetes mellitus (non-OAB 3.6%; OAB 11.3%;  $P = 0.064$ ). A comparative assessment of subjective symptoms between both groups showed that all subscale and total scores estimated using the OABSS questionnaire were higher in the OAB group than in the non-OAB group. Comparative assessment of objective signs showed that both the voided volume and maximal flow rate of urine were lower in the OAB group than in the non-OAB group (voided volume,  $P < 0.001$ ;  $Q_{\max}$ ,  $P < 0.001$ ; Table 1).

Table 2 summarizes the differences in the values of AC and parameters indicative of visceral fat accumulation between both study groups. OAB and non-OAB participants did not differ significantly with respect to parameters including AC ( $P = 0.145$ ), SFA ( $P = 0.714$ ), SFV ( $P = 0.882$ ) and TAV ( $P = 0.097$ ). However, significantly higher values were shown by the OAB group participants than their non-OAB counterparts for body fat parameters, including VFA ( $P < 0.001$ ), VFV ( $P < 0.001$ ), VFA/SFA ( $P = 0.014$ ), VFV/SFV ( $P < 0.001$ ) and VFV/TAV ( $P < 0.001$ ). Conversely, the SFV/TAV ratio estimated in the OAB group was lower than that calculated in the non-OAB group ( $P < 0.001$ ). In addition, participants were divided into three groups according to their total OABSS (i.e. the absence of OAB, non-OAB; 3–5 points, mild OAB; 6–15 points, moderate/severe OAB; Table 3). Similar to the results shown in Table 2, there were statistically significant differences between the group without OAB and the groups with OAB, including VFV. However, no significant difference was found between the groups with OAB (Table 3).

We found no statistically significant correlation between total OABSS and parameters including AC, BMI, SFA, SFV, VFA and TAV. However, a significant positive correlation with OABSS was shown by parameters specifically indicative of visceral fat accumulation, including VFV, VFA/SFA, VFV/SFV and VFV/TAV. Conversely, a significantly negative correlation was observed between total OABSS and the SFV/TAV ratio. The correlation between the VFV/TAV ratio and the total OABSS was found to be the strongest (Table 4). When plotting a receiver operating characteristic curve to assess the suitability of using the VFV/TAV value to assess the presence or absence of OAB, the area under the curve was found to be 0.742 ( $P < 0.001$ ). With a cut-off value set to 0.381, the VFV/TAV ratio showed a sensitivity and

**Table 1** Patient characteristics

	Entire	Non-OAB	OAB	<i>P</i> -value
No. patients (%)	182 (100)	111 (61.0)	71 (39.0)	–
Age (years)	$57.7 \pm 15.3$	$52.7 \pm 14.8$	$65.5 \pm 12.6$	$<0.001$
BMI (kg/m <sup>2</sup> )	$22.4 \pm 4.2$	$21.9 \pm 3.1$	$23.1 \pm 5.3$	0.071
<18.5 kg/m <sup>2</sup> (%)	32 (17.6)	18 (16.2)	14 (19.7)	0.148
18.5 to <25 kg/m <sup>2</sup> (%)	115 (63.2)	76 (68.5)	39 (54.9)	
$\geq 25$ kg/m <sup>2</sup> (%)	35 (19.2)	17 (15.3)	18 (25.4)	
Comorbidities				
Hypertension (%)	46 (25.3)	17 (15.3)	29 (40.9)	$<0.001$
Diabetes mellitus (%)	12 (6.6)	4 (3.6)	8 (11.3)	0.064
Hyperlipidemia (%)	24 (13.2)	9 (8.1)	15 (21.1)	0.001
Renal dysfunction (%)	50 (27.5)	22 (19.8)	28 (27.5)	0.006
OABSS				
Q1 daytime frequency	$0.3 \pm 0.6$	$0.2 \pm 0.5$	$0.5 \pm 0.7$	$<0.001$
Q2 nocturia	$1.2 \pm 1.0$	$0.7 \pm 0.8$	$1.9 \pm 0.9$	$<0.001$
Q3 urgency	$1.2 \pm 1.4$	$0.2 \pm 0.4$	$2.7 \pm 0.9$	$<0.001$
Q4 urgency incontinence	$0.4 \pm 1.0$	$0.1 \pm 0.4$	$1.0 \pm 1.4$	$<0.001$
Total OABSS	$3.2 \pm 3.1$	$1.3 \pm 1.4$	$6.2 \pm 2.6$	$<0.001$
Uroflowmetry				
Voided volume (mL)	$207.3 \pm 109.7$	$232.8 \pm 115.7$	$167.4 \pm 86.2$	$<0.001$
$Q_{\max}$ (mL/s)	$18.4 \pm 9.6$	$20.3 \pm 9.9$	$15.5 \pm 8.4$	$<0.001$
PVR (mL)	$28.8 \pm 39.7$	$30.8 \pm 44.7$	$25.7 \pm 30.4$	0.401

