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The role of prostatic urethral angle and intravesical prostatic protrusion on surgical capsule calculi formation in the prostate: A retrospective study

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Purpose: To investigate the relationship between prostatic urethral angle (PUA) and the development of surgical capsule calculi (SCC) within the prostate, and to examine the presence and impact of intravesical prostatic protrusion (IPP).

Materials and Methods: A retrospective analysis was conducted on 90 patients who underwent radical prostatectomy, with preoperative assessments using both transrectal ultrasound of the prostate (TRUS) and magnetic resonance imaging. Patients were divided into groups with and without SCC and further categorized into type 1 and type 2 stones based on the location and severity of the calculi. Statistical analysis included chi-square and independent sample t-tests, with $p<0.05$ considered significant.

Results: Of the patients, 82.2% were diagnosed with SCC. No significant difference in PUA was found between patients with and without SCC. However, a notable disparity in IPP presence was observed, suggesting an inverse correlation with SCC development. Additionally, no significant differences were identified when comparing the two types of SCC based on PUA and IPP measurements.

Conclusions: The presence of IPP exhibited an inverse relationship with SCC, suggesting diminished urine flow pressure over the prostatic urethra may reduce the likelihood of SCC formation. However, no direct association between PUA and the presence or severity of SCC was identified. These findings highlight the complexity of factors contributing to prostatic calculi development and the potential role of IPP in this context.

Keywords: Calculi; Magnetic resonance imaging; Prostate; Ultrasonography; Urethral diseases

INTRODUCTION

Prostatic calculi, typically discovered incidentally during examinations for benign prostatic hyperplasia, have been proved to be linked to the exacerbation of lower urinary tract symptoms (LUTS) in men [1,2]. While the precise un-

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derlying mechanism remains controversial, potential causes for the formation of prostatic calculi include urine obstruction, urine stasis, and intraprostatic urine reflux [3,4].

The prostatic urethral angle (PUA), conventionally assessed via transrectal ultrasound of the prostate (TRUS), has been implicated in the worsening of LUTS and demonstrated an inverse correlation with urinary flow rate [5,6]. The curvature of the prostatic urethra results in energy loss during urinary flow, leading to a reduction in urinary flow rate [7]. However, variations in practitioner skills and experience could affect the accuracy of PUA measurement by TRUS [8]. The presence of an acoustic shadow induced by prostatic calculi could potentially influence the ultrasound-based detection of the prostatic urethra.

Our hypothesis suggests that an elevated PUA may play a contributory role in the development of prostatic calculi. The dissipation of energy during urinary flow acts as a driving force for heightened urine reflux into the space between the transitional zone and peripheral zone of the prostate, ultimately leading to the formation of prostatic calculi over the surgical capsule. In the context of endoscopic enucleation of the prostate [9], we identify the interface targeted during this procedure as the surgical capsule. We refer to this type of prostatic stone, formed within this specific interface, as surgical capsule calculi (SCC) (Fig. 1), distinguishing them from calcifications occurring over the transitional or peripheral zones. Notably, there is a dearth of research investigating the relationship between prostatic stones and the angulation of the prostatic urethra. Furthermore, due to inconsistencies in ultrasound-based measurements of PUA [8], and the absence of systematic visualization of the entire urethra by urologists during TRUS examinations, which contributed to the challenge of accurately measuring the PUA, we opted to employ magnetic resonance imaging (MRI) for PUA measurement in our study. Additionally, the identification of calcifications was facilitated by the incorporation of TRUS, as calcifications are challenging to visualize on MRI. This approach was undertaken to elucidate the potential correlation between PUA and the presence of SCC.

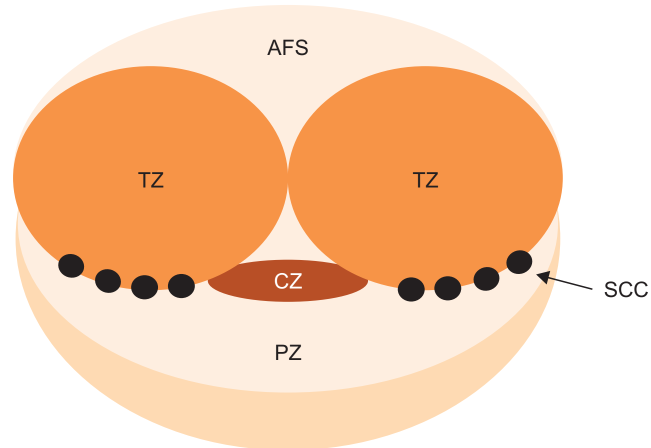

Fig. 1. The surgical capsule stones presented over the space between the transitional zone and peripheral zone of the prostate. AFS, anterior fibromuscular stroma; TZ, transitional zone; PZ, peripheral zone; CZ, central zone; SCC, surgical capsule calculi.

