Vitamin D Deficiency as a Potential Marker of Benign Prostatic Hyperplasia

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OBJECTIVE To determine whether prostatic volumes and urinary flow changes were higher in old Chinese men with vitamin D deficiency than in those without vitamin D deficiency.

METHODS This was an observational case-control study of 224 old Chinese men. End point variables were prostatic volume, measured by transrectal ultrasound, and urinary flow, measured by urinary flowmetry. The International Prostate Symptom Score and International Index of Erectile Function score were determined.

RESULTS Two hundred and thirty-one (71.7%) out of the 322 were defined as vitamin D deficiency. The vitamin D deficiency group had a significantly higher prostate volume (42 mL vs 28 mL, $P < .001$), aldosterone (293 pg/mL vs 220 pg/mL, $P < .001$), prostate-specific antigen value (3.28 ng/mL vs 2.55 ng/mL, $P < .001$), and IPSS (4.47 vs 1.98, $P < .001$), and a significantly lower maximum urinary flow (13.44 mL/s vs 29.98 mL/s, $P < .001$) vs free of vitamin D deficiency group. Binary logistic regression analysis showed a strong association between the presence of vitamin D deficiency and benign prostatic hyperplasia (BPH) after adjusting for age, International Prostate Symptom Score, urination time, urinary volume, abdominal obesity, aldosterone, glucose, insulin, parathyroid hormone, and C-reactive protein (odds ratio 5.22, 95% confidence interval 1.96-12.76, $P = .001$).

CONCLUSION There is a relationship between the presence of vitamin D deficiency and prostate growth-associated urinary symptoms, likely attributable to their pathophysiological similarity. This study suggests that vitamin D deficiency may be a marker of BPH. Thus, it may be used as a future therapeutic target in patients with BPH. Further studies were necessary to confirm this association. UROLOGY 97: 212–218, 2016. © 2016 Elsevier Inc.

Benign prostatic hyperplasia (BPH) is a common cause of lower urinary tract symptoms among older men.[1] BPH has a significant impact on the health of older men and healthcare costs. As the world population ages, the incidence and prevalence of BPH have increased rapidly. In a meta-analysis, Wang et al[2] reported that the pooled overall prevalence of BPH among Chinese men aged 40 years and older was 36.6% (95% confidence interval [CI] 32.3-44.8) from 1989 to 2014. BPH is due to the excess growth of both stromal and epithelial cells of the prostate. Fifty percent of men over the age of 50 will have BPH, whereas 90% of men at the age of 80 will have an enlarged prostate.[3] Whereas aging and androgens are considered to have a role in BPH development,[4] the role of other risk factors, namely, inflammation,[5] inflammatory mediators, oxidative stress, hormones,[6] physical activity, dietary factors, cardiovascular disease, obesity, and diabetes[7] had been under investigation.

Vitamin D has a well-known role in calcium metabolism and bone health. It may also help prevent a number of chronic diseases, including cardiovascular disease, diabetes, and malignancies such as breast, colorectal, and prostate cancer.[8] Epidemiological studies have suggested the association between vitamin D deficiency and BPH.[1] In a cohort study, Pitman et al[9] found that 52% of the urological patients were frankly deficient (less than 20 ng/mL) in vitamin D. They also reported that vitamin D deficiency was more common in patients younger than age 50 years (44.5%), black (53.2%) and Hispanic (41.6%) patients ($P < .001$), and patients without an existing urological malignancy (35.4%, $P < .001$). Low vitamin D promotes cell proliferation and decreases apoptosis in normal prostate cells, whereas prostate cells express vitamin D receptors.[10] The link between low vitamin D and BPH was explored by Crescioli et al.[11] In addition, an epidemiological study showed a small decrease in the risk of symptomatic BPH

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in men using supplemental vitamin D.[12] The objective of this study was to determine whether prostatic volumes and urinary flow changes were higher in old Chinese men with vitamin D deficiency than in those without vitamin D deficiency.

