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The severity of visceral obesity is associated with an increased risk of urolithiasis

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OBJECTIVE **To assess the relationship between urolithiasis and obesity related parameters measured by computed tomography (CT) abdominal scan. The relationships between visceral obesity and the severity of urinary stone disease, and between the severity of visceral obesity and urolithiasis were evaluated.** METHOD **A retrospective case-control design was used, with one control subject for each patient, matched for age and sex. The participants were 100 adult patients with urolithiasis diagnosed by CT scan at our hospitals between October 2014 and September 2016. The control group consisted of 100 adults attending the hospital for trauma, with no past medical history of urological disease, who underwent abdominopelvic CT scan. The visceral fat area and other obesity related parameters were measured using the CT scan, on one cross-sectional cut at the level of the umbilicus.** RESULTS **All the obesity related parameters were significantly higher in the urolithiasis group than in the control group. The largest effect size was in the mean visceral fat area, which was higher in the patient group with visceral obesity than in the control group with visceral obesity (p=0.03). No statistically significant relationship was found between visceral obesity and the severity of urinary stone disease.** CONCLUSIONS **These results indicate that obesity, especially visceral obesity, is related to urinary stone disease. Individuals with severe obesity were at higher risk of urinary stone formation than individuals with mild obesity.**

Η βαρύτητα της σπλαγχνικής παχυσαρκίας σχετίζεται με αυξημένο κίνδυνο ουρολιθίασης

Περίληψη στο τέλος του άρθρου

Key words

Computed tomography
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Computed tomography (CT) scan is the gold standard technique for the measurement of visceral fat.[1] Epidemiological data show a relationship between obesity and urinary stone disease.[2] Few studies have assessed the relationship between urinary stone disease and the amount of visceral fat measured on CT.[3,4]

This study investigated the relationship between urolithiasis and obesity related parameters measured by CT scan. The relationships between visceral obesity and the severity of urinary stone disease, and between the severity of visceral obesity and urolithiasis were evaluated.

MATERIAL AND METHOD

Patients

A retrospective matched case-control design was used, with one matched control subject for each patient. The study participants were 100 adult patients (75 men and 25 women) with urinary stone disease diagnosed by CT scan at our hospitals between October 2014 and September 2016. Patients with bladder stone, congenital urinary tract anomalies, single kidney, ureteral stricture and chronic renal failure were excluded from the study.

The control group consisted of 100 adults investigated for trauma, with no past medical history of urological diseases, who underwent abdominopelvic CT scan in the same period, matched by age (±2 years) and gender with the study patients. Individuals with trauma induced gross pathology in the relevant CT cut were excluded.

For the purpose of the study, the data relating to the patients' age and sex, number of stones and recurrence of disease were retrieved from the records. Imaging had been performed on all patients and control subjects using 16-slice CT scanners in the supine position. Image analysis software previously used for this purpose (Image J, version 1.50 g; National Institutes of Health, USA) was used to quantify the abdominal fat area.[5]

Measurements

The total fat area (TFA), visceral fat area (VFA) and subcutaneous fat area (SFA) were measured on the CT abdominal scan on one cross-sectional cut at the level of the umbilicus. For measuring TFA, the threshold was determined with an attenuation range of -190 to -30 Hounsfield units.[6] The fat area reserved within abdominal muscles was defined as VFA and the fat area reserved between abdominal muscles and skin was defined as SFA. Non-adipose areas, such as bowel contents, were excluded. Fat area was measured in square centimeters (cm^2). Figure 1 shows the objective data on the obesity related parameters.

The most common parts of non-fat area in the defined CT cut were muscles. The fat area to non-fat area ratio (FNR) was defined as the ratio of the amount of fat area to non-fat area on one cross-sectional cut at the level of the umbilicus. The definitions of the obesity parameters used in the study are shown in table 1.

The patients and control subjects were divided into two subgroups, with and without visceral obesity. The results of a previous study were considered to determine the cut-off points for the definition of visceral obesity.[7] The cut-off point for VFA for men was 96 cm^2 and for women 75 cm^2. The VFA mean values of patients and control subjects with visceral obesity were compared to evaluate the relationship between urolithiasis and the severity of obesity. Based on a previous study, the multiplicity of stones and disease recurrence were considered as the markers of severity of urinary stone disease.[8] The study was approved by the University Ethical Committee.

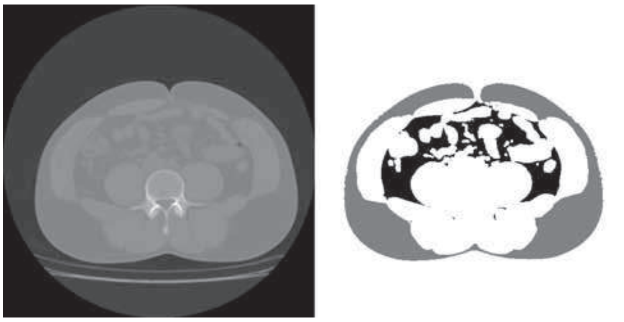

Figure 1. Computed tomography (CT) imaging in visceral obesity: The left image shows the CT cut at the level of the umbilicus. In the right image, the black area shows the visceral fat area (VFA), the gray area shows the subcutaneous fat area (SFA) and the white area shows the non-fat area (NFR).

