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Visceral Obesity and Urinary Stone Disease: A Systematic Review

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Abstract

Background: Incidence of obesity is on rise worldwide due to several risk factors, including lifestyle changes and genetic causes. Obesity can be diagnosed with different anthropometric tools, such as body mass index, visceral fat, subcutaneous fat and waist circumference. The incidence of urinary stones disease has been linked to obesity as well as metabolic syndrome (MetS). The aim of the present study was to determine the relationship between obesity defined by visceral adipose tissue (VAT) and urolithiassis.

Methods: The search engines utilized for finding relevant studies were Medline, ScienceDirect, and Cochrane databases between January 2001 and January 2019. Published articles written in the English language and reporting an association between visceral obesity, urolithiasis and MetS were included.

Results: Obesity defined by visceral fat estimation is associated with increased risk of MetS and urinary stone formation. Insulin resistance, low urinary pH, hyperuricemia, hyperuricosuria and hyperoxaluria were the main observed metabolic derangements behind the pathogenesis and the increased risks of stone development in obese patients.

Conclusion: The role of VAT reduction in prevention of urinary stones disease is not yet established, and for this reason more studies are required in the future to clarify this sequence of events. (**International Journal of Biomedicine. 2019;9(2):87-90.**)

Key Words: visceral obesity • visceral adipose tissue • metabolic syndrome • urolithiassis

Abbreviations

BMI, body mass index; **IR**, insulin resistance; **MetS**, metabolic syndrome; **USD**, urinary stones disease; **VAT**, visceral adipose tissue; **VO**, visceral obesity; **WC**, waist circumference

Introduction

Nephrolithiasis is a morbid condition with increasing prevalence worldwide. Multifactorial causes, such as genetic factors and lifestyle, are thought to play significant roles in kidney stone formation.[1] Obesity and MetS have been shown to be significant risk factors for nephrolithiasis and various urinary biochemical abnormalities, including high excretion of calcium, oxalate, uric acid, and lower levels of citrate and pH.[2]

The relationship between obesity defined by BMI and nephrolithiasis has been reported by several studies. The higher fat mass and its abnormal distribution have a greater impact than total body weight on MetS.[3] Abnormal body fat with higher VAT distribution appears to have even a greater influence in MetS than does total body weight on cardiovascular disease and diabetes risk.[4] The National Cholesterol Education Program Adult Treatment Panel III considers WC, and thus VO, one of the major clinical criteria to diagnose MetS.[5] However, measurements of BMI and WC cannot distinguish VAT from subcutaneous fat, which is subject to inherent differences in fat distribution between subjects.[6] Measurement of visceral fat volume from a single axial CT slice at different levels has been developed and validated.[7]

Obesity has been linked in several studies to changes in serum and urine composition. Urinary excretion of oxalate and uric acid was higher in obese patients compared to non-obese. On the other hand, lower levels of stone inhibitors, such as citrate, pyrophosphate and magnesium (other causative factors for stone formation), are observed in these patients.[8]

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Acidic urine is an important promoter for the most common types of stones, including calcium oxalate, calcium phosphate and uric acid stones.[9] Low urinary pH has been observed in individuals with obesity and MetS. The exact pathophysiology is not clear, but a possible cause is IR, which decreases excretion of renal ammonia and derangement of the hydrogen ion buffering system.[10] In addition, IR leads to lower insulin bioactivity in the proximal renal tubules, which affect ammonium metabolism and ultimately changes in urinary pH.[11] The aim of the present study was to determine the relationship between obesity defined by VAT and urolithiassis.

Materials and Methods

The prevalence, risk factor and morbidity of obesity defined by VAT and its association with urolithiasis and MetS are the main objectives of this systematic review. The search engines utilized for finding relevant studies were Medline, ScienceDirect, and Cochrane databases between January 2001 and January 2019. The Cochrane Collaboration and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were carried out for this review. All identified studies that met the inclusion criteria for this review were included and analyzed. The search for relevant studies was performed using the following keywords: "obesity," "visceral obesity," "visceral fat," "visceral adipose tissue," "insulin resistance," "nephrolithiasis," "uric acid," "hypercalciuria," "metabolic syndrome," "renal," "kidney," "calculi," "stone(s)," and "urolithiasis." The Boolean operator (OR, AND) combining the keywords was used to refine the search results. Published articles written in the English language and reporting an association between VO, urolithiasis and MetS were included. Exclusion criteria were case reports, brief notes, reviews, editorials, letters to editors and conference proceedings (Table 1).

