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SYSTEMATIC REVIEW AND META-ANALYSIS

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The Association Between Metabolic Syndrome and Characteristics of Benign Prostatic Hyperplasia

A Systematic Review and Meta-Analysis

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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 prostate 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.

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.

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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.

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]

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Furthermore, recent evidence is suggesting a link between MS and prostatic hyperplasia and LUTS.[5,10–13] In contrast with results from the United States and European countries, results from Asian populations have been inconsistent.[1] One study indicated that MS was not clearly correlated with LUTS/BPH in Korean men in their 50s,[1] whereas the results of another study indicated that MS was associated with an increased total volume and annual prostate growth rate.[14] 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.[15]

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.[16] 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.[17] 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.[18] Pooled mean differences were compared between groups. Heterogeneity among the studies was assessed by the Cochran Q and the I^2 statistic.[19] If either the Q statistic value of P was <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.[20] All analyses were performed with Comprehensive Meta-Analysis software, version 2.0 (Biostat, Englewood, NJ).

ETHICS

This study did not involve human subjects, so informed consent was not required. In addition, no approval was required from an institutional review board.

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.[21–28] The study by Aktas et al[29] 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.[25,27,28] 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 $= 0.67$ 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.[21–28] Significant 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 $= 6.8$ 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).

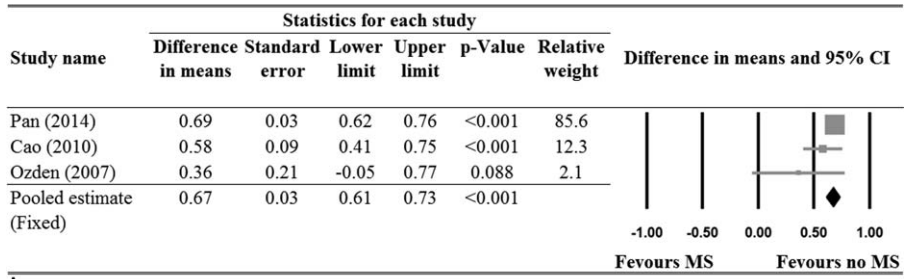
TABLE 1. Basic Characteristics of Included Studies

First Author (Publication Year)	Population	Study Design	Definition of Metabolic Syndrome	Imaging Techniques for Prostate Volume	Group	Number of Patients	Age, y	BMI, kg/m^2	IPSS	Newcastle-Ottawa Scale
Gacci et al (2015)[21]	Italy	Prospective	NCEP-ATP III[43]	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	
Cyrus et al (2014)[22]	Iran	Cohort	WHO criteria[44]	Transrectal ultrasonography	With MS	47	62.5 ± 9.6	NR	16.95 ± 8.54	8
					Without MS	53		NR	16.81 ± 7.01	
De Nunzio et al (2014)[23]	Italy	Cohort	NCEP-ATP III	Transrectal ultrasonography	With MS	103	68.8 ± 6.3	29.8 ± 4.3	9.7 ± 6.8	8
					Without MS	328	65.9 ± 8.4	26.5 ± 3.3	9.6 ± 7.2	
Zhang et al (2014)[24]	China	Cohort	NCEP-ATP III	Transrectal ultrasonography	With MS	222	76.93 ± 5.85	26.18 ± 2.78	11.18 ± 7.52	8
					Without MS	179	77.75 ± 5.78	23.45 ± 2.50	11.20 ± 7.96	
Pan et al (2014)[25]	China	Retrospective cohort	NCEP-ATP III	Ultrasonography	With MS	418	68.44 ± 9.82	28.20 ± 2.16	24.80 ± 3.93	7
					Without MS	634	71.24 ± 5.93	24.14 ± 1.20	18.58 ± 2.87	
Gacci et al (2013)[26]	Italy	Retrospective	IDF and AHA/ NHLBI[45]	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	
Aktas et al[29] (2011)*	Turkey	Cohort	NCEP-ATP III	Transrectal and transabdominal ultrasonography	With MS	33	60.41 ± 6.75	NR	IPSS 0–7: 14 IPSS 8–19: 16 IPSS 20–35: 3	8
					Without MS	73		NR	IPSS 0–7: 19 IPSS 8–19: 50 IPSS 20–35: 4	
Cao et al (2010)[27]	Chinese	Retrospective cohort	Modified IDF[46]	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	20.41 ± 4.98	
Ozden et al (2007)[28]	Turkey	Prospective	NCEP ATP III	Transrectal ultrasonography	With MS	38	59 (50–83)†	28.7 (21.2–36.7)†	22 (10–32)†	8
					Without MS	40	60 (50–72)†	25.4 (19.5–31.9)†	20 (10–33)†	

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.