METHODS

Study Subjects and Design

This study included 364 Chinese men participants aged 60 to 75 years consecutively examined in the Medical Center of Zhongnan Hospital of Wuhan University, Wuhan, China from July 2015 to September 2015. Men previously diagnosed with prostate disease (N = 15); neurogenic bladder (N = 5); previous consultation with urologist or family physician for prostate problems (N = 12); and treatment with minoxidil, a-blockers, testosterone, 5-alpha-reductase inhibitors (N = 7; in the previous 6 months), or any other hormone therapy (N = 3; in previous 6 months) were excluded from study, leaving 322 available for analysis. The study was approved by the Wuhan University ethics committee. Written informed consents were obtained from all study participants.

Clinical Variables and Prostate Volume

Body height and weight were measured using standard equipment. Body mass index (BMI) was calculated by body height and weight. Lean body mass, total body fat mass, and trunk fat mass were assessed using the DXA QDR 4500/A-Delphi device (Hologic Inc., MA). Systolic and diastolic blood pressure was measured after a 5-minute rest and again 10 minutes later, recording the mean value. The prostate gland was examined by digital rectal examination and by ultrasound using 2002 ADI Panther equipment (BK Medical, Gentofte, Denmark). Prostate volume was determined by ultrasound using the ellipsoid method.[13] All participants underwent transrectal ultrasound examination at the urology department (by a single examiner who did not know the purpose of the study) to determine the prostate volume and were studied with urinary flowmetry to determine the maximum flow rate, the urination time, and volume. Tests were performed after a minimum of 4 hours without urinating.

Participants completed the International Prostate Symptom Score (IPSS) and the International Index of Erectile Function (IIEF) questionnaires. The IPSS (for prostate symptoms) comprises 7 items scored from 0 to 5, giving a maximum global score of 35 points. The IIEF test comprises 30 items on the frequency of erection during sexual activity, number of sexual partners, and ejaculation and satisfaction in sexual relationships, yielding a maximum score of 30 points. BPH was defined by the following: prostate volume greater than 30 mL (by transrectal ultrasound), peak urinary flow rate less than 15 mL/s, mean urinary flow rate less than 10 mL/s, void volume of 200 to 400 mL, and prostate-specific antigen (PSA) less than 10 ng/mL.[14] Two hundred and fifteen out of the 322 participants were defined as BPH according to the above criteria.

Blood Sampling and Laboratory Testing

All tests were done after an overnight fast and at least 8 hours of nonsmoking on morning blood samples that were never previously thawed. After centrifugation, serum of the samples were immediately stored at −80°C before assay. Serum 25(OH) D levels were measured by the E601 modular (Roche Diagnostics, Mannheim, Germany). In our study, the limit of detection was 3 ng/mL and calibration range was from 3 to 75 ng/mL. The intra-assay coefficient of variation and interassay coefficient of variation were 1.8%-3.0% and 2.0%-3.5%, respectively. Vitamin D status was classified by the serum 25(OH) D levels into vitamin D deficiency (<20 ng/mL) and vitamin D insufficiency (20~ 30 ng/mL).[15] In addition, aldosterone, total testosterone, parathyroid hormone (PTH), prolactin, estrogen, albumin, PSA, sex hormone-binding globulin, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, glycemia, insulin, and C-reactive protein (CRP) were also tested by routine techniques.

Statistical Analyses

In our study, results are expressed as medians (interquartile ranges) or means (standard deviation) for the continuous variables and percentages for categorical variables. Variables were compared between groups by using Mann-Whitney *U* test or chi-square test as appropriate. The Spearman rank-correlation coefficient was used to assess correlations among continuous variables. The participants were divided into 2 groups according to serum 25(OH) D levels, namely, vitamin D deficiency group and control group (included vitamin D insufficiency and normal levels). Associations between vitamin D deficiency and prostate volume and urinary flow were assessed using linear regression models in multivariate adjustment for possible confounders. The results are expressed as adjusted odds ratios (ORs) with the corresponding 95% CIs. Vitamin D levels were also examined as a continuous variable in multivariate logistic regression models to predict BPH. Receiver operating characteristic curve was also utilized to evaluate the accuracy of serum 25(OH) D to diagnose BPH. Area under the curve (AUC) was calculated as measurements of the accuracy of the test. Statistical significance was defined as $P < .05$. All statistical analysis was performed with SPSS for Windows (version 20.0, SPSS Inc., Chicago, IL).

