The Association Between Metabolic Syndrome and Characteristics of Benign Prostatic Hyperplasia
A Systematic Review and Meta-Analysis

Jian-Ye Wang, MD, PhD, Yan-Yan Fu, MD, PhD, and De-Ying Kang, MD

Abstract: The purpose of this systematic review was to examine the association of metabolic syndrome (MS) with measures of benign prostatic hyperplasia (BPH) including prostate growth rate, prostate volume, International Prostate Symptom Score (IPSS), prostate-specific antigen (PSA) level, and maximal flow rate.

Medline, Cochrane CENTRAL, EMBASE, CBM, and Google Scholar databases were searched until March 23, 2015 using combinations of the keywords benign prostatic hyperplasia/BPH, metabolic syndrome, total prostate volume, prostate growth rate, prostate specific antigen, International Prostate Symptom Score/IPSS, maximal flow rate. Cohort or case-control studies of patients with BPH and MS that reported quantitative outcomes were included. The pooled mean differences of the outcome measures were compared between patients with and without MS.

INTRODUCTION
Benign prostatic hyperplasia (BPH), characterized by enlargement of the prostate gland and narrowing of the urethra, affects >50% of men older than 60 years and the majority older than 80 years, and is a major cause of lower urinary tract symptoms (LUTS).1,2 LUTS can be obstructive and/or irritative, and can significantly affect quality of life.1,2 BPH is the result of a nonmalignant proliferation of cells in the prostate gland, and although the etiology of the proliferation is not well understood, known factors associated with BPH are aging and androgen metabolism.3 Recent evidence has also suggested that metabolic disorders, including hyperinsulinemia, dyslipidemia, and obesity may play a role in the development of prostate hyperplasia.4–7

Metabolic syndrome (MS) is a cluster of medical conditions including hypertension, impaired glucose metabolism, abdominal obesity, hypertriglyceridemia, and low high-density lipoprotein cholesterol (HDL-C).8 The underlying feature of MS is insulin resistance, and MS is associated with an increased risk of type 2 diabetes mellitus and cardiovascular disease.8 Similar to BPH, the prevalence of MS increases with age.9

A total of 158 potentially relevant studies were identified, and 8 were included in the meta-analysis. The 8 studies included in the meta-analysis contained a total of 3093 BPH patients, wherein 1241 had MS and 1852 did not have MS. BPH patients with MS had a significantly higher prostate growth rate (pooled mean difference = 0.67 mL/y, P < 0.001) and larger prostate volume (pooled mean difference = 6.8 mL, P = 0.010) than the BPH patients without MS. There was no significant difference in IPSS score (pooled mean difference = 1.58, P = 0.202) or maximal flow rate (pooled mean difference = –1.41 mL/s, P = .345) between BPH patients with and without MS. A borderline nonsignificant difference in PSA (pooled mean difference = 0.24 ng/mL, P = 0.056) was noted between BPH patients with and without MS.

The results of this meta-analysis are consistent with literature indicating that BPH patients with MS have a higher prostate growth rate and larger prostate volume than those without MS; however, further study is necessary to determine the association of BPH and metabolic disorder elements and the potential risk of disease progression in BPH patients with MS.

Abbreviations: BMI = body mass index, BPH = benign prostatic hyperplasia, CI = confidence interval, ED = erectile dysfunction, HDL-C = high-density lipoprotein cholesterol, HOMA-IR = homeostatic model assessment of insulin resistance, IPSS = International Prostate Symptom Score, LUTS = lower urinary tract symptoms, MS = metabolic syndrome, PSA = prostate specific antigen.
Furthermore, recent evidence is suggesting a link between MS and prostatic hyperplasia and LUTS. In contrast with results from the United States and European countries, results from Asian populations have been inconsistent. One study indicated that MS was not clearly correlated with LUTS/BPH in Korean men in their 50s, whereas the results of another study indicated that MS was associated with an increased total volume and annual prostate growth rate. A recent meta-analysis indicated that patients with MS have a higher total prostate volume than those without MS, yet International Prostate Symptom Scores (IPSS) were not different between those with and without MS.

As there are a number of different measures of determining BPH, the purpose of this meta-analysis was to examine the association of MS with measures of BPH including prostate growth rate, prostate volume, IPSS, prostate-specific antigen (PSA) level, and maximal flow rate.