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

†Data are presented as median (full range). All other data are presented as mean ± standard deviation.



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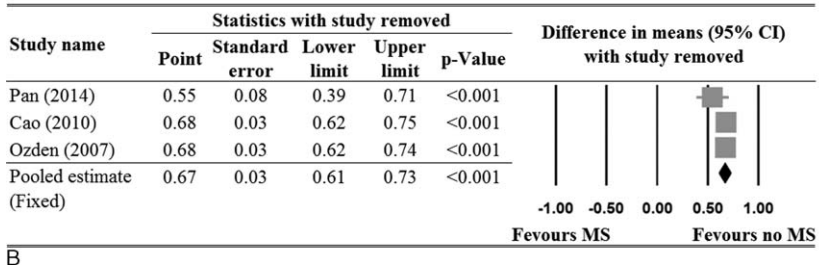

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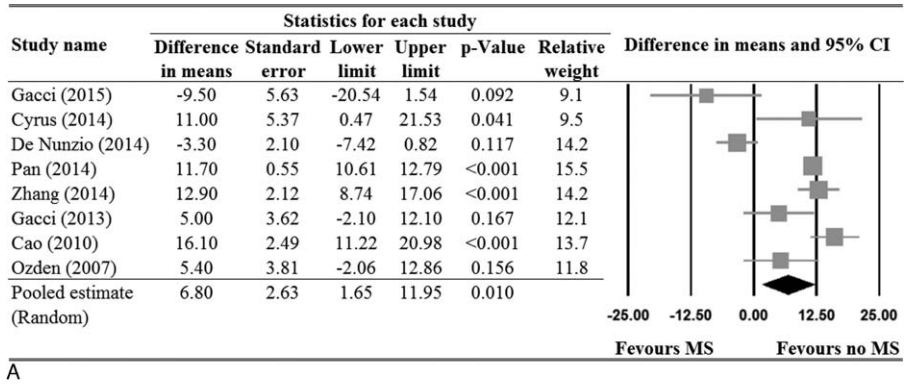
FIGURE 1. Meta-analysis for prostate growth rate. (A) Pooled estimate. (B) Sensitivity analysis.

PSA

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, $P = .056$; Figure 3A). The pooled mean differences of PSA with each of the studies removed



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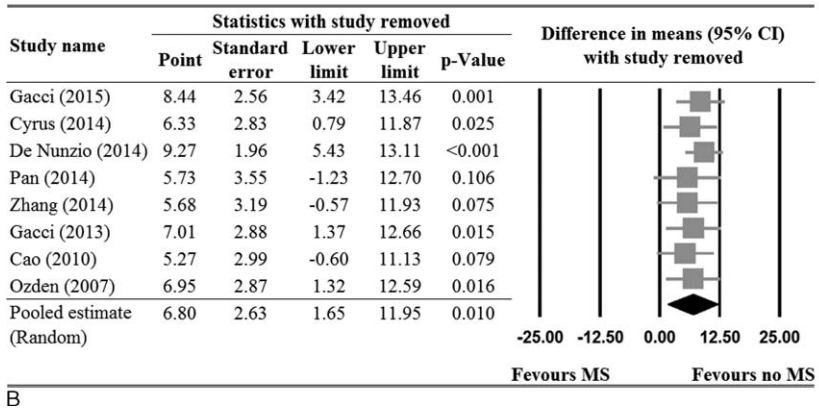

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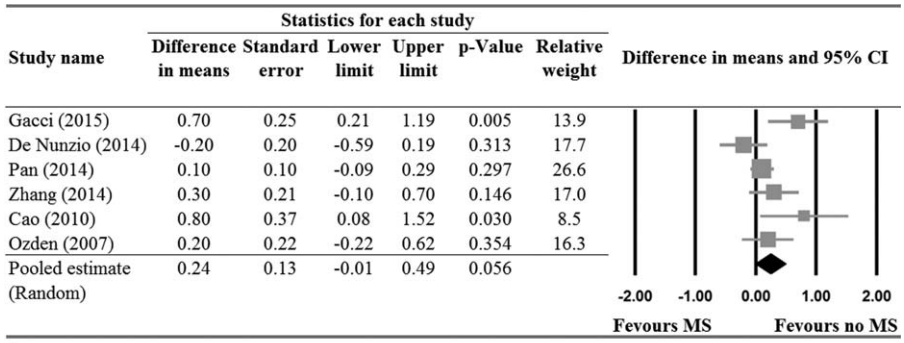
FIGURE 2. Meta-analysis for prostate volume. (A) Pooled estimate. (B) Sensitivity analysis.