RESULTS

All 322 participants completed the study. The median serum level of 25(OH) D in our participants was 14.95 ng/mL. Two hundred and thirty-one (71.7%) out of the 322 were defined as vitamin D deficiency. In addition, the proportions of participants with insufficiency and normal levels were 21.7% and 6.6%, respectively. The baseline subject characteristics were listed in Table 1. Participants with vitamin D deficiency were older and more frequently of TDM, and with family history of BPH. Participants with vitamin D deficiency had a significantly greater abdominal perimeter (112.5 cm vs 94.3 cm, $P < .001$) and glucose levels (111.5 mg/dL vs 85.4 mg/dL, $P = .013$) than control subjects, respectively. No significant differences were observed in body mass index, blood

Table 1. Baseline subject characteristics

Baseline Characteristics	Participants (N = 322)
Age (years, IQR)	67 (63-72)
BMI (kg/m^2, IQR)	27.5 (24.6-29.3)
Cardiovascular and cerebrovascular diseases, n (%)	112 (34.8)
T2DM, n (%)	81 (25.2)
Maximum flow (mL/s, IQR)	17.55 (11.13-22.02)
IIEF score (IQR)	30.05 (22.98-36.69)
IPSS (IQR)	3.76 (2.24-4.76)
CRP (mg/L)	6.3 (3.2-10.2)
Triglycerides (mmol/L)	1.55 (1.22-1.78)
Cholesterol (nmol/L)	
LDL	3.54 (2.66-4.02)
HDL	1.27 (0.98-1.66)
25(OH) vitamin D (ng/mL)	14.95 (10.98-21.02)
Albumin corrected serum calcium (mg/dL)	4.24 (3.88-4.40)
Fasting serum insulin (mU/L)	10.2 (4.5-18.8)
Fasting serum glucose (mmol/L)	5.65 (5.12-6.04)
Estradiol (pg/mL)	26.7 (15.4-34.8)
SHBG (nM)	48.5 (24.5-67.4)
Testosterone (ng/mL)	4.85 (4.00-6.08)
Aldosterone (pg/mL)	275 (163-443)
PTH (pg/mL)	41.2 (32.4-53.8)
PSA (ng/mL)	2.98 (2.55-4.04)

BMI, body mass index; CRP, C-reactive protein; IIEF, International Index of Erectile Function; IPSS, International Prostate Symptom Score; IQR, interquartile range; PSA, prostate-specific antigen; PTH, parathyroid hormone; SHBG, sex hormone-binding globulin; T2DM, type 2 diabetes mellitus.

pressure, total testosterone, sex hormone-binding globulin, free testosterone, estradiol, albumin, triglyceridemia, high-density lipoprotein cholesterol, or low-density lipoprotein cholesterol in participants with vitamin D deficiency and control subjects ($P > .05$, respectively). Biochemical analyses revealed that participants with vitamin D deficiency presented higher significant insulin levels (11.7 U/mL vs 7.0 U/mL, $P \leq .001$), CRP (0.52 mg/dL vs 0.30 mg/dL, $P = .005$), PTH (44.5 pg/mL vs 37.2 pg/mL; $P = .002$), and aldosterone (293 pg/mL vs. 220 pg/mL, $P < .001$) than the control group. No differences in IIEF score, alcohol consumption, diet (sodium intake), sedentarism, smoking, antihypertensives, anticholesterolemics, or oral antidiabetic intake were found between groups.