MATERIALS AND METHODS

Literature Search and Study Selection

This systematic review and meta-analysis was performed in accordance with MOOSE guidelines. Medline, Cochrane, EMBASE, Google Scholar databases, and CBM were searched from inception until March 23, 2015 using combinations of the keywords: benign prostate hyperplasia/BPH, metabolic syndrome, total prostate volume, prostate growth rate, prostate specific antigen, International Prostate Symptom Score/IPSS, maximal flow rate. Inclusion criteria for the analysis were: cohort or case-controlled studies; patients had BPH with or without LUTS and were older than 18 years; compared patients with and without MS; quantitative outcomes of interest were reported. Letters, comments, editorials, case reports, proceedings, and personal communications were excluded, as were studies in which no quantitative outcome was reported. Reference lists of relevant studies were hand-searched. Searches were conducted by 2 reviewers, and a third reviewer was consulted for resolution of disagreements.

The following information/data were extracted from studies that met the inclusion criteria: the name of the first author, year of publication, number of patients in each group, age, BMI, IPSS, and quantitative outcomes.

Quality Assessment

The Newcastle-Ottawa scale was used to assess the quality of the included studies. Briefly, the instrument contains 8 items categorized into 3 dimensions: selection, comparability, and exposure (outcome). A point system is used for a semi-quantitative assessment of study quality.

Outcome Measures and Data Analysis

The primary outcome was the association of prostate growth rate and MS, and secondary outcomes were the associations of prostate volume, PSA level, IPSS, and maximal flow rate with MS. Data reported as median and range were converted to mean and standard deviation. Pooled mean differences were compared between groups. Heterogeneity among the studies was assessed by the Cochran Q and the I² statistic. If either the Q statistic value of $P < 0.1$ or $I^2$ was $>50\%$, a random-effects model of analysis (DerSimonian-Laird method) was used. Otherwise, a fixed-effects model (Mantel-Haenszel method) was used. Sensitivity analyses based on the leave-one-out approach were performed to evaluate the robustness of the pooled estimates of the primary and secondary outcomes.

Publication bias was not evaluated in this study because there were only 3 studies included for the primary outcome (prostate growth rate), which is insufficient to detect funnel plot asymmetry. All analyses were performed with Comprehensive Meta-Analysis software, version 2.0 (Biostat, Englewood, NJ).

RESULTS

Literature Search and Study Characteristics

A flow diagram of study selection is shown in Supplemental Figure 1, http://links.lww.com/MD/A920. A total of 158 potentially relevant studies were identified, and 118 remained after duplicates were excluded. After screening by title and abstract, 31 articles were excluded, the reasons for which are shown in Supplemental Figure 1, http://links.lww.com/MD/A920. Nine full-text articles were assessed for eligibility, and of these, 8 were included in the meta-analysis.

The study by Aktas et al was included in the qualitative synthesis, but did not include measures appropriate for the meta-analysis. The characteristics of the included studies were summarized in Table 1. The 8 studies included in the meta-analysis contained a total of 3093 BPH patients, wherein 1241 had MS and 1852 did not have MS. The primary and secondary outcomes of the included studies are summarized in Supplemental Table 1, http://links.lww.com/MD/A920.

Quality Assessment

Results of the Newcastle-Ottawa scales assessment of the included studies are shown in Table 1. Six studies had a total score of 8 points, and 3 studies a total score of 7 points, indicating that the overall quality of the included studies was acceptable.

Primary Outcome (Prostate growth Rate)

Three studies reported prostate growth rate data. No significant heterogeneity was observed (Cochran $Q = 3.6$, $P = 0.167$; $I^2 = 44.1\%$), and thus a fixed-effects model of analysis was performed. BPH patients with MS had a significantly higher prostate growth rate than the BPH patients without MS (pooled mean difference $= 0.67 \text{ mL/y}$, $P < 0.001$; Figure 1 A). The pooled mean differences of prostate growth rate with each of the studies removed were similar (range, 0.55–0.68 mL/y), and remained statistically significant (all, $P < 0.001$), indicating good reliability in the pooled estimate (Figure 1B).

