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The changes of serum prostate specific antigen level in advanced prostate cancer patients undergoing palliative transurethral prostate resection

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Original Article

ABSTRACT

Background: Total Prostate specific antigen (tPSA) is a substance secreted by the prostate gland. It levels vary depending on the condition of the prostate and typically increase in response to increased prostate volume, cancer, infection, urinary retention and others. Conversely, tPSA levels decrease following a reduction in prostate volume. Palliative transurethral resection of the prostate (pTURP) is a procedure performed to relieve urinary retention in patients with metastatic prostate cancer who are not candidates for, or do not consent to, definitive treatment.
Objective: This study aims to compare tPSA levels before and after pTURP in patients with advanced prostate cancer.
Method: Using retrospective cross-sectional studyutilized patient medical records and laboratory results to compare pre- and post-operative tPSA levels. Data were collected from the UGM Academic Hospital's medical record between 2019 and 2022. Inclusion criteria included patients with available pre-operativeand post-operative tPSA levels and anatomic pathology results. Tumor characteristics were classified as cT3-4 or cN+ with any PSA level and any ISUP grade. Patients presented with symptoms such as urinary obstruction, pelvic pain, and/or haematuria, and all diagnoses were confirmed via prostate biopsy. Data were analyzed using the Mann-Whitney U test.
Results: A total of 40 patients met the inclusion criteria. The mean average age was 72.45 years. The average resection time was 60.42 ± 5.41 minutes, and the mean resected tissue weight was 27.50 ± 8.06 grams. Complications occurred in 30% of patients within 90 days post-pTURP. A significant decrease in tPSA levels was observed after pTURP ($p<0.05$). Furthermore, the change in tPSA (delta tPSA) showed a linear and positive correlation with the weight of resected tissue.
Conclusion: Palliative transurethral resection of the prostate in patients with advanced prostate cancer significantly reduces serum tPSA levels.

INTRODUCTION

Globally, prostate cancer ranks as the fifth leading cause of cancer-related death and is the second most commonly diagnosed cancer among men. It is most prevalent in middle-aged men between the ages of 45 and 60 and is the leading cause of cancer-related mortality in Western countries. According to GLOBOCAN 2018, prostate cancer accounted for 1,276,106 new cases worldwide. with a higher incidence in industrialized countries. The incidence and mortality rates of prostate cancer are strongly correlated with age, with the highest rates observed in men over 65 years of age.[1,2] In developing countries, prostate cancer is often diagnosed at an advanced stage, typically when patients present with lower urinary tract symptoms (LUTS) or urine retention.[3] Previous studies report that approximately 83.3% of individuals with prostate cancer experience bladder outlet obstruction (BOO), a condition that significantly impairs patients' quality of life. According to current clinical guidelines, patients with BOO who fail

medical therapy or have absolute indications for surgery are advised to undergo surgical intervention.[4]

Most patients diagnosed with prostate cancer are elderly and ineligible for curative therapy, making palliative care the mainstay of management. Accurate survival prediction helps physicians and patients plan for end-of-life care. Many men diagnosed with prostate cancer markedly elevated PSA levels are concerned about their life expectancy.[5] Modern oncology acknowledges that palliative care should not be limited to end-of-life treatment but should instead address physical and emotional distress throughout the disease trajectory. A clear understanding of prognosis empowers patients to make informed decisions about care, including evaluating the benefits and risks of various treatments, which ultimately affects their quality of life.[5-7]

One the palliative approaches that may improve quality of life is Palliative Transurethral Resection of the Prostate (pTURP). pTURP is performed to relieve urinary retention by resecting obstructive prostatic tissue without extending to the prostatic capsule.[8,9] In the context of advanced prostate cancer with BOO, pTURP has been reported to offer the advantages of minimal invasiveness and rapid symptom relief.[10] However, the oncologic benefit of pTURP remains uncertain, as long-term outcomes and randomized controlled trials are limited. In addition, data on the impact of pTURP in advanced prostate cancer are scarce. While some small-scale studies support the safety and feasibility of pTURP, the potential for significant complications and delayed recovery, especially in terminally ill patients, must also be considered.[4,11,12]