The vitamin D deficiency group had a significantly higher prostate volume, aldosterone, PTH and PSA value, and IPSS, and a significantly lower maximum urinary flow vs the control group (Table 2). In addition, the vitamin D deficiency group had a significantly lower mean urinary *flow rate* vs the control group (8.56 mL/s vs 18.13 mL/s). 25(OH) D levels decreased with increasing prostate volume. There was a significantly negative correlation between levels of 25(OH) D and prostate volume ($r = -0.399$, $P < .001$). There was no direct association between serum PSA and 25(OH) D in participants with vitamin D deficiency and participants free of vitamin D deficiency ($P > .05$, respectively). Levels of 25(OH) D were compared based on 4 seasons of blood sampling. Significant seasonal differences in 25(OH) D levels were observed (analysis of variance, $P = .003$). In addition, prostate volume was also negatively correlated with maximum urinary flow ($r = -0.406$, $P < .001$) and positively correlated with IPSS ($r = 0.443$, $P < .001$).

The vitamin D deficiency group had a significantly lower urination volume (255.43 mL vs 332.54 mL, $P = .005$) and lower urination time (45.34 seconds vs 54.43 seconds, $P = .012$) in comparison with control group. The prostate volume was greater than 30 mL in 91.3% of participants with vitamin D deficiency vs 39.6% of control subjects ($P < .0001$). Maximum urinary flow was greater than 15 mL/s in 87.9% of control subjects vs 21.6% of participants with vitamin D deficiency ($P < .001$). BPH diagnostic criteria were met by 86.6% of participants with vitamin D deficiency vs 16.5% of control subjects ($P < .001$).

In our study, 215 participants were defined as BPH. We found serum aldosterone levels significantly higher in BPH patients ($P = .008$). BPH patients had significantly higher serum PSA levels ($P = .01$). The median serum levels of 25(OH) D in participants with BPH were significantly lower when compared with controls (12.75 [interquartile range, 11.22-15.76] ng/mL vs 14.84 [12.05-21.59] ng/mL; $P < .0001$). Based on the receiver operating characteristic

Table 2. Median (IQRs) levels of various parameters in participants with vitamin D deficiency and control subjects

	Vitamin D Deficiency	Control Group†	*P* Value*
N	231	91	
Prostate volume (mL, IQR)	42 (33-49)	28 (22-36)	<.001
Maximum flow (mL/s, IQR)	13.44 (9.75-18.87)	23.44 (14.98-29.75)	<.001
IIEF score (IQR)	30.12 (22.65-36.48)	29.98 (23.12-37.01)	.252
IPSS (IQR)	4.47 (3.02-5.85)	1.98 (1.23-3.01)	<.001
Serum levels (IQR)			
Testosterone (ng/mL)	4.87 (4.02-6.11)	4.93 (4.05-6.04)	.332
Aldosterone (pg/mL)	293 (188-478)	220 (155-308)	<.001
Albumin (mg/dL)	4.22 (3.89-4.42)	4.25 (3.87-4.37)	.530
PTH (pg/mL)	44.5 (33.2-61.9)	37.2 (32.3-50.5)	.002
SHBG (nmol/L)	40.12 (28.09-59.32)	41.05 (27.65-60.22)	.192
PSA (ng/mL)	3.28 (2.94-4.49)	2.55 (2.02-3.27)	<.001

Abbreviations as in Table 1.

* Mann-Whitney *U* test for comparison of quantitative variables after establishing their non-normal distribution by means of Shapiro-Wilk test and Levene test for equality of variance.

† Control group was defined as participants with vitamin D insufficiency and normal levels.

Table 3. Binary logistic regression analyses showed a strong association between the presence of vitamin D deficiency and a prostate volume greater than 30 mL after adjusting for age, aldosterone, CRP, PTH, glucose, insulin, urination volume, urination time, and IPSS

Predictor	OR*	95% CI	*P*
Vitamin D deficiency	10.12	2.23-25.32	.002
Age	1.10	1.01-1.35	.041
Aldosterone	1.08	1.02-1.15	.015
CRP	1.35	1.19-1.72	.037
PTH	2.02	1.36-3.07	.005
Glucose	1.75	0.92-3.47	.426
Insulin	2.10	0.68-5.43	.225
Urination time	0.99	0.95-1.04	.073
Urinary volume	1.17	0.95-3.87	.332
IPSS	1.49	1.15-2.04	.014

CI, confidence interval; OR, odds ratio; other abbreviations as in Table 1.
* Note that the OR corresponds to a unit increase in the explanatory variable.