MATERIALS AND METHODS

This retrospective study evaluated a cohort of patients who underwent radical prostatectomy between 2021 and 2022 at Linkou Chang Gung Memorial Hospital, Taiwan. Patients undergoing preoperative assessments with both TRUS and MRI were included. Baseline characteristic data, encompassing age, body mass index (BMI), total prostate volume (TPV), transitional zone volume (TZV), maximum flow rate (Qmax), initial prostate-specific antigen (iPSA), and residual urine (RU), were collected. Exclusion criteria encompassed individuals with a history of prior prostate surgery (e.g., transurethral resection of the prostate, laser prostatectomy), those lacking preoperative TRUS or MRI examinations, and individuals with prostatic calculi diffusely distributed over the transitional or peripheral zones.

This research employed sagittal views of the prostatic urethra obtained from MRI to assess PUA. PUA was defined as the angle of intersection between the proximal and distal portions of the prostatic urethra, divided by the verumontanum [5,10]. The measurement of the PUA was conducted by a single urologist to minimize detection variation and ensure consistency and comparability. SCC presence was determined through TRUS and subsequently categorized into two distinct types. By identifying the interface of the transitional and peripheral zones, referred to as the surgical capsule, SCC were classified based on the position of stones: type 1 denoting unilateral prostatic calculi covering 33% or less of the surface, and type 2 indicating unilateral prostatic calculi covering more than 33% of the surface, bilateral prostatic calculi, or those displaying an acoustic shadow. Severity and burden of calcification were indicated by these classifications. Additionally, the presence of intravesical prostatic protrusion (IPP) was recorded with the aid of TRUS and MRI.

The research plan received the endorsement of the Institutional Review Board of Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan (IRB number: 202400487B0). Given the study's retrospective design, the IRB exempted it from the need to secure consent from patients for the examination of their health records. All patient information was

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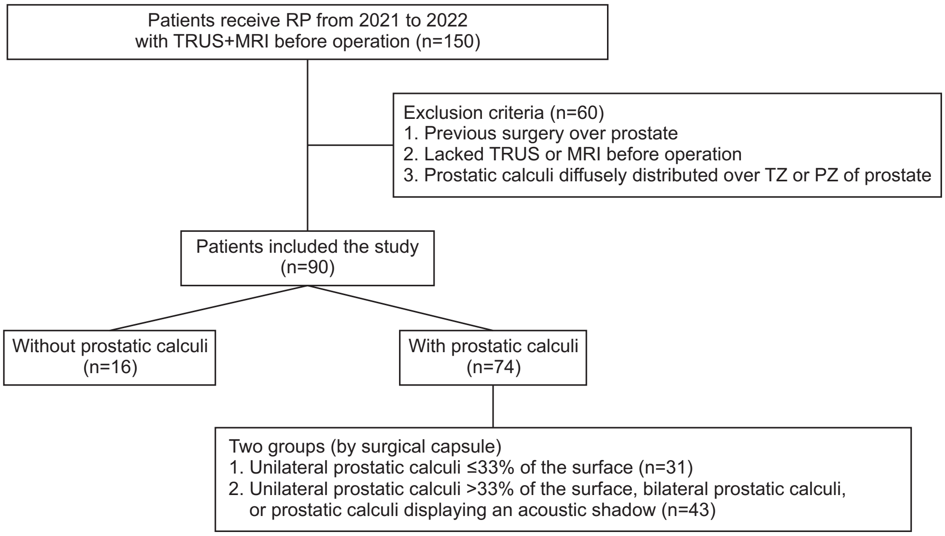

Fig. 2. The flow chart of study design. RP, radical prostatectomy; TRUS, transrectal ultrasound of the prostate; MRI, magnetic resonance imaging; TZ, transitional zone; PZ, peripheral zone.

safeguarded following the principles set forth in the Declaration of Helsinki to ensure privacy and confidentiality. Statistical analyses were conducted using IBM SPSS Statistics software version 20 (IBM Corp.). Categorical variables and the relationship between SCC and IPP were analyzed using the chi-square test, whereas continuous variables and the comparison between SCC and PUA were evaluated using the independent sample t-test. A p-value less than 0.05 was considered statistically significant (two-tailed test).

