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Association of midline prostatic cysts and lower urinary tract symptoms: A case-control analysis of 606 transrectal ultrasound findings

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Abstract

Objective: To evaluate the association between midline prostatic cysts (MPCs) and lower urinary tract symptoms (LUTS).

Methods: A total of 606 patients who underwent transrectal ultrasound of the prostate (TRUS) were retrospectively reviewed. Patients were divided into two groups based on the presence of MPCs for comparison. We used the International Prostate Symptom Score (IPSS) as a LUTS parameter. Multivariate analysis was performed to find out independent predictors for moderate to severe LUTS. An MPC subgroup analysis was done to look for linear correlation between the size of MPCs and LUTS.

Results: Patients with no MPCs were of higher age, had more history of diabetes, were taking more urological medications, and had more IPSS storage symptoms. No significant differences were found in body mass index, total IPSS, voiding IPSS, bother score, total prostate-specific antigen level, and the prostate size. Multivariate analysis revealed age, history of diabetes, taking urological medications, and the prostate size as independent predictors of moderate to severe LUTS. The presence of MPCs was not an independent factor. Subgroup analysis failed to show significant correlation between the size of MPCs and the LUTS scores.

Conclusions: The presence of MPCs is not an independent factor for moderate to severe LUTS, and the size of the MPCs does not have any correlation to LUTS scores either.

KEYWORDS

cysts, lower urinary tract symptoms, prostatic neoplasms, urination

1 | INTRODUCTION

A midline prostatic cyst (MPC) is a cystic lesion found in the midline area of the prostate, which is commonly detected on transrectal ultrasound of the prostate (TRUS) in urologic clinical settings. It has been reported that 7.6% of asymptomatic patients, and 5% of patients with urological symptoms, have MPCs.[1,2] Traditionally, MPCs have been classified as Müllerian duct cysts, prostatic utricle cysts, ejaculatory duct cysts, prostatic retention cysts, or cystic dilatation of the utricle, but still there is no standardized classification system, and it remains controversial.[3-7] Even though the above classification can be anatomically clear, it is rarely pertinent to actual clinical practice, and it is hard to differentiate between the abovementioned classifications with imaging studies. Recently, efforts have been made to simplify the classification system. Furuya et al classified MPCs into four categories: type 1 (MPC with no communication into the urethra), type 2a (MPC with communication into the urethra), type 2b (cystic dilatation of the prostatic utricle with communication into the seminal tract), and type

3 (cystic dilatation of the ejaculatory duct).[6] Shebel et al classified prostatic cysts into three categories: median cysts (prostatic utricle cysts, Müllerian duct cysts), paramedian cysts (ejaculatory duct cysts), and lateral cysts (prostatic retention cysts, cystic degeneration of benign prostatic hyperplasia, cysts associated with tumors, prostatic abscess).[7]

It is generally known that MPCs do not cause LUTS, but there have been several case reports that suggest MPCs lead to LUTS.[8-12] Furthermore, a few studies have even shown that a significant number of patients with MPCs showed urological symptoms.[1,13] Even though MPCs are one of the common abnormalities on TRUS, there have been no well-established studies so far, and there has been a clinical dilemma, especially when urologists explain the findings of MPCs to patients in routine practice. Therefore, we conducted this study to evaluate if MPCs are associated with LUTS.

2 | METHODS

2.1 | Study design and patient population

We retrospectively reviewed and analyzed the medical records of 606 patients who received TRUS between October 2013 and March 2015. Enrolled patients for this study consisted of new outpatient urology patients presenting with LUTS or those examined at the Health Screening Center for routine health maintenance at Kangnam General Hospital, according to the hospital's health screening policy. Patients who underwent TRUS for follow-up purposes were excluded. If a patient underwent two or more TRUSs, only the initial TRUS was chosen for the study. Patients were divided into two groups according to the presence of MPCs on TRUS.

2.2 | Variables

In each group, variables such as age, history of diabetes mellitus (DM; which can potentially affect LUTS), concurrent urological medications (defined as alpha-blockers, 5-alpha reductase inhibitors, and/or anti-muscarinics), body mass index (BMI), International Prostate Symptom Score (IPSS) with bother score, prostate-specific antigen (PSA) levels, and TRUS findings (MPCs, prostate size) were collected. If MPCs were detected during the TRUS exam, the transverse diameter was measured. In this study, MPCs were defined as any low echoic or anechoic smooth-surfaced cystic lesion located in the midline of the prostate on the axial TRUS image. Examples of variable-sized MPCs are demonstrated in Figure 1. A single urologist (BP) performed all TRUS procedures and measured the size of the MPCs.