Statistical analysis

Independent samples t-test was used to compare the means. Effect sizes were calculated using Cohen's d formula.[9] Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS), version 15.0 (SPSS Inc, Chicago, IL). A p-value <0.05 was considered significant.

RESULTS

The mean age of the patients in the study group was 42.7±15.4 (range: 19–86) years, and of the subjects in the control group 42.6±15.7 (range: 19–88) years ($p>0.05$). The mean age of the men was 42.3±15.2 years in the study group and 42.3±15.3 years in the control group ($p>0.05$). The mean age of the women was 43.7±16.4 years in the study group, and 43.6±17.0 years in the control group ($p>0.05$).

All of the obesity related parameters were significantly higher in urinary stone group than in the control group. The largest effect size was in VFA, followed by FNR and TFA (tab. 2).

Visceral obesity was detected in 77 patients (58 men and 19 women) with urolithiasis, and 40 control subjects (30 men and 10 women). Significant differences were demonstrated in VFA between the two groups. The mean VFA was higher in patients with visceral obesity (173.4±61.8) than in the control subjects with visceral obesity (151.2±40.6). According to the study protocol, each patient had one matched control subject. Of the 77 patients with visceral obesity, 40 patients had a matched control subject with visceral obesity. Analysis of the data of these 40 cases and 40 matched control subjects revealed a significant difference in the VFA between the two groups (tab. 3). Regarding the

Table 1. Definitions of the fat measurement parameters used in the study.

Parameter	Definition
Total fat area (TFA)*	Area with fat attenuation in the selected computed tomography (CT) cut
Visceral fat area (VFA)*	Area with fat attenuation in the selected visceral part
Subcutaneous fat area (SFA)*	TFA subtracted from the VFA
Fat area to non-fat area ratio (NFR)	TFA/non-fat area
The percentage of VFA	(VFA/TFA)×100
Ratio of VFA to SFA	VFA/SFA

*Square centimeters (cm^2)

Table 2. The relationship between urolithiasis and obesity related parameters.

Parameters	Urinary stone group (n=100)	Control group (n=100)	p value	Effect size
Visceral fat area (VFA) (mean±SD)	145.4±75.5	86.7±62.0	<0.001	0.85
Fat area to non-fat area ratio (NFR) (mean±SD)	1.31±0.60	0.87±0.57	<0.001	0.75
Total fat area (TFA) (mean±SD)	367.0±160.3	250.5±162.0	<0.001	0.72
The percentage of VFA (mean±SD)	40.1±11.1	34.1±10.0	<0.001	0.57
Subcutaneous fat area (SFA) (mean±SD)	221.8±105.5	163.8±110.3	<0.001	0.54
Ratio of VFA to SFA (mean±SD)	0.75±0.45	0.56±0.28	<0.001	0.51

Table 3. The relationship between urolithiasis and the severity of obesity.

Variable	Patients with visceral obesity	Control subjects with visceral obesity	p value
Visceral fat area (VFA) (mean±SD) (77 patients versus 40 control subjects)	173.4±61.8	151.2±40.6	0.02
VFA (mean±SD) (40 patients versus 40 matched control subjects)	183.6±53.9	151.2±40.6	0.03

clinical characteristics of the study patients, 35 (35%) were suffering from a single stone while 65 patients (65%) had multiple stones; 56 patients (56%) presented one episode, while 44 (44%) had recurrent disease. As shown in table 4, no significant relationship was detected between VFA and the parameters of severity.

DISCUSSION

The role of obesity and its various different aspects in urinary stone disease is ambiguous, although it is generally regarded as an accompanying factor. For this reason, specific obesity parameters measured on abdominal CT scan were evaluated in this study, to better clarify the possible role of obesity in stone formation and disease severity.

A few studies have focused on the relationship between visceral obesity and urinary stone disease.[3,4] One recent study concluded that VFA and VFA% were significantly higher in patients with urolithiasis compared to a control group, while SFA was not significantly higher in patients with urolithiasis.[3] The present study also indicated that VFA and VFA% were significantly higher in a group of patients with urinary stone disease than in a control group of matched subjects. In this study, however, the SFA also was significantly higher in patients with urinary stone disease than in the control subjects. The differences in the results of the two studies may be attributed to the selection of the control group. The earlier researchers selected for their control group individuals with flank pain but with no urinary stone identified by CT scan.[3] It is therefore possible that patients who had passed out a urinary stone might have been included in the control group. In one previous study, SFA was found to be significantly higher in patients with the metabolic syndrome,[5] and another study concluded that increase in VFA is a risk factor for urinary stone disease.[4] In that study individuals without urinary stone disease who underwent CT scan were selected as control subjects.[4] Thus, all other patients with diseases associated with visceral obesity were named as "controls".

Based on the results of the present study, all the obesity related parameters measured were significantly higher in patients with urinary stone disease than in the control subjects. In addition, the largest effect size was related to VFA. The effect size shows the strength of a relationship.