**Table 2** Body fat accumulation

	Entire	Non-OAB	OAB	P-value
AC (cm)	81.6 ± 9.7	80.8 ± 7.6	82.9 ± 12.2	0.145
SFA (cm <sup>2</sup> )	150.0 ± 74.8	151.6 ± 67.7	147.4 ± 85.2	0.714
SFV (cm <sup>3</sup> )	3701.9 ± 1927.2	3718.9 ± 1650.4	3675.3 ± 2307.0	0.882
VFA (cm <sup>2</sup> )	79.2 ± 49.9	69.4 ± 39.3	94.7 ± 60.2	<0.001
VFV (cm <sup>3</sup> )	2022.6 ± 1371.1	1705.6 ± 1009.8	2518.2 ± 1688.1	<0.001
TAV (cm <sup>3</sup> )	5724.5 ± 3051.8	5424.5 ± 2440.3	6193.5 ± 3789.3	0.097
VFA/SFA	0.68 ± 1.39	0.48 ± 0.22	1.00 ± 2.17	0.014
VFV/SFV	0.61 ± 0.59	0.47 ± 0.21	0.84 ± 0.87	<0.001
SFV/TAV	0.65 ± 0.12	0.69 ± 0.09	0.59 ± 0.13	<0.001
VFV/TAV	0.35 ± 0.12	0.31 ± 0.09	0.41 ± 0.13	<0.001

**Table 3** Differences of body fat accumulation among the severity of OAB

	Non-OAB	OAB mild	OAB moderate/severe	P-value
No. patients	111	35	36	–
AC (cm)	80.8 ± 7.6	83.8 ± 8.0	82.1 ± 15.3	0.260
SFA (cm <sup>2</sup> )	151.6 ± 67.7	154.5 ± 59.1	140.5 ± 105.0	0.689
SFV (cm <sup>3</sup> )	3718.9 ± 1650.4	3868.4 ± 1917.4	3487.6 ± 2645.7	0.702
VFA (cm <sup>2</sup> )	69.4 ± 39.3	104.1 ± 49.1**	85.5 ± 68.8**	<0.001
VFV (cm <sup>3</sup> )	1705.6 ± 1009.8	2635.2 ± 1311.5**	2404.5 ± 2000.4*	<0.001
TAV (cm <sup>3</sup> )	5424.5 ± 2440.3	6503.6 ± 3003.0	5892.0 ± 4446.0	0.178
VFA/SFA	0.48 ± 0.22	0.70 ± 0.27	1.30 ± 3.04*	0.009
VFV/SFV	0.47 ± 0.21	0.71 ± 0.27*	0.96 ± 1.19**	<0.001
SFV/TAV	0.69 ± 0.09	0.60 ± 0.09**	0.59 ± 0.15**	<0.001
VFV/TAV	0.31 ± 0.09	0.40 ± 0.09**	0.41 ± 0.16**	<0.001

\* $P < 0.05$  versus non-OAB. \*\* $P < 0.001$  versus non-OAB.

**Table 4** Body fat accumulation and OAB symptom score

	<i>r</i>	P-value
AC (cm)	0.053	0.477
BMI (kg/m <sup>2</sup> )	0.082	0.273
SFA (cm <sup>2</sup> )	−0.081	0.277
SFV (cm <sup>3</sup> )	−0.078	0.295
VFA (cm <sup>2</sup> )	0.125	0.092
VFV (cm <sup>3</sup> )	0.191	0.010
TAV (cm <sup>3</sup> )	0.037	0.624
VFA/SFA	0.269	<0.001
VFV/SFV	0.330	<0.001
SFV/TAV	−0.394	<0.001
VFV/TAV	0.394	<0.001