Prostate Volume

All 8 studies reported prostate volume data. Significantly heterogeneity was observed (Cochran $Q = 70.6$, $P < 0.001$; $I^2 = 90.1\%$), and thus a random-effects model of analysis was performed. BPH patients with MS had a significantly larger prostate volume than BPH patients without MS (pooled mean difference $= 6.8 \text{ mL}$, $P = 0.010$; Figure 2A). The pooled mean differences of prostate volume with each of the studies removed were similar (range, 5.27–9.27 mL), indicating acceptable reliability in the pooled estimate (Figure 2B).
| First Author (Publication Year) | Population | Study Design | Definition of Metabolic Syndrome | Imaging Techniques for Prostate Volume | Group | Number of Patients | Age, y | BMI, kg/m² | IPSS | Newcastle-Ottawa Scale |
|---------------------------------|------------|--------------|----------------------------------|---------------------------------------|-------|-------------------|--------|------------|------|-----------------------|
| Gacci et al. (2015)             | Italy      | Prospective  | NCEP-ATP III                    | Ultrasound                            | With MS | 140               | 69.7 ± 7.4 | 27.4 ± 3.5 | 20.0 ± 5.7 | 8                   |
|                                 |            |              |                                  |                                       | Without MS | 238              | 68.5 ± 8.8 | 25.7 ± 2.3 | 20.5 ± 4.8 |                    |
|                                 |            |              |                                  |                                       | With MS | 47               | 62.5 ± 9.6 | NR         | 16.95 ± 8.54 | 8               |
|                                 |            |              |                                  |                                       | With MS | 53               | 68.8 ± 6.3 | NR         | 29.8 ± 4.3    | 8               |
|                                 |            |              |                                  |                                       | Without MS | 103              | 26.5 ± 3.3 | 9.6 ± 7.2  | 16.81 ± 7.01 | 8               |
|                                 |            |              |                                  |                                       | Without MS | 328              | 76.93 ± 5.85 | 26.18 ± 2.78 | 11.18 ± 7.52 | 8               |
| Cyrus et al. (2014)             | Iran       | Cohort       | WHO criteria                     | Transrectal ultrasonography           | With MS | 47               | 62.5 ± 9.6 | NR         | 24.80 ± 3.93 | 7               |
|                                 |            |              |                                  |                                       | With MS | 179              | 77.75 ± 5.78 | 23.45 ± 2.50 | 11.20 ± 7.96 | 7               |
|                                 |            |              |                                  |                                       | Without MS | 418              | 68.44 ± 9.82 | 28.20 ± 2.16 | 22.5 ± 5.7    | 7               |
| De Nunzio et al. (2014)         | Italy      | Cohort       | NCEP-ATP III                     | Transrectal ultrasonography           | With MS | 103              | 69 ± 7.4   | 24.14 ± 1.20 | 11.52 ± 7.01 | 8               |
|                                 |            |              |                                  |                                       | Without MS | 634              | 71.24 ± 5.93 | 27.4 ± 3.5  | 18.58 ± 2.87 | 7               |
|                                 |            |              |                                  |                                       | With MS | 86               | 69 ± 7.4   | 27.4 ± 3.5  | 22.5 ± 5.7    | 7               |
| Zhang et al. (2014)             | China      | Cohort       | NCEP-ATP III                     | Transrectal ultrasonography           | With MS | 185              | 68 ± 7.5   | 25.4 ± 3.6  | 20.9 ± 5.7    | 8               |
|                                 |            |              |                                  |                                       | Without MS | 33               | 60.41 ± 6.75 | NR         | 18.58 ± 2.87 | 7               |
| Pan et al. (2014)               | China      | Retrospective cohort | NCEP-ATP III | Ultrasonography | With MS | 179              | 77.75 ± 5.78 | 23.45 ± 2.50 | 11.20 ± 7.96 | 7               |
|                                 |            |              |                                  |                                       | Without MS | 418              | 68.44 ± 9.82 | 28.20 ± 2.16 | 22.5 ± 5.7    | 7               |
| Gacci et al. (2013)             | Italy      | Retrospective | IDF and AHA/NHLBI               | Transrectal ultrasonography           | With MS | 86               | 69 ± 7.4   | 27.4 ± 3.5  | 22.5 ± 5.7    | 7               |
|                                 |            |              |                                  |                                       | Without MS | 185              | 68 ± 7.5   | 25.4 ± 3.6  | 20.9 ± 5.7    | 8               |
|                                 |            |              |                                  |                                       | With MS | 33               | 60.41 ± 6.75 | NR         | 18.58 ± 2.87 | 7               |
| Aktas et al. (2011)             | Turkey     | Cohort       | NCEP-ATP III                     | Transrectal and transabdominal        | With MS | 185              | 68 ± 7.5   | 25.4 ± 3.6  | 20.9 ± 5.7    | 8               |
|                                 |            |              |                                  | ultrasonography                      | Without MS | 33               | 60.41 ± 6.75 | NR         | 18.58 ± 2.87 | 7               |
|                                 |            |              |                                  |                                       | Without MS | 73               | NR         | IPSS 0–7: 14 |                    | 8               |
| Cao et al. (2010)               | Chinese    | Retrospective | Modified IDF                  | Transabdominal ultrasonography       | With MS | 187              | 70.14 ± 8.59 | 26.19 ± 2.82 | 23.10 ± 4.44 | 7               |
|                                 |            |              |                                  |                                       | Without MS | 195              | 71.79 ± 9.02 | 23.25 ± 2.78 | 22.10 ± 3.23 | 8               |
|                                 |            |              |                                  |                                       | With MS | 38               | 59 (50–83)  | 28.7 (21.2–36.7) | 20 (10–32) | 8               |
|                                 |            |              |                                  |                                       | With MS | 40               | 60 (50–72)  | 25.4 (19.5–31.9) | 20 (10–33) | 8               |