2.3 | Outcome measures

To address LUTS, IPSS with bother score was used as a tool. "Storage IPSS" was defined as the sum of items 2, 4, and 7, while "voiding IPSS" was defined as the sum of items 1, 3, 5, and 6. "Mild LUTS" was defined as IPSS ≤7, while "moderate/severe LUTS" was defined as IPSS ≥8, based on the American Urological Association Measurement Committee.[14]

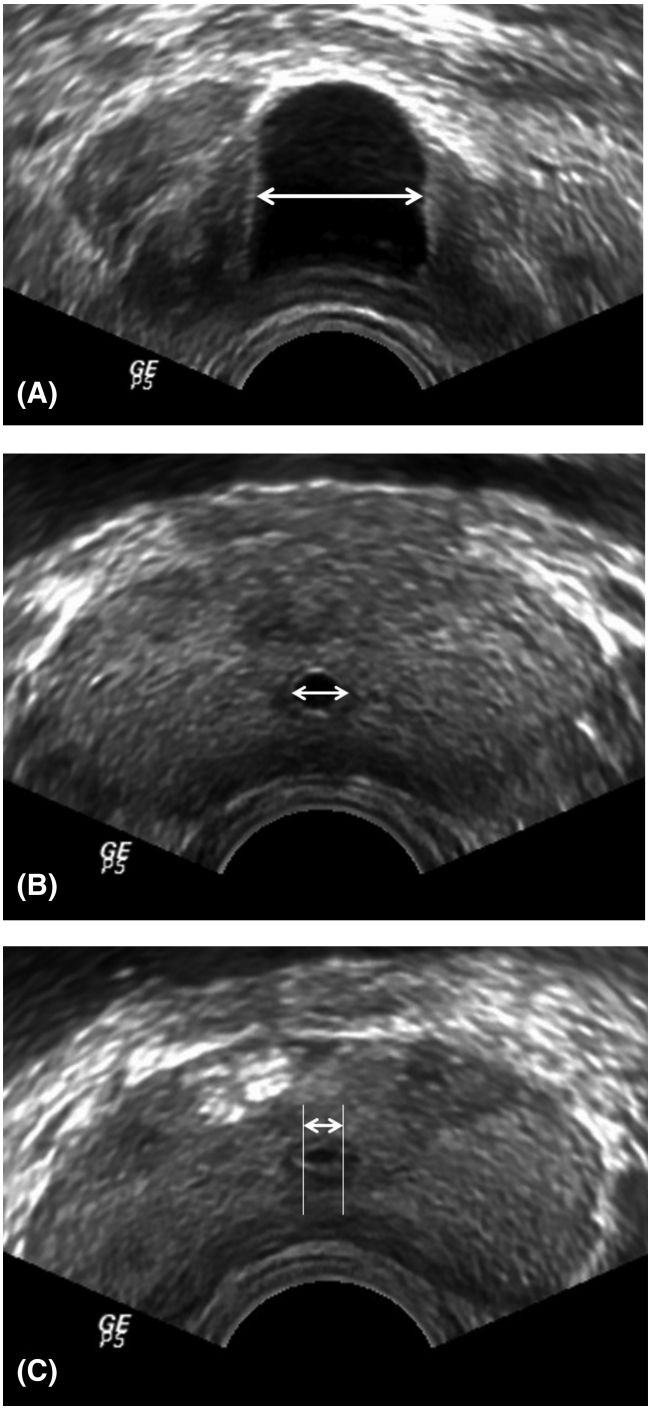

FIGURE 1 Examples of measuring the transverse diameter of the cysts for large (A), small (B), and tiny (C) midline prostatic cysts

2.4 | Statistical analysis

We used the independent *t* test, chi-square test, and Fisher's exact test to compare the distribution of clinical variables across the presence of MPCs. For univariate and multivariate analysis to determine

independent predictors for moderate/severe LUTS, the binary logistic regression test was used. We set the moderate/severe LUTS as the multivariate analysis endpoint because guidelines generally recommend to start pharmacologic treatment for moderate/severe LUTS.[15,16] Step-wise regression techniques were used to build multivariate models using a significance level of 0.15 for the covariate to remain in the model. Some covariates with no significance on univariate analysis were also included in the model if the authors were interested in investigating their association with LUTS. On the other hand, we performed a subgroup analysis to find out whether the size of the MPCs may affect LUTS within the MPC group. A partial correlation test was conducted to evaluate a linear correlation between the size of the MPCs and each element of the IPSS questionnaire (total IPSS, storage IPSS, voiding IPSS, and bother score), while adjusting age, history of DM, concurrent urological medications, and prostate size that might act as confounders. All analyses were performed using PASW Statistics 18 (SPSS Inc., Chicago, Illinois), and a P value <.05 was considered statistically significant.