**Table 5** Relationship between objective findings and body fat accumulation

	Voided volume		$Q_{\max}$		PVR	
	<i>r</i>	P-value	<i>r</i>	P-value	<i>r</i>	P-value
AC (cm)	−0.150	0.044	−0.005	0.819	−0.052	0.488
BMI (kg/m <sup>2</sup> )	−0.245	<0.001	−0.088	<0.001	−0.093	0.211
SFA (cm <sup>2</sup> )	−0.029	0.695	0.022	0.765	−0.092	0.216
SFV (cm <sup>3</sup> )	−0.051	0.493	0.016	0.826	−0.060	0.422
VFA (cm <sup>2</sup> )	−0.300	<0.001	−0.248	<0.001	−0.088	0.236
VFV (cm <sup>3</sup> )	−0.304	<0.001	−0.210	0.004	−0.089	0.235
TAV (cm <sup>3</sup> )	−0.169	0.023	−0.084	0.259	−0.078	0.298
VFA/SFA	−0.101	0.176	−0.154	0.038	0.100	0.183
VFV/SFV	−0.158	0.033	−0.209	0.005	0.178	0.016
SFV/TAV	0.291	<0.001	0.289	<0.001	0.040	0.588
VFV/TAV	−0.291	<0.001	−0.289	<0.001	−0.040	0.588

specificity of 0.563 and 0.811, respectively, for detecting OAB (data not shown). Of all body fat accumulation parameters assessed in the present study, VFV and the VFV/TAV ratio showed the strongest negative correlation with voided volume and  $Q_{\max}$  of urine, respectively. Furthermore, a statistically significant relationship was observed between VFV/SFV and PVR (Table 5).

Based on these aforementioned findings, we carried out multivariate analyses to verify the impact of independent variables found to be significant in the univariate analysis on the presence of OAB (Table 6). Multivariate analysis showed

that the VFV/TAV ratio, the patient's age and the MetS-related condition (including hypertension, diabetes mellitus, hyperlipidemia and renal dysfunction) were independent risk factors associated with OAB (VFV/TAV OR 3.79, 95% CI 1.87–7.80,  $P < 0.001$ ; patients' age OR 1.02, 95% CI 1.01–1.03,  $P = 0.044$ ; MetS-related condition OR 2.91, 95% CI 1.47–5.78,  $P = 0.002$ , respectively). Conversely, BMI and AC were not found to be risk factors for OAB in the present study (Table 6).



**Table 6** Univariate and multivariate analysis for OAB

	Univariate analysis			Multivariate analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Age	1.07	1.09–1.10	<0.001	1.02	1.01–1.03	0.044
BMI	1.07	0.87–1.01	0.072	–	–	–
AC	1.10	0.95–1.01	0.144	–	–	–
VFV/TAV	7.04	3.34–12.5	<0.001	3.79	1.87–7.80	<0.001
MetS-related diseases	4.25	2.26–8.02	<0.001	2.91	1.47–5.78	0.002

## Discussion

The present study investigated the relationship between parameters denoting the level of body fat accumulation, which were assessed using CT and a 3-D image analysis system, and the presence and severity of urinary symptoms associated with OAB. A comparative analysis of relevant parameters was carried out between patients with OAB and those without the disorder. A significantly higher proportion of patients in the OAB group presented with systemic comorbidities, including hypertension and dyslipidemia, which are the components of MetS, than those in non-OAB group. Furthermore, although the amount of subcutaneous fat did not correlate with the presence of OAB, parameters of visceral fat accumulation, especially the VFV level and the VFV/TAV ratio, correlated not only with reported subjective symptoms, but also with objective examination findings, including voided volume and  $Q_{\max}$  of urine in affected patients. Finally, the VFV/TAV ratio was found to be a significant, possibly predictive, factor for OAB in the present study.