Table 4. Binary logistic regression analysis showing that vitamin D deficiency was found to be an independent risk factor for maximum urinary flow less than 15 mL/s after adjusting for age, aldosterone, CRP, PTH, glucose, insulin, prostate volume, urination time, urinary volume, and IPSS

Predictor	OR*	95% CI	*P*
Vitamin D deficiency	6.99	1.49-21.16	.011
Age	1.23	0.99-2.03	.079
Aldosterone	1.04	1.01-1.09	.027
CRP	1.44	0.92-3.37	.328
PTH	1.87	1.29-3.16	.006
Glucose	1.05	0.99-1.27	.063
Insulin	1.79	1.05-3.02	.036
Prostate volume	1.15	0.99-1.40	.075
Urination time	1.09	1.02-1.21	.022
Urinary volume	0.94	0.87-0.98	.002
IPSS	1.54	1.16-1.99	.009

Abbreviations as in Tables 1 and 2.
* Note that the OR corresponds to a unit increase in the explanatory variable.

curve, the optimal cutoff value of serum 25(OH) D levels as an indicator for diagnosing of BPH was projected to be 15.55 ng/mL, which yielded a sensitivity of 78.3% and a specificity of 71.4%, with the AUC at 0.74 (95% CI 0.65-0.82). With an AUC of 0.74, 25(OH) D showed a significantly greater discriminatory ability as compared with CRP (AUC 0.64; 95% CI 0.56-0.73; $P = .03$), age (AUC 0.59, 95% CI 0.53-0.66; $P < .001$), and aldosterone (AUC 0.65, 95% CI, 0.57-0.73; $P = .03$). The 15.55 ng/mL defined as the optimal cutoff value for diagnosing of BPH yielded a false positive rate of 44.1% and a false negative rate of 16.3%. 25(OH) D levels were also examined as a continuous variable in logistic regression models to predict BPH. With an unadjusted OR of 0.848 (95% CI 0.799-0.906, $P < .0001$), 25(OH) D had a strong association with BPH. After adjusting for all other significant predictors, 25(OH) D remained an independent BPH predictor with an adjusted OR of 0.902 (95% CI 0.864-0.943, $P < .0001$).

Binary logistic regression analysis showed a strong association between the presence of vitamin D deficiency and a prostate volume greater than 30 mL after adjusting for age, aldosterone, CRP, glucose, insulin, urination volume, urination time, and IPSS (OR 10.12, 95% CI 2.23-25.32; $P = .002$; Table 3). Vitamin D deficiency was found to be an independent risk factor for a urinary flow less than 15 mL/s after adjusting for age, aldosterone, CRP, glucose, insulin, prostate volume, urination time, urinary volume, and IPSS (OR 6.99, 95% CI 1.49-21.16; $P = .011$; Table 4). The presence of vitamin D deficiency was also an independent risk factor for the presence of BPH after adjusting for age, IPSS, urination time, urinary volume, abdominal obesity, aldosterone, glucose, insulin, PTH, and CRP (OR 5.22, 95% CI 1.96-12.76, $P = .001$).