2.5 | Ethics statement

The study protocol was approved by the Institutional Review Board of Ajou University Hospital (IRB File No. AJIRB-MED-MDB-15-052). Ajou University Hospital has an educational affiliation with Kangnam General Hospital. Informed consent was waived by the board.

3 | RESULTS

MPCs of any size were present in 199 (32.8%) of the 606 participants. Age (58.92 vs 56.69 years, P =.038), the number of patients with a history of DM (87 vs 26; P =.014), the number of patients who are on concurrent urological medications (53 vs 12; P =.008), and storage IPSS (5.60 vs 4.80, P =.016) were significantly higher in the no-MPC group than in the MPC group. No significant differences in BMI, total IPSS, voiding IPSS, bother score, total PSA, or prostate size were observed between the groups (Table 1). A multivariate analysis showed that age (odds ratio [OR], 1.040; 95% confidence interval [CI], 1.022-1.058), history of DM (OR, 1.887; 95% CI, 1.057-3.368), concurrent urological medications (OR, 3.386; 95% CI, 1.298-8.833), and prostate size (OR, 1.029; 95% CI, 1.004-1.055) significantly predicted moderate/severe LUTS. However, the presence of MPCs was not an independent predictor of moderate/severe LUTS (Table 2). The MPC subgroup analysis failed to reveal any linear correlation between the size of MPCs and total IPSS (r = 0.010), storage IPSS (r = −0.061), voiding IPSS (r = 0.049), or bother score (r = −0.106).

TABLE 1 Comparison of clinical variables between the two groups

	No MPCs (n = 407)	MPCs (n = 199)	*P* value
Mean age, years	58.92 ± 12.53	56.69 ± 12.05	.038[a]
Mean BMI, kg/m^2	23.67 ± 4.22	24.08 ± 3.35	.233[a]
History of DM (%)	87 (21.4)	26 (13.1)	.014[b]
Medications (%)[c]	53 (13.0)	12 (6.0)	.008[b]
Total IPSS	14.17 ± 8.87	12.71 ± 9.16	.060[a]
Storage IPSS	5.60 ± 3.79	4.80 ± 3.84	.016[a]
Voiding IPSS	8.55 ± 6.06	7.83 ± 6.07	.169[a]
Bother score	3.22 ± 1.60	2.98 ± 1.64	.088[a]
Mean total PSA, ng/mL	3.58 ± 26.67	2.48 ± 9.58	.574[a]
Mean prostate size, mL	26.16 ± 9.81	26.17 ± 9.62	.990[a]

Abbreviations: BMI, body mass index; DM, diabetes mellitus; IPSS, International Prostate Symptom Score; MPC, midline prostatic cyst; PSA, prostate-specific antigen.
[a]Independent t test.
[b]Fisher's exact test.
[c]Concurrent urological medications affecting voiding condition such as alpha-blockers, 5-alpha reductase inhibitors, and antimuscarinics.

TABLE 2 Univariate and multivariate analysis of variables to predict independent factors for moderate/severe lower urinary tract symptoms

	Univariate OR (95% CI)[a]	Multivariate OR (95% CI)[a]
Age	1.056 (1.040-1.073)	1.040 (1.022-1.058)
BMI	0.968 (0.922-1.016)	0.966 (0.918-1.016)
History of DM	2.713 (1.567-4.699)	1.887 (1.057-3.368)
Medications[b]	5.593 (2.207-14.178)	3.386 (1.298-8.833)
PSA	1.048 (0.993-1.106)	1.005 (0.983-1.027)
Prostate size	1.049 (1.026-1.072)	1.029 (1.004-1.055)
Presence of MPC	0.730 (0.506-1.053)	0.839 (0.568-1.240)

Abbreviations: BMI, body mass index; CI, confidence interval; DM, diabetes mellitus; MPC, midline prostatic cyst; OR, odds ratio; PSA, prostate-specific antigen.
[a]Binary logistic regression test.
[b]Concurrent urological medications affecting voiding condition such as alpha-blockers, 5-alpha reductase inhibitors, and antimuscarinics.

4 | DISCUSSION

It was the objective of our study to investigate the impact of MPCs on LUTS, as the clinical significance of MPCs in the urological outpatient setting is unclear, even though urologists have believed that most of MPCs are asymptomatic. Our study does not show any significant difference in LUTS parameters (IPSS and bother score) according to the presence of MPCs.