AHA/NHLBI = American Heart Association/National Heart, Lung, and Blood Institute, BMI = body mass index, IDF = International Diabetes Foundation, IPSS = International Prostate Symptom Score, MS = metabolic syndrome, NCEP ATP III = National Cholesterol Education Program Adult Treatment Panel III, NR = not reported, WHO = World Health Organization.

1The study by Aktas et al. was retained for systematic review only, as its outcomes were not appropriate for the meta-analysis.

2Data are presented as median (full range). All other data are presented as mean ± standard deviation.
Six studies reported PSA data.\(^{21,23-25,27,28}\) Significant heterogeneity was observed (Cochran $Q = 11.8$, $P = 0.038$; $I^2 = 57.5\%$), and thus a random-effects model of analysis was performed. BPH patients with and without MS had a borderline nonsignificant difference in PSA (pooled mean difference $= 0.24$ ng/mL, $P = 0.056$; Figure 3A). The pooled mean differences of PSA with each of the studies removed was performed. BPH patients with and without MS had a borderline nonsignificant difference in PSA (pooled mean difference $= 0.24$ ng/mL, $P = 0.056$; Figure 3A). The pooled mean differences of PSA with each of the studies removed was performed. BPH patients with and without MS had a borderline nonsignificant difference in PSA (pooled mean difference $= 0.24$ ng/mL, $P = 0.056$; Figure 3A). The pooled mean differences of PSA with each of the studies removed was performed. BPH patients with and without MS had a borderline nonsignificant difference in PSA (pooled mean difference $= 0.24$ ng/mL, $P = 0.056$; Figure 3A). The pooled mean differences of PSA with each of the studies removed was performed. BPH patients with and without MS had a borderline nonsignificant difference in PSA (pooled mean difference $= 0.24$ ng/mL, $P = 0.056$; Figure 3A). The pooled mean differences of PSA with each of the studies removed.
were similar (range, 0.15–0.32 ng/mL), which indicated an acceptable reliability in the pooled estimate (Figure 3B).

**IPSS**

All 8 studies reported IPSS data.21–28 Because significant heterogeneity was observed between studies (Cochran \( Q = 250.8, \ P < 0.001; I^2 = 97.2\% \)), a random-effects model of analysis was performed. There was no significant difference in IPSS score between BPH patients with and without MS (pooled mean difference \( = 1.58, \ P = 0.202; \) Figure 4A). The pooled mean differences of IPSS with each of the studies removed were similar and remained statistically nonsignificant (all, \( P > 0.05 \)), which indicated a good reliability in the pooled estimate (Figure 4B).

**Maximal Flow Rate**

Four studies reported maximal flow rate data.21,24–26 Because significant heterogeneity was observed between studies (Cochran \( Q = 297.8, \ P < 0.001; I^2 = 99.0\% \)), a random-effects model of analysis was performed. There was no difference in maximal flow rate between BPH patients with and without MS (pooled mean difference = 1.85, \( P = 0.202; \) Figure 5A). The pooled mean differences of maximal flow rate with each of the studies removed were similar (range, \(-1.92 \) to \(-0.27 \) mL/s) and remained statistically nonsignificant (all, \( P > 0.05 \)), indicating good reliability in the pooled estimate (Figure 5B).