Table 4. The relationship between urolithiasis disease severity and visceral obesity.

Variable	Single stone versus multiple stones	One episode versus recurrence	Single stone and one episode versus multiple stones and or recurrence
Visceral fat area (VFA) (mean±SD)	156.0±86.9 versus 139.8.0±68.6 (p=0.31)	142.9±76.0 versus 148.6±75.5 (p=0.71)	165.5±86.4 versus 141.0±72.7 (p=0.22)

Based on these results, the hypothesis that "obesity, especially visceral obesity, is related to urinary stone disease" is confirmed. A previous study found that body mass index (BMI) was not related to the severity of urolithiasis, as an independent variable.[8] We used VFA rather than BMI as the index of obesity, but also found no significant relationship with the severity of urinary stone disease.

Another previous study concluded that obesity was associated with an increased risk of urolithiasis, although the risk of urolithiasis remained stable with increasing degrees of obesity.[10] In the present study, VFA measured with CT scan rather than BMI was used to evaluate the severity of obesity. VFA is more precise than BMI in evaluation of the risk of the metabolic syndrome.[11] According to the study data, an increase in VFA results in increasing stone formation, even in morbidly obese patients. It appears that individuals with severe obesity are at higher risk of urinary stone formation than those with mild obesity. Proteins or hormones related to the adipose cells, especially the visceral adipose cells may be considered as regulators of such effects.

In conclusion, visceral obesity, as a marker of the metabolic syndrome, had a significant relationship with urinary stone formation, but did not play an obvious role in the severity of urinary stone disease. In contrast with the results of a previous study,[10] in our series, risk of stone formation was higher in the individuals with severe obesity than in those with mild obesity, which may be due to the selection of VFA, rather than BMI, as the marker of the severity of obesity.

ΠΕΡΙΛΗΨΗ

Η βαρύτητα της σπλαγχνικής παχυσαρκίας σχετίζεται με αυξημένο κίνδυνο ουρολιθίασης

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ΣΚΟΠΟΣ Εκτίμηση του συνδυασμού μεταξύ ουρολιθίασης και παραμέτρων σχετιζόμενων με την παχυσαρκία που μετρώνται με αξονική τομογραφία. Επί πλέον, διενεργήθηκε αξιολόγηση της σχέσης μεταξύ σπλαγχνικής παχυσαρκίας και βαρύτητας της λιθίασης των ουροφόρων. **ΥΛΙΚΟ-ΜΕΘΟΔΟΣ** Χρησιμοποιήθηκε αναδρομική ελεγχόμενη μελέτη με έναν μάρτυρα για κάθε ασθενή και συμβατό ως προς την ηλικία και το φύλο. Έγινε επιλογή 200 ενηλίκων ατόμων, από τα οποία 100 είχαν ουρολιθίαση και 100 ήταν μάρτυρες. Η διάγνωση της ουρολιθίασης των 100 ατόμων τέθηκε με αξονική τομογραφία μεταξύ Οκτωβρίου 2014 και Σεπτεμβρίου 2016. Οι 100 μάρτυρες παρουσίαζαν τραύματα και δεν είχαν προηγούμενο ιστορικό ουρολογικής νόσου και υποβλήθηκαν σε αξονική τομογραφία της κοιλιακής και της πυελικής περιοχής. Το σπλαγχνικό λίπος και οι άλλες παράμετροι παχυσαρκίας μετρήθηκαν με μια τομή στο ομφαλικό επίπεδο με αξονική τομογραφία. **ΑΠΟΤΕΛΕΣΜΑΤΑ** Όλες οι παράμετροι που σχετίζονταν με την παχυσαρκία ήταν σημαντικά υψηλότερες στην ομάδα με ουρολιθίαση σε σχέση με την ομάδα ελέγχου. Το μεγαλύτερο αποτέλεσμα παρατηρήθηκε στη μέση σπλαγχνική λιπώδη περιοχή, στην ομάδα των ασθενών με σπλαγχνική παχυσαρκία σε σύγκριση με την ομάδα ελέγχου η οποία εμφάνιζε επίσης σπλαγχνική παχυσαρκία (p=0,03). Τελικά, δεν βρέθηκε σημαντική συσχέτιση μεταξύ της σπλαγχνικής παχυσαρκίας και της βαρύτητας της ουρολιθίασης. **ΣΥΜΠΕΡΑΣΜΑΤΑ** Τα αποτελέσματα έδειξαν ότι η παχυσαρκία και ιδιαίτερα η σπλαγχνική σχετίζεται με την ουρολιθίαση. Επί πλέον, τα άτομα με πολύ βαριά παχυσαρκία βρίσκονται σε υψηλότερο κίνδυνο για σχηματισμό ουρολίθων σε σύγκριση με άτομα με ήπια παχυσαρκία.

Λέξεις ευρετηρίου: Αξονική τομογραφία, Ουρολιθίαση, Παχυσαρκία, Σοβαρότητα, Σπλαγχνική παχυσαρκία

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