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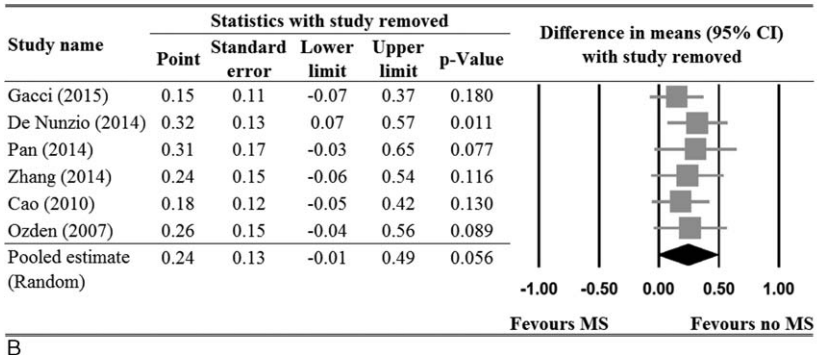

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FIGURE 3. Meta-analysis for prostatic specific antigen. (A) Pooled estimate. (B) Sensitivity analysis.

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, $P = .202$; 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 = −1.41 mL/s, $P = 0.345$; 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)

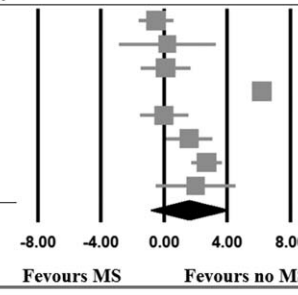
Subgroup analyses by region (Asia and Europe) for prostate volume, PSA, IPSS, and maximal flow rate were performed to reduce the heterogeneity among the included studies. Four studies from Asia[22,24,25,27] reported prostate volumes for patients with and without MS, and the mean differences of prostate 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 Europe[21,23,26] 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 Asia[24,25,27] 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 Europe[21,23] 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 Asia[22,24,25,27] and 3 from Europe[21,23,26] 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 Asia[24,25] reported maximal flow rate data, and there was obvious heterogeneity among studies

Study name	Statistics for each study						Difference in means and 95% CI
	Difference in means	Standard error	Lower limit	Upper limit	p-Value	Relative weight	
Gacci (2015)	-0.50	0.55	-1.58	0.58	0.362	13.0	
Cyrus (2014)	0.20	1.55	-2.84	3.24	0.897	11.0	
De Nunzio (2014)	0.10	0.80	-1.47	1.67	0.901	12.6	
Pan (2014)	6.20	0.21	5.79	6.61	<0.001	13.3	
Zhang (2014)	0.00	0.78	-1.52	1.52	1.000	12.7	
Gacci (2013)	1.60	0.74	0.14	3.06	0.031	12.7	
Cao (2010)	2.70	0.48	1.75	3.65	0.000	13.1	
Ozden (2007)	2.00	1.28	-0.51	4.51	0.119	11.7	
Pooled estimate (Random)	1.58	1.24	-0.85	4.01	0.202		



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Study name	Statistics with study removed					Difference in means (95% CI) with study removed
	Point	Standard error	Lower limit	Upper limit	p-Value	
Gacci (2015)	1.90	1.23	-0.50	4.31	0.121	
Cyrus (2014)	1.75	1.32	-0.83	4.33	0.183	
De Nunzio (2014)	1.80	1.32	-0.79	4.38	0.174	
Pan (2014)	0.89	0.59	-0.27	2.04	0.131	
Zhang (2014)	1.81	1.32	-0.77	4.39	0.168	
Gacci (2013)	1.58	1.37	-1.12	4.27	0.251	
Cao (2010)	1.40	1.51	-1.56	4.37	0.353	
Ozden (2007)	1.53	1.34	-1.10	4.15	0.255	
Pooled estimate (Random)	1.58	1.24	-0.85	4.01	0.202	

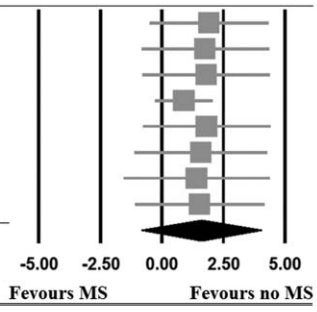

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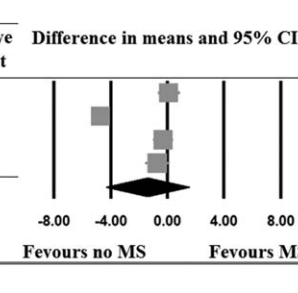
FIGURE 4. Meta-analysis for International Prostate Symptom Score (IPSS). (A) Pooled estimate. (B) Sensitivity analysis.