RESULTS

A total of 90 patients were enrolled in the analysis, with 74 patients diagnosed with SCC, representing 82.2% of the cohort. Among patients with SCC, 31 were classified as type 1 prostatic stones, and 43 were classified as type 2. The study design flow chart is illustrated in Fig. 2.

Statistical analysis of the basic characteristics between patients with and without SCC was showed in Table 1. The demographic breakdown revealed no statistically significant age difference between patients with SCC (67.73±5.67 years) and those without (64.75±5.85 years), with a p-value of 0.061, indicating a marginally higher age average among the SCC group. For the remaining basic characteristic parameters, such as BMI, TPV, TZV, Qmax, iPSA, and RU, the statistical analysis indicated similar values between patients in two groups.

In a striking contrast, the comparison between PUA and IPP between the two patient groups illuminated a significant correlation. Despite the PUA values showing no significant difference (39.92°±9.77° for SCC vs. 37.13°±10.27° for non-SCC, p=0.307), the presence of IPP exhibited a stark disparity. A notable 81.3% of non-SCC patients demonstrated IPP, compared to only 32.4% within the SCC group, with a statistically significant p-value of <0.001. This pronounced difference underscores the potential role of IPP in the context of SCC, as depicted in Table 2.

In the comparative analysis of the two types of SCC within the cohort of 74 affected patients, those with type 2 prostatic stones exhibited a tendency toward larger TPV and TZV (34.90±9.02 mL for type 1 stones vs. 38.94±15.42 mL for type 2 stones by TPV; 12.30±7.45 mL for type 1 stones vs. 15.90±6.84 mL for type 2 stones by TZV). However, these observations did not reach statistical significance (p=0.166 for TPV and 0.058 for TZV). The detailed findings are outlined in Table 3. Moreover, no statistically significant differences were identified when comparing the two types of prostatic calculi based on PUA and IPP measurements. The comprehensive results are presented in Table 4.

Table 1. Demographic data of patients with/without SCC

	With SCC (n=74)	Without SCC (n=16)	p-value
Age (y)	67.73±5.67	64.75±5.85	0.061
BMI (kg/m^2)	25.38±3.14	24.26±2.94	0.196
TPV (mL)	37.22±13.17	40.39±15.53	0.402
TZV (mL)	14.13±7.31	15.42±7.29	0.625
Qmax (mL/s)	12.37±4.69	12.14±9.41	0.922
iPSA (ng/mL)	20.89±28.06	15.56±9.14	0.456
RU (mL)	30.61±47.35	25.55±33.48	0.740

Values are presented as mean±standard deviation.
SCC, surgical capsule calculi; BMI, body mass index; TPV, total prostate volume; TZV, transitional zone volume; Qmax, maximum flow rate; iPSA, initial prostate-specific antigen; RU, residual urine.

Table 2. Comparison of the PUA and IPP between patients with/without SCC

	With SCC (n=74)	Without SCC (n=16)	p-value
PUA (°)	39.92±9.77	37.13±10.27	0.307
IPP			<0.001*
Yes	24 (32.4)	13 (81.3)	
No	50 (67.6)	3 (18.8)	

Values are presented as mean±standard deviation or number (%).
PUA, prostatic urethral angle; IPP, intravesical prostatic protrusion; SCC, surgical capsule calculi.
*p<0.05, statistically significant differences.

Table 3. Demographic data of patients with surgical capsule calculi by types

	Type 1 stone (n=31)	Type 2 stone (n=43)	p-value
Age (y)	67.61±4.93	67.81±6.20	0.882
BMI (kg/m^2)	25.39±3.42	25.37±2.97	0.982
TPV (mL)	34.90±9.02	38.94±15.42	0.166
TZV (mL)	12.30±7.45	15.90±6.84	0.058
Qmax (mL/s)	11.06±5.12	13.32±4.22	0.146
iPSA (ng/mL)	26.85±40.49	16.59±12.33	0.181
RU (mL)	27.59±32.64	32.52±55.17	0.741

Values are presented as mean±standard deviation.
Type 1 stone: unilateral prostatic calculi ≤33% of the surface of surgical capsule; Type 2 stone: unilateral prostatic calculi >33% of the surface of surgical capsule, bilateral prostatic calculi, or prostatic calculi displaying an acoustic shadow.
BMI, body mass index; TPV, total prostate volume; TZV, transitional zone volume; Qmax, maximum flow rate; iPSA, initial prostate-specific antigen; RU, residual urine.