Prostate-specific antigen (PSA) is a glycoprotein secreted by normal and malignant prostate tissue.[13] The total PSA (tPSA) level represents both free and protein-bound PSA in the bloodstream. Elevated tPSA levels are commonly associated with prostate cancer, benign prostatic hyperplasia (BPH), trauma, or infection.[14] It is the most widely used biomarker for prostate cancer screening and prognosis.[3] Prognostic factors in prostate cancer include the patient's age, general health, tumor stage, PSA levels, and younger age at diagnosis.[15] A decrease in PSA following treatment typically reflects tumor cell death, while an increase may indicate disease progression.[16–18] PSA levels exceeding 20 ng/mL are strongly correlated with the risk of metastases, particularly to bone.[19] PSA expression is regulated not only by androgen signaling but also by tumor volume.[20,21]

pTURP may be indicated in cases with significant tumor burden, especially in the transitional or anterior zome of the prostate. By removing part of the tumor-laden tissue, TURP can reduce tumor volume and consequently decrease PSA levels. This reduction in PSA may reflect a diminished tumor burden and is sometimes associated with improved outcomes such as longer progression-free survival.[14] While pTURP has long been employed for palliation in prostate cancer with BOO, its morbidity and impact on long-term prognosis in advanced prostate cancer remain unclear..[13] Although several studies have explored the effects of pTURP in metastatic prostate cancer its influence on tPSA level is is not yet well defined. pTURP reduced prostate volume, and any alteration in the condition of the prostate should be mirrored by changes in serum tPSA levels.

The aim of this study is to evaluate whether pTURP affect serum tPSA levels in patients with advanced prostate cancer. The novelty of this research lies in its focus on patients with advanced prostate adenocarcinoma, whereas most existing studies have focused on BPH or early stage prostate cancer.[13]

METHODS

Research Methods

The study is an observational cross-sectional review utilizing a retrospective approach. Clinical data were collected from the hospital's clinical health information system. Medical records from 1 January 2019 to 31 December 2022, were reviewed. A total sampling method was used. All data was anonymized, and the identities of research subjects were kept confidential and secure. This study was conducted at UGM Academic Hospital in Yogyakarta.

Study Population

The inclusion criteria for this study were patients who had pre-operative tPSA, post-operative tPSA, and anatomic pathology findings available, and who visited UGM Academic Hospital. Included patients were those diagnosed with advanced prostate cancer, including those with probable bladder neck stenosis due to prior radiotherapy. The exclusion criteria were patients with an initial diagnosis other than prostate adenocarcinoma and those who had undergone pTURP before the study period.

Research Variables

Clinical tumor classification of prostate cancer, were T1 is clinically inapparent tumor that is not palpable, T2 is tumor that is palpable and confined within the prostate, T3 is tumor extends palpably through the prostatic capsule, T4 is tumor is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles, and/or pelvic wall.[12] Based on the metastasis, it is separated into two parts, namely no distant metastasis and distant metastasis [non-regional lymph node(s), bone(s), or other site(s)]. International Society of Urological Pathology (ISUP) adopt using the Gleason Score (GS), a grading limiting the number of prostate cancer grades, ranging them from 1 to 5.[12] ISUP grade 1 (GS 2-6), ISUP grade 2 (GS 7 [3+4]), ISUP grade 3 (GS 7 [4+3]), ISUP grade 4 (GS 8 [4+4 or 3+5 or 5+3]), ISUP grade 5 (GS 9-10 [4+5 or 5+4 or 5+5]). The lower the score, the less likely cancer spreads. The classification of prostate cancer divided into: Localised [Low-risk (PSA < 10 ng/mL, ISUP 1, or cT1-2a), Intermediate-risk (PSA 10-20 ng/mL, ISUP 2/3, or cT2b), High-risk (PSA >20 ng/mL, ISUP 4/5, or cT2c)] and Locally advanced [High-risk (any PSA, any grade, or cT3-4 or cN+)].