Study name	Statistics for each study						Difference in means and 95% CI
	Difference in means	Standard error	Lower limit	Upper limit	p-Value	Relative weight	
Gacci (2015)	0.10	0.38	-0.64	0.84	0.792	24.9	
Pan (2014)	-4.70	0.13	-4.95	-4.45	<0.001	25.3	
Zhang (2014)	-0.30	0.36	-1.01	0.41	0.408	25.0	
Gacci (2013)	-0.70	0.43	-1.54	0.14	0.104	24.8	
Pooled estimate (Random)	-1.41	1.50	-4.35	1.52	0.345		



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Study name	Statistics with study removed					Difference in means (95% CI) with study removed
	Point	Standard error	Lower limit	Upper limit	p-Value	
Gacci (2015)	-1.92	1.69	-5.23	1.40	0.257	
Pan (2014)	-0.27	0.22	-0.71	0.17	0.230	
Zhang (2014)	-1.78	1.78	-5.28	1.72	0.318	
Gacci (2013)	-1.65	1.83	-5.22	1.93	0.367	
Pooled estimate (Random)	-1.41	1.50	-4.35	1.52	0.345	

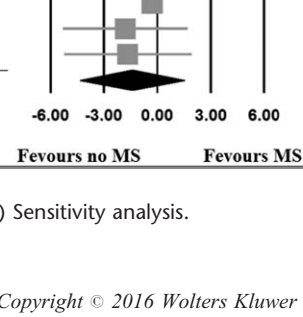

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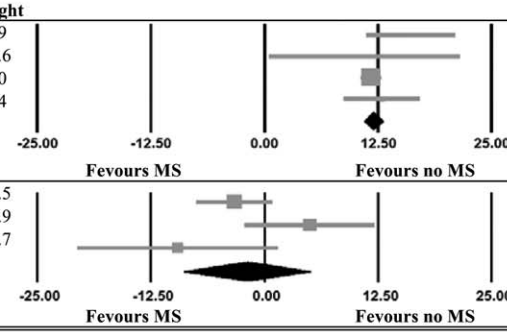
FIGURE 5. Meta-analysis for maximal flow rate. (A) Pooled estimate. (B) Sensitivity analysis.

Subgroup by area	Study name	Statistics for each study: Difference in means	Standard error	Lower limit	Upper limit	p-Value	Relative weight
Asia	Cyrus (2014)	11.00	5.37	0.47	21.53	0.041	0.9
	Pan (2014)	11.70	0.55	10.61	12.79	0.000	88.6
	Zhang (2014)	12.90	2.12	8.74	17.06	0.000	6.0
	Cao (2010)	16.10	2.49	11.22	20.98	0.000	4.4
	Pooled estimate (Fixed)	11.96	0.52	10.94	12.98	0.000	
Europe	Gacci (2015)	-9.50	5.63	-20.54	1.54	0.092	22.5
	De Nunzio (2014)	-3.30	2.10	-7.42	0.82	0.117	43.9
	Gacci (2013)	5.00	3.62	-2.10	12.10	0.167	33.7
	Pooled estimate (Random)	-1.90	3.55	-8.85	5.05	0.592	



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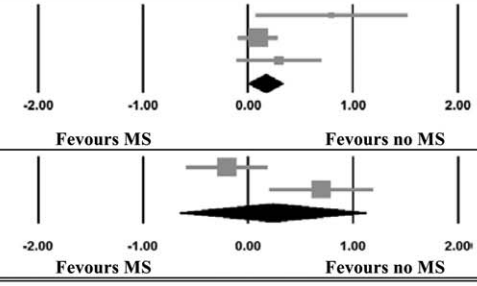
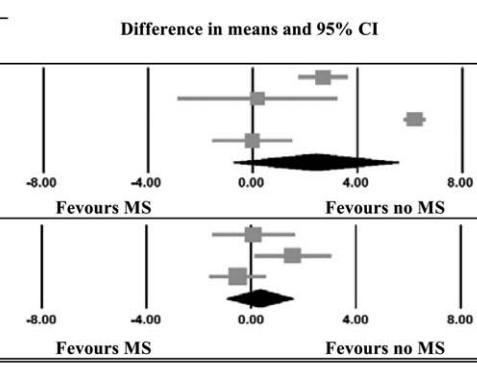
Subgroup by area	Study name	Statistics for each study: Difference in means	Standard error	Lower limit	Upper limit	p-Value	Relative weight
Asia	Pan (2014)	0.10	0.10	-0.09	0.29	0.297	77.9
	Zhang (2014)	0.30	0.21	-0.10	0.70	0.146	16.8
	Cao (2010)	0.80	0.37	0.08	1.52	0.030	5.3
	Pooled estimate (Fixed)	0.17	0.08	0.00	0.34	0.044	
Europe	Gacci (2015)	0.70	0.25	0.21	1.19	0.005	48.5
	De Nunzio (2014)	-0.20	0.20	-0.59	0.19	0.313	51.5
	Pooled estimate (Random)	0.24	0.45	-0.65	1.12	0.599	