Dik et al evaluated 704 TRUS findings and found 34 (5%) MPCs. The authors reported that 32% of the patients with MPC had impaired micturition.[1] Coppens et al enrolled 65 patients with MPCs retrospectively and found that 25% of the patients demonstrated LUTS.[17] Zhang and associates reported that 10 (67%) out of 15 MPC patients that were enrolled showed prostatitis-like symptoms.[13] However, the purpose of all the above studies was to address the impact of endourological intervention of MPCs, and still there have been no case-control studies thus far to our best knowledge. Most of the articles regarding MPCs in the literature are case reports that have shown

the impact of therapeutic procedures on symptomatic MPCs. Interestingly, case reports show that most of the MPCs that caused symptoms such as LUTS or urinary retention were anatomically projecting to the bladder outlet and subsequently caused outlet obstruction.[8,18-26] Radiographically, they were shown on transabdominal ultrasound as protruding cystic masses originating in the prostatic urethra upward into the bladder neck. Of the 606 patients who underwent TRUS in our study, there were no cases of MPCs protruding into the bladder neck, and this could be one of the reasons why the MPCs in our study were not significantly more symptomatic than no MPCs.

Table 3 shows the size distribution of the MPCs in our cohort. As there were large MPCs with more than 10 cm in transverse diameter, we assessed if the size of the MPCs correlated with the symptom score among the patients with MPCs, but we failed to obtain any linear correlation between the size of MPCs and the LUTS symptom score. As many of the case reports suggest, anatomical location rather than the size of the MPCs might be an important factor to predict LUTS, and this should be considered in a future study.

Cysts can occur in any organs in the human body, and they are commonly found on imaging studies such as ultrasound, computed tomography, or magnetic resonance imaging. Most of the clinical concerns that arise from cysts are regarding malignant transformation, but cysts usually do not result in clinical symptoms unless rare complications such as rupture, compression and mass effect, infection, or bleeding occurs. Skolarikos et al reviewed about 100 articles regarding simple renal cysts and found that only 2% to 4% of the cases became symptomatic due to enlargement or complications such as hemorrhage, infection, or rupture.[27] Another body organ where cysts are commonly detected is the liver. A review article by Mavilia et al described that 15% to 16% of hepatic cysts can become symptomatic with causing abdominal pain, early satiety, nausea, or vomiting, but it depends on the size and the growth of the cysts.[28] Likewise, in the prostate, based on the results of our study, the presence of MPCs alone does not predict the development of moderate to severe LUTS, and this can suggest that it might be rare that MPCs become symptomatic.

It is not surprising that our multivariate analysis shows that age and prostate size are independent predictors of moderate to severe LUTS. Interestingly, history of DM and concurrent urological medications can predict moderate/severe LUTS. This can be explained by the fact that more patients with moderate to severe LUTS were taking urological medications such as alpha-blockers, 5-alpha reductase inhibitors, or antimuscarinics. Also, several studies show association of type 2 DM and LUTS.[29-31] This should be further investigated in the future.

TABLE 3 Size distribution of the midline prostatic cysts

Size (cm)	Number (%)
1.9 or below	47
2.0-2.9	43
3.0-3.9	31
4.0-4.9	29
5.0-5.9	16
6.0-6.9	11
7.0-7.9	12
8.0-8.9	1
9.0-9.9	4
10.0 or above	5

Out study has several limitations that should be discussed. Given its retrospective nature, there has been no randomization, raising a risk of selection bias. Another important limitation is that there were significant differences between the MPC and no-MPC groups, given no randomization. As seen in Table 1, the group without MPCs were of higher age, had more diabetic history, were taking more urological medications (which was an independent predictor of moderate to severe LUTS), and had more storage symptoms. These significant differences might have affected the result of our study that MPCs did not significantly affect the LUTS parameters. However, the presence of MPCs still was not an independent predictor for moderate to severe LUTS, even after we adjusted other significant factors in the multivariate model; therefore the conclusion of our study can still be justified. One very critical point in our study is that we did not measure the sagittal diameter of the cysts in delineating the burden of MPCs. Given the three-dimensional nature of the cysts, we should have measured the volume of the cysts instead of measuring the transverse diameter only; and this could have affected our study result. Another important point is that we only analyzed the sum of the total IPSS, storage IPSS, and voiding IPSS without subanalyzing each component of the IPSS (frequency, nocturia, urgency, etc) as exampled in a study by Lee et al.[32] Given the significant difference in storage IPSS between the MPC and no-MPC groups (Table 1), this subanalysis would have provided further insight in the association of MPC and LUTS. Another relevant point in our study is that we did not analyze the association of MPCs and prostatic surgery, which could be a future investigation.

In conclusion, our study shows that the presence of MPCs does not independently predict moderate to severe LUTS. Therefore, it is generally thought that MPCs themselves are less likely to become symptomatic unless there are specific anatomical variations such as bladder outlet obstruction seen in numerous case reports. Even though our study failed to demonstrate any positive associations, we believe that our study has its own meaningfulness in that it is, to our best knowledge, potentially the first large retrospective case-control study to address the association between MPCs and LUTS. Further prospective randomized trials will be needed for better clarification.

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DISCLOSURE

The authors declare no conflict of interest.

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