Data analysis

Data were analyzed using SPSS statistical software. Continuous variables (age, resection time, and resection weight) were reported as medians with interquartile ranges or means with standard deviations. Categorical variables were presented as frequencies and percentages. A paired t-test was used to compare tPSA levels before and after pTURP in patients with advanced prostate cancer. Additionally, box plots were used to visualize the distribution difference and change in tPSA levels post-pTURP. Regression analysis was conducted to determine the effects of age and resection weight on changes in serum tPSA levels.

In this study, the results were divided into 2 (primary results and secondary results). The primary outcome is the change in tPSA levels after pTURP. Meanwhile, secondary outcomes are patient and tumor characteristics, the condition of patients who underwent pTURP (symptoms triggering pTURP, resection time (min), resection weight (g), perioperative transfusion, complications within 90 days, as well as correlation between resection weight (the amount of prostate tissue resected during pTURP surgery) and age regarding changes in serum tPSA levels. Delta tPSA is determined by the difference between tPSA pre-pTURP and tPSA post-pTURP. The scatter plot depicts the correlation between delta tPSA and resection weight.

Ethical Consideration

All procedures conducted in this study adhered to the Declaration of Helsinki (2013 revision). The study received ethical approval from the Medical and Health Research Ethics Commission, Public Health and Nursing Faculty, Gadjah Mada University - Dr. Sardjito Hospital, with reference number: KE/FK/1485/EC/2023.

RESULTS

Forty males with confirmed prostate cancer met the inclusion criteria, with a total of 40 pTURP procedures performed during the review period. No samples were excluded from the study. Table 1 presents the characteristics of the subject, including age, Gleason score at diagnosis, clinical T stage, and the presence of metastatic at diagnosis.

Table 1. Patient and tumor characteristics

Variable	N = 40
Age (year)	72.45 ± 4.78
Gleason at diagnosis	
5-6	4 (10%)
7	13 (32.5%)
8-10	23 (57.5 %)
Clinical T stage	
T2	16 (40%)
T3	3 (7.5%)
T4	21 (52.5%)
Metastatic at diagnosis	
Yes	11 (27.5%)
No	29 (72.5%)

Table 2 summarizes the clinical condition of patients who underwent pTURP. Urinary retention was the most common indication for the procedure (67.5%), followed by hematuria (25%), bladder stones (2.5%), and hydronephrosis (5%). The mean resection time was 60.42 minutes, and the average resected prostate tissue weight was 27.5 grams. Nine patients (22.5%) required perioperative blood transfusions. Within 90 days psot-procedure, 12 patients (30%) experienced complications, with hematuria being the most common (12.5%).

Table 2. The condition of patients who went through pTURP

Variable	N = 40
Symptoms triggering pTURP	
Urinary Retention	27 (67.5%)
Bladder Stone	1 (2.5%)
Haematuria	10 (25%)
Hydronephrosis	2 (5%)
Resection time (min)	60.42 ± 5.41
Resection weight (g)	27.50 ± 8.06
Perioperative transfusion	9 (22.5%)
Complications within 90 days	
Hematuria	5 (12.5%)
Acute urinary retention	3 (7.5%)
Febrile UTI	1 (2.5%)
Azotemia	1 (2.5%)
Diarrhea	1 (2.5%)
Leg or scrotal edema	1 (2.5%)

pTURP: palliative transurethral resection of the prostate; UTI: urinary tract infection

Figure 1 shows the results of non-parametric statistical test comparing serum tPSA level before and after pTURP. The mean tPSA level before surgery was 68.10 ng/ml; and after surgery it decreased to 39.28 ng/ml. The difference wasstatistically significantly ($p < 0.05$), indicating a reduction in tPSA levels following the procedure.