**Subgroup Analysis By Region (Asia And Europe)**

Subgroup analyses by region (Asia and Europe) for prostate volume, PSA, IPSS, and maximal flow rate were performed to reduce the heterogeneity among the included studies. Four studies from Asia22,24,25,27 reported prostate volumes for patients with and without MS, and the mean differences of prostate volume showed no obvious heterogeneity (\( Q = 3.2, df = 3, P = 0.360; I^2 = 6.7\% \)); thus, a fixed-effects model was used. The pooled estimate showed that patients with MS had higher prostate volume than those without MS (pooled mean difference = 11.96, 95% confidence interval [CI]: 10.94–12.98, \( P < .001 \)). Three studies from Europe21,23,26 reported prostate volumes for patients with and without MS, and the mean differences of prostate volume showed obvious heterogeneity (\( Q = 5.9, df = 2, P = 0.053; I^2 = 66.1\% \)); thus, a random-effects model was used. The pooled estimate showed no significant difference in prostate volume between patients with and without MS (Figure 6A).

Three studies from Asia24,25,27 reported PSA for patients with and without MS, and the mean differences of PSA showed minor heterogeneity (\( Q = 3.9, df = 2, P = 0.146; I^2 = 48.1\% \)); thus, a fixed-effects model was used. The pooled estimate showed that patients with MS had higher PSA than those without MS (pooled mean difference = 0.17, 95% CI: 0.00–0.34, \( P = 0.044 \)). Two studies from Europe21,23 showed obvious heterogeneity (\( Q = 7.9, df = 1, P = 0.005; I^2 = 87.3\% \)); thus, a random-effects model was used. The pooled estimate showed no significant difference in PSA between patients with and without MS (Figure 6B).

Four studies from Asia22,24,25,27 and 3 from Europe21,23,26 reported IPSS data, and obvious heterogeneity was present in both groups (Asia: \( Q = 104.7, P < 0.001; I^2 = 97.1\% \); Europe: \( Q = 5.2, P = 0.075; I^2 = 61.4\% \)); thus, random-effects models were used. For both Asia and Europe, the pooled estimate of included studies showed no significant difference in IPSS between patients with and without MS (Figure 6C).

Two studies from Asia24,25 reported maximal flow rate data, and there was obvious heterogeneity among studies.

---

**FIGURE 3.** Meta-analysis for prostatic specific antigen. (A) Pooled estimate. (B) Sensitivity analysis.
FIGURE 4. Meta-analysis for International Prostate Symptom Score (IPSS). (A) Pooled estimate. (B) Sensitivity analysis.

FIGURE 5. Meta-analysis for maximal flow rate. (A) Pooled estimate. (B) Sensitivity analysis.
FIGURE 6. Subgroup analysis by area (Asia and Europe) (A) prostate volume (B) PSA (C) IPSS, and (D) maximal flow rate.
(Q = 130.9, P < 0.001; F = 99.2); thus, a random-effects model was used. Two studies from Europe\(^{11,26}\) reported maximal flow rate data, and minor heterogeneity was present (Q = 1.9, \(P = 0.163; F = 48.5\%\)); thus, a fixed-effects model was used. For both Asia and Europe, the pooled estimates showed no significant difference in maximal flow rate between patients with and without MS (Figure 6D).

**DISCUSSION**

This study aimed to evaluate the association of MS with characteristics of BPH. The results showed that BPH patients with MS had a significantly higher prostate growth rate and larger prostate volume than those without MS. However, IPSS and maximal flow rate were not different between BPH patients with and without MS, and a borderline nonsignificant difference in PSA between patients with and without MS was seen. Subgroup analysis by region, however, indicated that Asian patients with MS had a larger prostate volume and PSA than those without MS, but this finding was not present in European patients. Although there have been other studies examining the association between MetS and BPH, this was the first to provide a comprehensive examination of MS and various measures of BPH.