DISCUSSION

BPH is a prevalent and chronic progressive disease that may be correctly defined as prostate gland enlargement secondary to hyperproliferation of stromal and glandular cells, with predominance of mesenchymal cells.[16] Aging and the presence of androgens are necessary for the development of BPH, but the pathogenesis of BPH is still unresolved. Recent clinical trials have suggested a relationship between prostatic inflammations and lower urinary tract symptoms related to BPH.[17] In this study, old Chinese men with vitamin D deficiency were found to have a larger prostate, higher IPSS, and lower urinary flow value in comparison with men free of vitamin D deficiency, suggesting that the vitamin D deficiency could be implicated in the pathophysiology of BPH in old Chinese men and can be used as an independent risk factor for BPH. Consistently with our findings, Haghsheno et al[4] reported that low vitamin D might be an important factor contributing to BPH development. In addition, vitamin D deficiency (55%) is highly prevalent among adult men in the United States.[18] Similarly, vitamin D deficiency is very common in old Chinese men (71.7%).

Although the pathogenesis of BPH is not yet fully understood and several mechanisms seem to be involved in the development and progression, recent studies strongly suggest that BPH is an immune inflammatory disease.[19] Men with acute or chronic inflammation had larger prostate volumes (41.1 mL vs 36.8 mL; $P = .002$).[20] In another prospective study of autopsy specimens obtained from 93 men who had histologic evidence of BPH, chronic inflammation was found in 75% of prostates examined compared with 55% of prostates not affected by BPH.[21] Vitamin D deficiency might increase prostate volume through inflammation. However, in binary logistic regression analyses, vitamin D deficiency still was an independent risk factor for BPH after adjusted CRP. Some other possible mechanisms need to be considered.

Firstly, prostate epithelial cells can produce the biologically more active 1, 25-OH vitamin D3 from 25-OH vitamin D3.[22] Also, normal and prostate cancer epithelial cells express vitamin D receptor. By binding to vitamin

D receptor, vitamin D can increase cell differentiation, decrease cell proliferation, and increase apoptosis.[23] Secondly, Habuchi et al[24] indicated that the *BsmI* polymorphism in the vitamin D receptor (VDR) gene plays a significant role in protection against BPH. A review finished by Adorini et al[25] demonstrate that VDR agonists, and notably elocalcitol, reduce the static component of BPH by inhibiting the activity of intraprostatic growth factors downstream of the androgen receptor, the dynamic component by targeting the RhoA/ROCK pathway in prostate and bladder cells, and the inflammatory component by targeting the NF-kappaB pathway. Thirdly, patients with vitamin D deficiency have a higher prevalence of cardiovascular risk factors. Several pathogenic mechanisms have been suggested to explain the increase in cardiovascular risk.[26] Interestingly, some studies suggest that BPH is associated with abdominal obesity,[27] insulin levels, diabetes, hypertension,[28] and systemic inflammation. We also have found a positive significant correlation between some of these parameters and prostate volume. Fourthly, vitamin D deficiency can play a role in BPH through oxidative stress.[29] Lastly, a previous study strongly favored a link between the renin-angiotensin system and vitamin D and BPH pathogenesis.[30] Similarly, in our study we also found that the vitamin D deficiency and the BPH group had a significantly higher serum aldosterone value.

The current study has 5 important limitations. These are the following:

(1) In this context, the study population is somewhat small. Further, its members have a very high prevalence of both BPH and vitamin D deficiency.
(2) The study included only Chinese males who were mainly Chinese. Thus, our findings must be applied with caution to other populations.
(3) Third, we did not have the resources to measure serum vitamin D-binding protein and VDR in our samples. Vitamin D-binding protein and VDR might play role in the BPH.[24]
(4) We adjusted for many risk factors in the multivariate analysis, but the possibility of residual confounding remains. We cannot exclude the possibility that residual confounding factors, including dementia or a poorer health status, may have been missed. Moreover, we also did not obtain information about the daily diet and level of activity, which may affect 25(OH) D metabolisms. Therefore, we could not adjust multivariable analysis for these variables. In addition, previous study suggested that the avoidance of smoking may benefit BPH.[31] We did not collect the information about smoking status.
(5) Lastly, in our study, we found that vitamin D deficiency is still an independent risk factor for BPH. The more interesting question would be whether vitamin D supplements can decrease prostate volume in BPH patients or prevent prostatic hypertrophy in the normal population. However, the cross-sectional design severely limits the interpretability of the data. Previous study suggested that increasing intake of vitamin D from diet and supplements has shown a correlation with decreased BPH prevalence. Vitamin D analogues of up to 6000 IU/day have shown to decrease prostate volume in BPH patients.[12] Similarly, Colli et al[32] found that BXL628, a vitamin D3 analog, was able to arrest prostate growth within 12 weeks in men aged ≥50 years with prostatic volume ≥40 mL. Further subsequent longitudinal studies are necessary to determine the role of vitamin D on BPH in our population.