Although BMI tended to be slightly higher in the OAB group, the two groups did not differ significantly with respect to this parameter. Obese people are considered to be at a higher risk of developing OAB than non-obese individuals.<sup>6,7</sup> However, it should be noted that a large-scale epidemiological study reported that BMI did not always show a positive association with OAB. Although OAB showed a decreased presence in individuals with a BMI level  $<27.5 \text{ kg/m}^2$ , the rate of occurrence of related symptoms increased when its value was  $\geq 27.5 \text{ kg/m}^2$ .<sup>13</sup> Another study carried out in Japan also reported a lower correlation between LUTS and obesity defined according to BMI values.<sup>14</sup> Furthermore, although Ikeda *et al.* showed a relationship between obesity, as indicated by the BMI level and LUTS, it was observed in Japanese patients aged  $\geq 70$  years.<sup>15</sup> In the present study, the lack of association between OAB symptoms and BMI might be attributed to the relatively lower mean value of the latter parameter ( $22.4 \pm 4.2 \text{ kg/m}^2$ ) and the inclusion of comparatively younger patients ( $57.7 \pm 15.3$  years). There is a general agreement that so-called “hidden obesity” can only be diagnosed to a limited extent using just BMI estimation. Patients who suffer from MetS and show excessive visceral fat accumulation are known to experience related comorbidities, despite having BMI levels that do not meet obesity criteria. Asians, including the Japanese, differ vastly from the Western population in skeletal structure and body

composition, and OAB is found to present even in younger people. In particular, a meta-analysis including Japanese men and women showed that, regardless of sex, Japanese participants were more likely to accumulate visceral fat than Western participants, even in people with the same BMI.<sup>16</sup> In addition, the study found that the Japanese participants had high visceral fat accumulation, even after adjusting for age, sex and SFV.<sup>16</sup> Therefore, we want to emphasize that a study of the relationship between obesity defined using only BMI and LUTS, such as OAB, might be ineffectual, especially in younger Japanese patients.

In the present study, we measured the volume of visceral fat to evaluate its correlation to the presence of OAB. The methods for estimation of visceral fat levels included AC measurement, impedance analysis, CT scanning and magnetic resonance imaging. In Japan, the cut-off values for visceral fat accumulation, as denoted by AC, are set at  $\geq 85 \text{ cm}$  and  $\geq 90 \text{ cm}$  for men and women, respectively.<sup>17</sup> This cut-off is considered to correspond to  $100 \text{ cm}^2$  VFA at the umbilical level on CT.<sup>17</sup> The cut-off was determined based on the finding of a higher risk of occurrence of complications including hypertension, hyperglycemia and dyslipidemia, which are components of MetS, when VFA  $\geq 100 \text{ cm}^2$ .<sup>18</sup> However, studies involving Japanese patients, especially women, showed that VFA was not found to correlate with AC. An AC of  $90 \text{ cm}$  corresponded to a VFA of only approximately  $65 \text{ cm}^2$ .<sup>19,20</sup> Therefore, it might be difficult to accurately estimate the visceral fat mass by measuring the AC. In the present study, we measured visceral fat using CT for the following reasons. First, the Japanese are more likely to experience accumulation of visceral fat (than subcutaneous fat) in comparison with their Western counterparts.<sup>16,20</sup> The recent Westernization of the Japanese diet might have contributed to this trend. Second, we wanted to evaluate the degree of fat accumulation with higher accuracy to ensure validity of the study findings.

Many epidemiological studies have reported a strong association between OAB and MetS and other lifestyle-related diseases, which are caused by excessive accumulation of visceral fat. The detailed mechanisms have been elucidated by various basic studies. Abnormally excessive secretion of adipocytokines, such as tumor necrosis factor- $\alpha$ , free fatty acids, monocyte chemoattractant protein-1 and plasminogen activator inhibitor-1, leads to the development of insulin resistance. This is, in turn, considered to trigger hypertension, diabetes and dyslipidemia.<sup>10</sup> Reportedly, insulin resistance acquired secondarily to excessive accumulation of visceral fat

leads to chronic sympathetic hyperactivity and ischemia of the lower urinary tract.<sup>21</sup>