Epidemiological studies have indicated a possible association between MS and prostatic conditions,\(^{0,31}\) and some studies have shown a increased prostate growth and larger prostate volume in BPH patients with MS than those without.\(^{4-9}\) It has also been reported that MS is associated with an increased risk of LUTS as a result of prostatic enlargement.\(^{7,32}\) Age-related changes in androgens have been generally accepted to be the primary factor involved in the pathogenesis of BPH.\(^{33}\)

Although it is becoming apparent that there is an association with metabolic derangements and BPH, the mechanisms by which the derangements of MS may led to prostatic hyperplasia and LUTS remain to be fully elucidated. Some studies have suggested that insulin resistance and hyperinsulinemia are possible causative factors of BPH in patients with MS.\(^{5,34-38}\)

Other authors have suggested that chronic inflammation is the causative link between MS and LUTS and BPH. A recent systematic review of the literature by He et al\(^{39}\) suggested that the proinflammatory state present in patients with MS results in inflammatory cell infiltration of prostatic and adipose tissue with subsequent tissue remodeling and overgrowth. Prostate tissue specimens of patients with BPH have been shown to have elevated levels of inflammatory cells,\(^{39}\) and prostate volume and IPSS have been directly correlated with the level of inflammation in patients with BPH/LUTS.\(^{39}\)

In another recent meta-analysis, Giacci et al\(^{15}\) included 8 studies which enrolled 5403 patients, of which 1426 had MS. Patients with MS had a significantly higher total prostate volume as compared with those without MS (+1.8 mL, 95\% CI: 0.74–2.87; \(P < 0.001\)); however, there was no difference in IPSS or LUTS subdomain scores between the groups. Meta-regression analysis showed that differences in total prostate volume were significantly higher in older and obese patients in contrast to those with low HDL-C concentrations. The study did not examine other measures such as prostate growth rate or maximal flow. In the present study, the report by Aktas et al\(^{29}\) did not include outcome measures appropriate for the meta-analysis. The study examined the relationship between MS, erectile dysfunction (ED), and LUTS in 106 patients with BPH, account off 31.1\% (33) to whom had MS. The analysis showed a significant difference between ED groups with respect to the presence of MS (\(P = 0.032\)), but MS was not associated with the severity of LUTS (\(P = 0.144\)), nor was there a correlation between ED and LUTS severity (\(P = 0.303\)).

Other studies have examined the association of MS with various measures of BPH. In a study of 401 elderly Chinese men, Zhang et al\(^{22}\) found that body mass index (BMI), waist circumference, fasting glucose, glycosylated hemoglobin, triglyceride, fasting insulin, and insulin resistance assessed by homeostasis model assessment of insulin resistance (HOMA-IR) were higher and HDL-C was lower in BPH patients with MS than in those without MS. Furthermore, patients with MS had a significantly larger prostate volume (\(P = 0.000\)) and longer duration of LUTS (\(P = 0.006\)), and prostate volume was positively correlated with BMI (\(P = 0.000\)), fasting insulin (\(P = 0.001\)), HOMA-IR (\(P = 0.003\)) and inversely correlated with HDL-C (\(P = 0.000\)). In another study of 764 Chinese males older than 40 years, multivariate analysis showed that aging, cigarette smoking, lack of regular exercise, and larger prostate volume were independent predictors for moderate/severe LUTS, and risk factors for LUTS were influenced by the presence of MS.\(^{40}\) Ozden et al\(^{28}\) studied 78 patients with BPH and LUTS and found that those with MS had significantly higher median body weight, BMI, serum glucose, serum triglyceride, and PSA levels, but lower HDL-C level, compared with BPH patients without MS. The median annual total prostate growth rate (1.0 mL/y), and median annual transitional zone prostate growth rate (1.25 mL/y) were significantly higher in patients with MS than those without (0.64 mL/y and 0.93 mL/y, respectively, both \(P < 0.05\)). Interestingly, a study of only Chinese patients by Zou et al\(^{41}\) found that patients with MS had a significantly higher PSA level than those without MS, which is similar to the subgroup analysis of Asian patients in our study. Thus, race may be a factor contributing to the different results of different studies.

Studies have shown that the results from transabdominal ultrasonography, 1 study used transabdominal and transrectal ultrasonography, 1 study used transabdominal ultrasonography, and 2 studies used ultrasonography without mention of the site. Study has shown that the results from transabdominal ultrasonography are not consistent with those from transrectal sonography when used to measure prostate volume.\(^{42}\) and this may have led to bias in the measurement of prostate volume.
In conclusion, the results of this meta-analysis are consistent with literature indicating that BPH patients with MS have a higher prostate growth rate and larger prostate volume than those without MS. However, measures of LUTS were not different between patients with and without MS. Further study is necessary to elucidate the association of BPH and metabolic disorder elements and the potential risk of disease progression in BPH patients with MS.