Table 4. Comparison of the PUA and IPP between patients with surgical capsule calculi by types

	Type 1 stone (n=31)	Type 2 stone (n=43)	p-value
PUA (°)	40.13±11.79	39.77±8.17	0.884
IPP			0.978
Yes	10 (32.3)	14 (32.6)	
No	21 (67.7)	29 (67.4)	

Values are presented as mean±standard deviation or number (%).
Type 1 stone: unilateral prostatic calculi ≤33% of the surface of surgical capsule; Type 2 stone: unilateral prostatic calculi >33% of the surface of surgical capsule, bilateral prostatic calculi, or prostatic calculi displaying an acoustic shadow.
PUA, prostatic urethral angle; IPP, intravesical prostatic protrusion.

DISCUSSION

Prostatic calculi, traditionally considered a non-specific finding in patients with benign prostate hyperplasia or chronic pelvic pain syndrome, have garnered increasing attention due to recent studies suggesting their association with LUTS. This association is particularly noted in cases involving larger stones or those with an increased burden [1,2,11,12]. Chen et al. [13] have gone so far as to propose a connection between diminished sperm motility and the presence of larger and coarser prostatic calculi. In recent years, prostatic calculi have emerged as a valuable aspect in invasive procedures involving the prostate. O'Neill et al. [14] have even postulated the feasibility of utilizing prostatic calculi as guidance in prostatic image-guided radiotherapy. Furthermore, Li et al. [15] have highlighted improved postoperative LUTS in patients with a smaller burden of postoperative prostatic calculi, encompassing procedures such as transurethral plasmakinetic enucleation of the prostate and transurethral resection of the prostate.

The prevalence of prostatic stones exhibits significant variation, ranging widely from 7.35% to 88.6% [16,17]. Despite this variability, the precise mechanism underlying the formation of prostatic calculi remains a subject of controversy. The initial proposal for the etiology of prostatic calculi, dating back to 1927 by Thomas and Robert [18], attributed their formation to the calcification of the corpora amylacea. Subsequently, various theories have been postulated, including the roles of urine obstruction, urine stasis within the prostate tissue, and intraprostatic urine reflux as potential contributors to prostatic calculi formation [3,4]. Currently, two major theories are generally accepted regarding the formation of prostatic calculi: the prostatic inflammatory condition and urinary intraprostatic reflux [19]. These theories represent the prevailing understanding of the mechanisms involved in the genesis of prostatic stones.

Utilizing the proposed mechanisms to date, we aimed to elucidate the role of PUA in the formation of prostatic stones. Increased PUA has been previously investigated for its association with worsened LUTS and reduced peak flow rate [5,6,8]. A larger PUA signifies a more pronounced bending tube over the prostatic urethra. During urination, energy loss in the urine flow occurs not only due to friction along the urethral wall but predominantly at the angle of the bending tube, resulting in a decreased urinary flow rate [7]. Our hypothesis suggests that the dissipation of energy in urine flow may act as a force intensifying urine reflux into the space between the transitional and peripheral zones of the prostate, and an elevated PUA would be associated with the presence of SCC. However, according to our study results, although patients with SCC exhibited a larger PUA compared to those without (39.92° vs. 37.13°), this difference did not reach statistical significance. A plausible explanation for our study's findings may stem from the inclusion criteria

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for the patients under investigation. In order to obtain MRI examinations for PUA measurement, we specifically included patients diagnosed with prostate cancer. The relationship between prostate calculi and prostate cancer is currently a topic of controversy [19]. Notably, Smolski et al. [20] posited that the presence of peripheral zone calcification was associated with prostate cancer, with a relatively higher rate of transitional zone calcification observed in the cancer group compared to patients with benign pathology. Conversely, interface calcification occurred more frequently than transitional or peripheral calcification and was not associated with any specific pathology of the prostate [20]. Although our study specifically focused on interface prostatic calculi, analogous to SCC in our investigation, it is plausible that the inflammatory changes associated with prostate cancer played a role in the genesis of prostatic calculi. This involvement of cancer-related inflammation may elucidate the non-statistically significant findings regarding the influence of PUA on prostatic stone formation.

In our investigation, we systematically documented IPP findings during image examinations, and our observations revealed an inverse association between the presence of IPP and prostatic calculi. Previous studies have identified IPP as a reliable predictive factor for bladder outlet obstruction and have linked it to worsened LUTS [21-23]. According to Keqin et al. [22], the protrusion of the lateral and median lobes of the prostate into the bladder can create a ball-valve type of obstruction at the bladder neck, disrupting the funneling effect of urine flow. This ball-valve obstruction is particularly pronounced when the bladder is full, exacerbating urinary stasis and increasing intravesical pressure. The impact of IPP on the bladder neck and the urinary flow dynamics provides additional insight into our study findings. In the presence of IPP, obstruction at the bladder outlet results in decreased pressure transmission of urine flow to the prostatic urethra. The majority of the energy loss in urine flow occurs at the bladder neck (Fig. 3). Consequently, the pressure exerted by urine flow in the prostatic urethra is diminished, resulting in decreased intraprostatic urine reflux and a lower likelihood of SCC formation.