CONCLUSION

This preliminary study was the first, to our knowledge, to demonstrate a strong relationship between vitamin D deficiency and BPH in old Chinese men. It suggested that vitamin D deficiency was an independent risk factor of BPH after adjustment by variables. Thus, it may be used as a future therapeutic target in patients with BPH. Further studies are necessary to confirm this association.

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EDITORIAL COMMENT

This paper describes a cross-sectional association between lower 25-hydroxy Vitamin D (25(OH) vitamin D) levels and a working diagnosis of benign prostatic hyperplasia (BPH) in a cohort of men aged 60-75 seen at a single medical center in China.[1] BPH was defined primarily based on prostate volume and urinary flow rates, but not symptoms. There were 215/322 (72%) of participants who were defined as having BPH, and 231 (72%) were vitamin D deficient, as opposed to insufficient (22%) or normal (7%). Of participants with vitamin D deficiency, 87% met the criteria for a BPH diagnosis, as compared to 16% of controls with insufficiency or normal levels. The strong association persisted with adjustment for measured confounders, although no clear "dose response" relationship is described. Such a relationship might have been obscured by the small number of participants with normal 25(OH) vitamin D levels.

These results are consistent with several previous studies, including a study from Sweden showing an association between benign prostatic enlargement and lower 25(OH) vitamin D levels,[2] and an association between lower urinary tract symptoms (LUTS) and vitamin D deficiency among men in the National Health and Nutrition Examination Survey in the United States.[3] However, association does not prove causation.

The most important question regarding the relationship between 25(OH) vitamin D and BPH is whether treatment with vitamin D, particularly among men who are vitamin D deficient, would reduce bothersome lower urinary tract symptoms. In one 12-week randomized trial, 119 men with benign prostatic enlargement aged 50 and older were randomized to a vitamin D3 analog or placebo.[4] Active treatment showed a small but significant difference in prostate size favoring the vitamin D3 analog, but no difference in American Urological Association symptom scores. Larger and longer trials of vitamin D treatment are needed to determine whether the relationship between low vitamin D levels and BPH is of any clinical import.

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AUTHOR REPLY

We appreciate the comments of the editor and we have demonstrated a strong relationship between vitamin D deficiency and benign prostatic hyperplasia (BPH) in old Chinese men in this study.[1] We are pleased that our results are similar to those obtained by other groups, that is, a study from Sweden showing an association between benign prostatic enlargement and lower 25(OH) vitamin D levels,[2] and another study finished by Caretta et al[3] showing an association between 25(OH) vitamin D deficiency, lower urinary tract symptoms, and BPH in type 2 diabetes men.

We agree with the editor that the most important question regarding the relationship between 25(OH) vitamin D and BPH is whether vitamin D supplements could decrease prostate volume in BPH patients or prevent prostatic hypertrophy in the normal population.[4] However, the cross-sectional design in our research[1] and previous studies[2,3] severely limits the interpretability of the data.

Interestingly, a few previous studies have suggested that increasing intake of vitamin D from diet and supplements has shown a correlation with decreased BPH prevalence. Kristal et al[5] reported that vitamin D analogues of up to 6000 IU/day had shown decrease in prostate volume in BPH patients. Similarly, Colli et al[6] found that BXL628, a vitamin D3 analog, was able to arrest prostate growth within 12 weeks in men aged ≥50 years with prostatic volume ≥40 mL. Thus, proposing further subsequent longitudinal studies on vitamin D and BPH is necessary to conduct.

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