ACKNOWLEDGMENT

None.

REFERENCES

1. Park YW, Min SK, Lee JH. Relationship between lower urinary tract symptoms/benign prostatic hyperplasia and metabolic syndrome in Korean men. World J Mens Health. 2012;30:183–188.
2. Platz EA, Smit E, Curhan GC, et al. Prevalence of and racial/ethnic variation in lower urinary tract symptoms and noncancer prostate surgery in US men. Urology. 2002;59:877–883.
3. Wei JT, Calhoun E, Jacobsen SJ. Urologic diseases in America project: benign prostatic hyperplasia. J Urol. 2008;179(5 suppl): S75–S80.
4. Nandeesha H, Koner BC, Dorrarajan LN, et al. Hyperinsulinemia and dyslipidemia in non-diabetic benign prostatic hyperplasia. Clin Chim Acta. 2006;370:89–93.
5. Hammarsten J, Högstedt B. Hyperinsulinæmia as a risk factor for developing benign prostatic hyperplasia. Eur Urol. 2001;39:151–158.
6. Lee S, Min HG, Choi SH, et al. Central obesity as a risk factor for prostatic hyperplasia. Obesity (Silver Spring). 2006;14:172–179.
7. Lee RK, Chung D, Chughtai B, et al. Central obesity as measured by waist circumference is predictive of severity of lower urinary tract symptoms. BJU Int. 2011;10:540–545.
8. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/ National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 2005;112:2735–2752.
9. Churilla JR, Fitzhugh EC, Thompson DL. The metabolic syndrome: how definition impacts the prevalence and risk in U.S. adults: 1999–2004 NHANES. Metab Syndr Relat Disord. 2007;5:331–342.
10. Jiang M, Strand DW, Franco OE, et al. PPAR: a molecular link between systemic metabolic disease and benign prostate hyperplasia. Differentiation. 2011;82:220–236.
11. Donnell RF. Benign prostate hyperplasia: a review of the year’s progress from bench to clinic. Curr Opin Urol. 2011;21:22–26.
12. Vikram A, Jena GB, Ramarao P. Increased cell proliferation and contractility of prostate in insulin resistant rats: linking hyperinsuliniæmia with benign prostate hyperplasia. Prostate. 2010;70:79–89.
13. Hammarsten J, Hogstedt B, Holthuis N, et al. Components of the metabolic syndrome- risk factors for the development of benign prostatic hyperplasia. Prostate Cancer Prostatic Dis. 1998;1:157–162.
14. Pan JG, Jiang C, Luo R, et al. Association of metabolic syndrome and benign prostatic hyperplasia in Chinese patients of different age decades. Urol Int. 2014;93:10–16.
15. Gacci M, Corona G, Vignozzi L, et al. Metabolic syndrome and benign prostatic enlargement: a systematic review and meta-analysis. BJU Int. 2015;115:24–31.
16. Donna F, Stroup Jesse A, Berlin Sally C, et al. David Williamson Drummond Rennie David Moher Betsy J Becker Theresa Ann Sipe Stephen B. Thacker, for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. JAMA. 2000;283:2008–2012.
17. Wells GA, Shea B, O’Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm.
18. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol. 2005;5:13.
19. Higgins JPT, Green S, eds. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. The Cochrane Collaboration. 2011. Available at: http://www.cochrane-handbook.org. Updated in March 2011.
20. Sutton AJ, Duval SJ, Tweedie RL, et al. Empirical assessment of effect of publication bias on meta-analyses. BMJ. 2000;320:1574–1577.
21. Gacci M, Sebastianelli A, Salvi M, et al. Central obesity is predictive of persistent storage LUTS after surgery for benign prostatic enlargement: results of a multicenter prospective study. BJU Int. 2015;116:271–277.
22. Cyrus A, Kahib A, Goodarzi D, et al. Impact of metabolic syndrome on response to medical treatment of benign prostatic hyperplasia. Korean J Urol. 2014;55:814–820.
23. De Nunzio C, Cindolo L, Gacci M, et al. Metabolic syndrome and lower urinary tract symptoms in patients with benign prostatic enlargement: a possible link to storage symptoms. Urology. 2014;84:1181–1187.
24. Zhang X, Zeng X, Liu Y, et al. Impact of metabolic syndrome on benign prostatic hyperplasia in elderly Chinese men. Urol Int. 2014;93:214–219.
25. Pan JG, Liu M, Zhou X. Relationship between lower urinary tract symptoms and metabolic syndrome in a Chinese male population. J Endocrinol Invest. 2014;37:339–344.
26. Gacci M, Vignozzi L, Sebastianelli A, et al. Metabolic syndrome and lower urinary tract symptoms: the role of inflammation. Prostate Cancer Prostatic Dis. 2013;16:101–106.
27. Cao B, Sun HB, Su JH, et al. [Correlation between metabolic syndrome and clinical progression in patients with benign prostatic hyperplasia]. Zhonghua Yi Xue Za Zhi. 2010;90:2823–2825[Article in Chinese].
28. Ozden C, Ozdal OL, Urgancioglu G, et al. The correlation between metabolic syndrome and prostatic growth in patients with benign prostatic hyperplasia. Eur Urol. 2007;51:199–203.
29. Aktas BK, Gokkaya CS, Bulut S, et al. Impact of metabolic syndrome on erectile dysfunction and lower urinary tract symptoms in benign prostatic hyperplasia patients. Aging Male. 2011;14:48–52.
30. Kupelian V, McVary KT, Kaplan SA, et al. Association of lower urinary tract symptoms and the metabolic syndrome: results from the Boston area community health survey. J Urol. 2013;189(Suppl.):S107–S114.
31. De Nunzio C, Aronson W, Freedland SJ, et al. The correlation between metabolic syndrome and prostatic diseases. Eur Urol. 2012;61:560–570.
32. Laven BA, Orsini N, Andersson SO, et al. Birth weight, abdominal obesity and the risk of lower urinary tract symptoms in a population based study of Swedish men. J Urol. 2008;179:1891–1895.
33. Ho CK, Habib FK. Estrogen and androgen signaling in the pathogenesis of BPH. Nat Rev Urol. 2011;8:29–41.
34. Dahle SE, Chokkalingam AP, Gao YT, et al. Body size and serum levels of insulin and leptin in relation to the risk of benign prostatic hyperplasia. J Urol. 2002;168:599–604.
35. Landsberg L. Diet, obesity and hypertension: a hypothesis involving insulin, the sympathetic nervous system, and adaptive thermogenesis. *Q J Med.* 1986;61:1081–1090.