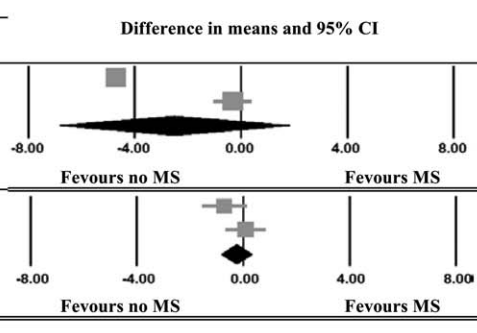
B

Subgroup by area	Study name	Statistics for each study: Difference in means	Standard error	Lower limit	Upper limit	p-Value	Relative weight
Asia	Cyrus (2014)	0.20	1.55	-2.84	3.24	0.897	21.5
	Pan (2014)	6.20	0.21	5.79	6.61	0.000	26.8
	Zhang (2014)	0.00	0.78	-1.52	1.52	1.000	25.3
	Cao (2010)	2.70	0.48	1.75	3.65	0.000	26.3
	Pooled estimate (Random)	2.42	1.61	-0.73	5.57	0.133	
Europe	Gacci (2015)	-0.50	0.55	-1.58	0.58	0.362	39.0
	De Nunzio (2014)	0.10	0.80	-1.47	1.67	0.901	29.5
	Gacci (2013)	1.60	0.74	0.14	3.06	0.031	31.5
	Pooled estimate (Random)	0.34	0.64	-0.92	1.60	0.599	



C

Subgroup by area	Study name	Statistics for each study: Difference in means	Standard error	Lower limit	Upper limit	p-Value	Relative weight
Asia	Pan (2014)	-4.70	0.13	-4.95	-4.45	0.000	50.3
	Zhang (2014)	-0.30	0.36	-1.01	0.41	0.408	49.7
	Pooled estimate (Random)	-2.51	2.20	-6.82	1.80	0.253	
Europe	Gacci (2015)	0.10	0.38	-0.64	0.84	0.792	56.3
	Gacci (2013)	-0.70	0.43	-1.54	0.144	0.10	43.7
	Pooled estimate (Fixed)	-0.25	0.28	-0.81	0.31	0.380	



D

FIGURE 6. Subgroup analysis by area (Asia and Europe) (A) prostate volume (B) PSA (C) IPSS, and (D) maximal flow rate.

($Q = 130.9$, $P < 0.001$; $I^2 = 99.2$); thus, a random-effects model was used. Two studies from Europe[21,26] reported maximal flow rate data, and minor heterogeneity was present ($Q = 1.9$, $P = 0.163$; $I^2 = 48.5\%$); 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,[30,31] and some studies have shown a increased prostate growth and larger prostate volume in BPH patients with MS than those without.[4–6] 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, Gacci 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[24] 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 in different studies.

Measures of clinical progression of BPH include quality of life, urinary retention, and risk of surgical intervention. However, these factors were not examined in the current analysis because of the 9 included studies, of which only 2 reported results of acute urinary retention, only 2 studies reported quality of life results, and only 1 study mentioned of risk of surgical intervention. Of the articles that reported rate of acute urinary retention, Pan et al[25] found acute urinary retention in 82% of patients with MS and in 17% of patients without MS, and Cao et al[27] reported a rate of 26.2% in patients with MS and 10.3% in patients without MS. Overall, the rate of acute urinary retention had tendency to be higher in patients with MetS than those without MS. As to quality of life, De Nunzio et al[23] reported no difference in quality of life between patients with and without MS. Pan et al,[25] however, reported that patients with MS had significantly higher IPSS quality of life score (4.94 ± 1.06) than did patients without MS (3.31 ± 0.95) ($P < 0.001$).

There are limitations of this analysis that have to be considered. The definition of MS used varied between the studies, and the number of available studies and data were limited. We did not examine characteristics of MS such as BMI and waist circumference, nor the mechanisms by which MS is associated with BPH examined. Five studies used transrectal 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.

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