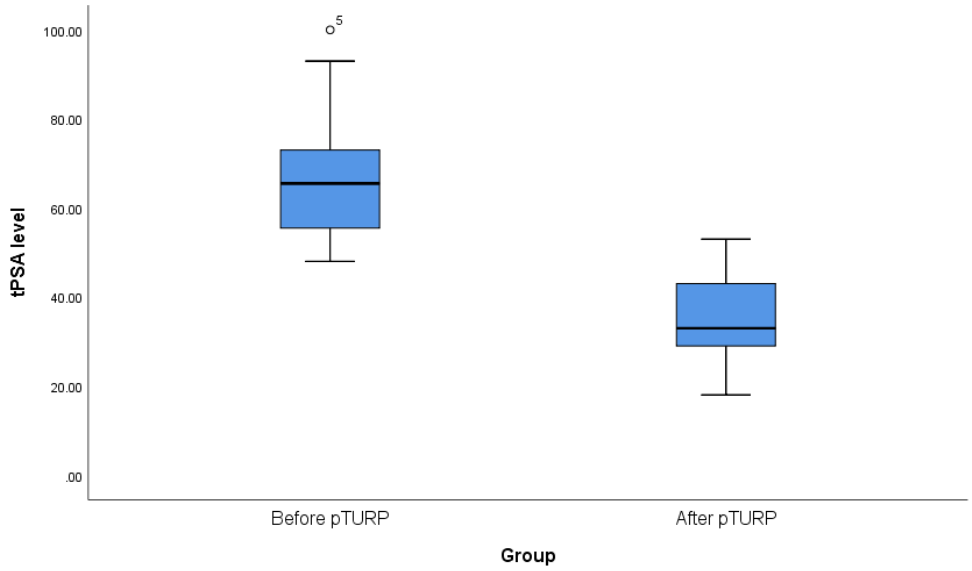

Figure 1. The change of tPSA level after pTURP

Table 3 presents the bivariate analysis results showing a significant negative correlation between resection weight and post-pTURP tPSA levels (p = 0.006). This suggests that a greater amount of prostate tissue removed during pTURP is associated with lower post-operative tPSA levels.

Table 3. Bivariate analysis of serum tPSA level in the advanced prostate cancer

Variable	Pearson correlation		p-value	
	tPSA before pTURP	tPSA after pTURP	tPSA before pTURP	tPSA after pTURP
Resection weight	0.212	-0.425	0.190	0.006*
Age	0.153	0.092	0.347	0.572

* p-value<0.05

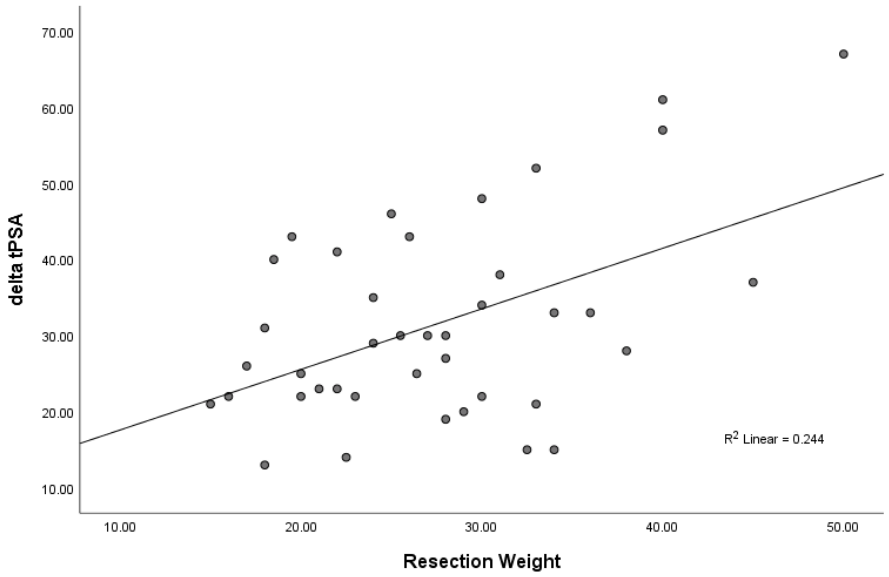

Figure 2. The correlation between tPSA difference (delta tPSA) and resection weight.