36. Peehl DM, Cohen P, Rosenfeld RG. The role of insulin-like growth factors in prostate biology. *J Androl.* 1996;17:2–4.

37. Kasturi S, Russell S, McVary KT. Metabolic syndrome and lower urinary tract symptoms secondary to benign prostatic hyperplasia. *Curr Urol Rep.* 2006;7:288–292.

38. Shieh SM, Sheu WH, Shen DC, et al. Glucose, insulin, and lipid metabolism in doxazosin-treated patients with hypertension. *Am J Hypertens.* 1992;5:827–831.

39. He Q, Wang Z, Liu G, et al. Metabolic syndrome, inflammation and lower urinary tract symptoms: possible translational links. *Prostate Cancer Prostatic Dis.* 2016;19:7–13.

40. Yeh HC, Liu CC, Lee YC, et al. Associations of the lower urinary tract symptoms with the lifestyle, prostate volume, and metabolic syndrome in the elderly males. *Aging Male.* 2012;15:166–172.

41. Zou C, Gong D, Fang N, et al. Meta-analysis of metabolic syndrome and benign prostatic hyperplasia in Chinese patients. *World J Urol.* 2016;34:281–289.

42. Babaei Jandaghi A, Shakiha M, Nasseh H, et al. Application of bland-altman method in comparing transrectal and transabdominal ultrasonography for estimating prostate volume. *Iran J Med Sci.* 2015;40:34–39.

43. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA.* 2001;285:486–497.

44. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med.* 1998;15:539–553.

45. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation.* 2009;120:1640–1645.

46. Song X, Ji L. [Global consensus on the International Diabetes Federation (IDF) about the metabolic syndrome]. *Chinese Journal of Diabetes.* 2005;13:178–180[Article in Chinese].