The predominant classification system for prostatic calculi has commonly categorized them as type A (discrete and small calculi) and type B (large calculi) [1,19,24]. Notably, recent work by Park and Choo [11] directly measured stone burden and unveiled an association between calculi burden and the exacerbation of storage symptoms. In the present study, we specifically defined interface prostatic calculi into type 1 and type 2, aiming to capture the severity and burden of the prostatic stones. However, our analysis did not reveal any significant differences between the two groups concerning PUA or the IPP.

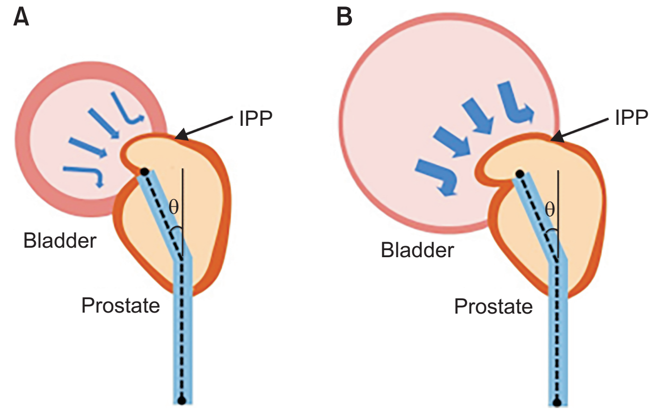

Fig. 3. (A) Disruption of the urine flow while intravesical prostatic protrusion (IPP) presented. (B) The ball-valve type of obstruction at the bladder neck induced by IPP became more apparent with increased bladder volume. θ, prostate urethral angle.

To the best of our knowledge, this study represents the inaugural investigation into examining the correlation between PUA and IPP in the context of SCC formation. Prior studies commonly relied on TRUS for PUA measurements, with MRI not having been utilized for this purpose before. However, PUA measurements may exhibit significant variability among practitioners with differing levels of experience [8]. Furthermore, the compression of the rectal wall by the ultrasound probe may not precisely reflect the natural angle of the prostatic urethra. Considering the widespread clinical use of TRUS for PUA detection, the application of MRI for PUA measurement is suggested for potentially improved accuracy in capturing the natural position of PUA [15].

Our study has notable limitations. Firstly, the data collection was retrospective in nature. Inevitable selection and recall biases may affect the results of the study. On the other hand, in an effort to include a maximal number of patients who underwent both MRI and TRUS examinations, we focused on individuals who had previously undergone radical prostatectomy, ensuring the availability of preoperative MRI images. This approach introduces selection bias, and as a result, the findings may not accurately represent the typical conditions of unselected patients, thereby affecting the generalizability of our hypothesis that a larger PUA may be associated with an increased formation of prostatic stones. Finally, the sample size of our study was relatively small, which may limit the study's power and the ability to draw definitive conclusions. A larger prospective cohort in the future is essential to objectively confirm the association between PUA/IPP and the presentation of prostatic calculi.

CONCLUSIONS

The presence of IPP demonstrated an inverse correlation with the incidence of prostatic calculi, potentially attributable to the diminished pressure of urine flow over the prostatic urethra. Nevertheless, the current study did not reveal a direct and statistically significant association between PUA and the presence or severity of prostatic calculi.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHORS' CONTRIBUTIONS

Research conception and design: Yu-Hsiang Lin and Horng-Heng Juang. Data acquisition: Jonathan YJ Chen. Statistical analysis: Han-Yu Tsai. Data analysis and interpretation: Shu-Han Tsao and Yu-Ting Chen. Drafting of the manuscript: Yu-Hsiang Lin, Horng-Heng Juang, Jonathan YJ Chen, Han-Yu Tsai, Chen-Pang Hou, Shu-Han Tsao, and Yu-Ting Chen. Critical revision of the manuscript: Yu-Hsiang Lin, Horng-Heng Juang, Jonathan YJ Chen, Han-Yu Tsai, Chen-Pang Hou, Shu-Han Tsao, and Yu-Ting Chen. Obtaining funding: Yu-Hsiang Lin. Administrative, technical, or material support: Chen-Pang Hou. Supervision: Horng-Heng Juang. Approval of the final manuscript: all authors.

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