Table 1.
Inclusion and exclusion criteria of the included records

Inclusion criteria	Exclusion criteria
Publication in the English language	Case reports
Original articles reporting the association between VAT, urolithiasis and MS	Brief notes
	Reviews
	Editorials
	Letters to editors and conference proceedings
	Languages other than English

Results

The initial search identified 1,811 related articles, from which, with a refined search, 1,759 records were excluded. Further filtration according to the inclusion and exclusion criteria determined 14 studies to be included for qualitative analysis in the present review (Fig.1).

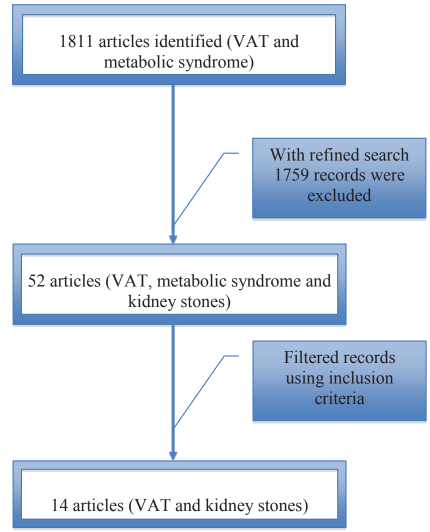

Fig. 1. *Flow diagram summarizing the literature search for this review.*

<u>Measurement of visceral fat volume</u>

With advances and revolutions in technologies, measurement of body fat distribution can be achieved utilizing different techniques. Examples of simple measures include waist-to-hip ratio and WC. These tests cannot distinguish between subcutaneous and visceral fat contents. CT and MRI have been considered the most accurate and reproducible techniques of abdominal fat assessment with the added advantage of distinguishing subcutaneous from visceral fat components.[7] The drawback of these techniques is the cost and radiation exposure, which can be minimized using a low dose CT scan or utilizing available images done for other purposes—most commonly CT being done for renal colic in patients with urolithiasis.[12,13]

CT-based fat delineation and calculation of visceral fat can be done either manually or with the help of automated image processing software to overcome the drawbacks of manual delineation.[14,15] To differentiate between visceral and subcutaneous fat, we used automatic fat analysis developed and evaluated by measures of accuracy and sensitivity in comparison to manual quantification. The differences between manual and automated techniques for estimating both subcutaneous and visceral fat were not significant.[16] The majority of the VAT and USD studies have been done by obtaining a single axial CT slice at the level of the fourth and fifth lumbar vertebrae (L4-5) (Fig.2), whereas some authors have suggested measurement of VAT at the level of the first and second lumbar vertebrae (L1-2) as a more accurate estimate (Fig.3). Kim et al. performed a study of VAT volume calculation by taking one slice of CT from the umbilicus level between fourth and fifth lumbar vertebrae and six additional CT slices from above and below the umbilicus level. Automated and manual evaluation methods were applied and found that more reliable results were obtained with assessments using a set of CT slices, compared to the use of a single CT slice.[17] VO was defined as a visceral fat volume more than 100 cm^2 and considered an important factor for MetS.[18]

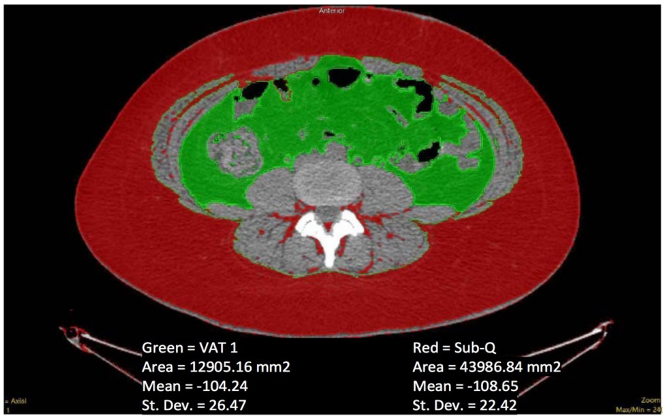

Fig. 2. *Axial CT slice at the level of the fourth and fifth lumbar vertebrae (L4–5).*