In the present study, we found that the OAB group showed higher levels of visceral fat (VFA, VFV) accumulation than that observed in the non-OAB group. However, the two groups did not significantly differ with respect to subcutaneous fat (SFA, SFV) levels. Among all visceral fat accumulation parameters assessed in the study, the VFV/TAV ratio showed the strongest positive correlation with the total OAB score. Furthermore, the present study showed that the VFV/TAV ratio, the patient's age, and the presence of MetS-related conditions were significant and independent predictive factors for OAB. Therefore, excessive accumulation of visceral fat is a risk factor that might directly or indirectly influence the onset of OAB, as described in previous reports.<sup>22</sup> The exact mechanism of the relationship between obesity and OAB is not fully understood. However, some researchers have reported that excess bodyweight and visceral fat increase intra-abdominal pressure that, in turn, increases bladder pressure and intravesical pressure, leading to excessive bladder activity.<sup>22–24</sup> This is thought to be a direct outcome caused by the excessive visceral fat mechanically compressing the bladder. In the present study, objective signs of OAB including  $Q_{\max}$  and voided volume of urine were both correlated with the level of visceral fat accumulation. The VFV/TAV ratio showed the strongest negative correlation with the maximum urine flow rate. The reasons for the effect of excessive body fat accumulation on the objective signs associated with OAB remain unclear, because we did not carry out the pressure flow study in this study. However, oxidative stress and chronic ischemia play important roles in urinary dysfunction.<sup>25,26</sup> In addition, basic research on the topic has shown that, while oxidative stress and inflammatory cytokines due to excessive body fat accumulation can lead to detrusor overactivity, when bladder ischemia is severe, detrusor contraction decreases.<sup>27–29</sup> In addition, OAB occurring over a long period of time, due to inflammation and detrusor overactivity in a chronically ischemic bladder, can lead to detrusor dysfunction by promoting fibrosis of the bladder musculature, dysfunction of the bladder epithelium and denervation.<sup>29,30</sup> Although the current study was restricted to women, MetS occurs in both men and women due to the accumulation of visceral fat, including obesity.<sup>31</sup> There is a strong correlation between an increase in visceral fat and prostate volume.<sup>31</sup> Furthermore, the imbalance in testosterone secretion with age further accelerates visceral fat accumulation, which also induces an increase in morphological prostate enlargement.<sup>32</sup> In addition to prostatic enlargement, excessive visceral fat accumulation induces oxidative stress and organ ischemia, resulting in various LUTS.<sup>32</sup> In a clinical study involving men, AC and BMI were not associated with the prevalence of OAB, whereas excess VFA was reported to be an independent risk factor for OAB.<sup>33</sup> Furthermore, a cross-sectional study that targeted only men also reported an association between OAB and VFA.<sup>7</sup> The relationship between LUTS and visceral fat needs to be further examined in the future, especially in Japanese men who are likely to accumulate visceral fat.<sup>34</sup>

The present study had certain limitations. First, the number of patients was relatively small and only included women to

rule out of the impact of benign prostate hyperplasia; and pressure flow studies were not carried out as a part of the protocol to evaluate the concomitant presence or absence of detrusor overactivity and detrusor hyperactivity with impaired contraction, which is a characteristic finding in older women. Second, we should note that OAB is multifactorial and can be caused by drugs and sleep disorders, which were not assessed in all patients during screening and selection. Currently, various new treatment strategies for urinary dysfunctions are developing.<sup>35–37</sup> In contrast, we emphasize the importance of a wide variety of information about the etiology of OAB to improve the QOL and outcomes of these new treatments. In that regard, we believe that the usefulness of the present results outweigh the limitations. In addition, a recently published cross-sectional study showed that OAB patients had more VFA than non-OAB patients.<sup>33</sup> However, we believe that the present study is the first to examine in detail the relationship between OAB and body fat mass including VFV and VFV/TAV in Japanese women. A prospective study reported that overweight female OAB patients who engaged in an intense exercise program showed improved OAB symptoms, as well as reduced bodyweight and VFA.<sup>22</sup> In future, it will be necessary to carry out a prospective study including the so-called “hidden obesity” OAB patients in order to investigate how changes in visceral fat as a result of behavior therapy, such as exercise and weight loss, affect OAB symptoms. In addition, we believe that it is necessary to evaluate lower urethral function using a pressure flow study and to examine the visceral fat relationship in detail. Furthermore, the present study included only female patients. Therefore, further detailed investigations including male patients are also necessary.

In conclusion, participants with OAB showed greater accumulation of visceral fat than those without the disorder. In addition, the degree of abdominal visceral fat accumulation was not only found to be associated with the severity of OAB, it was also shown to be a possible predictive factor. Conversely, AC and subcutaneous fat levels were not associated with LUTS. Based on the present findings, we suggest a correlation between visceral fat accumulation and OAB.

## Conflict of interest

None declared.

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