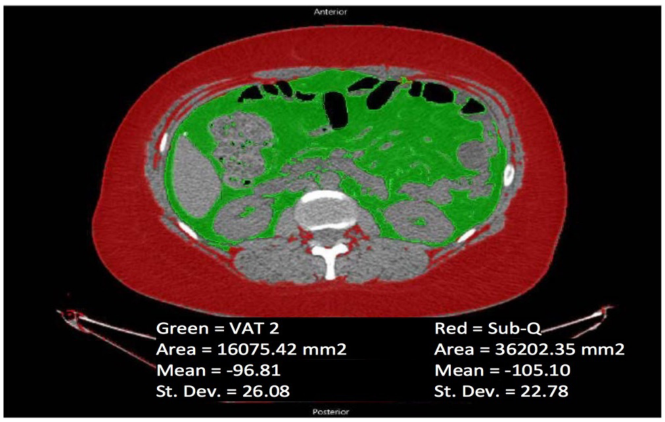

Fig. 3. *Axial CT slice at the level of the first and second lumbar vertebrae (L1–2).*

VAT and urolithiasis

In the literature, there is an inhomogeneous conclusion about the effect of obesity on urinary composition in patients with urolithiasis. Low urinary pH has been observed in obese patient as well as changes in urinary concentration of oxalate, phosphate, citrate, and uric acid.[19-21] Acidic urine is an important promoter of uric acid stone formation and has been found to have an inverse correlation with VAT.[22,23] Urinary concentration of uric acid was found to be higher when obesity defined by VAT, compared with calcium phosphate in obese patients, increases the risk for uric acid stone formation. Obesity defined by VAT was shown to have a strong association with the formation of calcium oxalate stones in comparison to calcium phosphate and mixed calcium oxalate phosphate stones.

Zhou and his colleagues analyzed 269 patients undergoing percutaneous nephrolithotomy and reported a significantly higher mean visceral fat volume in uric acid stone formers and found that the higher VAT level was an independent risk factor for the composition of uric acid stones after stone retrieval and chemical analysis.[24] Fujimura et al. looked at the association of VAT and the incidence of urolithiasis by measuring the VAT volume using a CT scan fat delineation. Increased VAT volume was associated with increased risk of urinary stone formation compared to BMI. They also noticed a strong association between VAT and IR and consequently an increase in the incidence of MetS.[25,26]

Ethan found that VAT was associated with increased quartile of creatinine, sodium, and urine volume in 24-h urine collection in men that was independent of BMI. Whereas in women, increased quartile phosphate urinary excretion was predicted only by increased VAT, while increased quartile of creatinine and oxalate were predicted by BMI. On multivariate regression analysis, VAT was found to be associated with uric acid stone formation, and none of the BMI or VAT estimation predicted the formation of other stone types.[27] Akarken demonstrated that the visceral abdominal area is a new and independent risk factor for urinary stone formation. The incidence of uric acid kidney stones was higher in patients with a high visceral abdominal area compared to those who do not have kidney stones.[28] A study of 98 kidney stone formers who had available a computerized tomography scan and twenty-four-hour urine for electrolytes showed that elevated VAT level was associated with low 24-hour urinary pH and higher urinary sodium excretion. As the level of VAT volume increases, urine pH becomes lower and the stone volume, greater. Formation of uric acid stones was associated with greater VAT volume and lower urinary pH.[29]

VAT, MetS and urolithiasis

MetS is a clinical diagnosis characterized by obesity, elevated blood pressure, dyslipidemia and elevated blood glucose.[30] IR and abdominal obesity are the principal risk factors for MetS development. People diagnosed with MetS are at higher risk of hyperuricemia, chronic kidney disease and cardiovascular disease. The risk of obesity-related disorders has been observed when VAT level exceeds 103.8 cm^2.[31] The incidence of urolithiasis has been observed to be on the rise in individuals with MetS.[32] Zhou et al.[24] found a significantly high level of VAT in patients with uric acid stones, and this proportion was not observed in patients who form non-uric acid stones. This finding was reinforced by a study done by Kim et al.[31] where obesity defined by VAT volume measured on a CT scan has a significant effect on the risk of forming uric acid stones compared with calcium phosphate and calcium oxalate stones. For obesity defined by BMI, no rules were found on the type of stones in adult patients who underwent surgical treatment for urinary stones. Daudon reported a strong association between type 2 diabetes and uric acid stones, with obesity being an additional risk factor in younger patients.[32,34] IR has been identified as a predisposing factor for uric acid stone formation and an important target to decrease the risk of nephrolithiasis.[35]

Conclusion

There is clear evidence for the increased prevalence and incidence of urinary stones in association with obesity. Obesity defined by visceral fat estimation is associated with increased risk of MetS and urinary stone formation. IR, low urinary pH, hyperuricemia, hyperuricosuria and hyperoxaluria were the main observed metabolic derangements behind the pathogenesis and the increased risks of stone development in obese patients. The role of VAT reduction in prevention of USD is not yet established, and for this reason more studies are required in the future to clarify this sequence of events.

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