Figure 2 illustrates a positive linear correlation between the change in the tPSA (delta tPSA) and resection weight, suggesting that as the amount of prostate tissue resected increases,

so does the change in tPSA level.

Table 4 shows the results of the regression analysis model between the resection weight of prostate tissue and age to the changes of serum tPSA level. This study shows that weight of the resected prostate tissue affected changes of serum tPSA level in advanced prostate cancer patients taken palliative transurethral prostate resection.

Table 4. Linear regression analysis which effect serum tPSA level changes

Variable	95% CI		R2	p-value
	tPSA before pTURP	tPSA after pTURP		
Resection weight	-0.166 – 0.230	0.066 – 0.621	0.473	0.024*
Age	-0.047 – 0.207	- 0.268 – 0.087	0.176	0.383

Cl: confidence interval; * p<0.05

DISCUSSION

Prostate cancer is a heterogeneous disease that can be entirely asymptomatic or rapidly progress to a life-threatening state. Diagnostic and therapeutic challenges become even more complex when patient present with exceptionally high PSA levels. Based on our findings, men with advanced prostate cancer can safely undergo pTURP, and the procedure's risks and effectiveness appear consistent with previous studies, ven in the current era of modern medicine. In lower-income countries, prostate cancer is often diagnosed at an advanced stage, commonly when patients present with urinary retention or frequent urination.[19-21] Enhancing the patient's quality of life requires surgical interventions that address these obstructive symptoms.[22-23] Timely and relevant data are essential to inform decision-making at this stage of the disease, especially as both patients and clinicians may be uncertain about the potential benefits of surgical intervention. Proper patient selection and counseling are critical for those undergoing pTURP.[24-26]

In this study, the mean age of patients with prostate cancer was 72.45 years. Older patients typically present with frailty, multiple comorbidities, and limited life expectancy, making them poor candidates for definitive treatments like radical prostatectomy, which carries significant risks. Additionally, patients with metastatic prostate cancer who have failed medical treatment and refuse long-term catheterization often seek less invasive alternatives.[26-28] Some elderly patients and their families may also be reluctant to undergo highly invasive procedures, preferring palliative measures that relieve urinary symptoms and improve quality of life. Transurethral resection of the prostate remains a recommended treatment for bladder outlet obstruction due to prostatic disease.[26-28]

According to the findings of this study, urine retention was the most common cause of pTURP in advanced prostate cancer patients (67.5%). A bigger prostate volume and a more aggressive or quickly developing growth can be associated with bladder outlet obstruction or hematuria. Hematuria may be caused by a higher ratio between microvessel density and irregular vessel lumen in aggressive or poorly differentiated prostate cancers. For patients with severe bladder outlet obstruction (urinary retention) who have failed medication therapy and do not wish to utilize an indwelling catheter, pTURP is an effective surgical alternative to relieve bladder outlet obstruction and improve symptoms.[5,27]

This study found that the average resection duration for pTURP was 60.42 minutes, with a resection weight of 27.50 grams. Although pTURP has benefits in improving the quality of life of patients (for managing patients' symptoms), it also has disadvantages. The primary tumor may not be completely removed by pTURP procedures. The majority of prostate tumors are found in the peripheral zone, however, prostatic malignancies in the transitional zone produce bladder outlet obstruction, so that pTURP was mostly used for these types of tumors. In addition, the less prostate tissue that is removed during pTURP, then there is greater chance of prostate cancer developing after surgery. New metastases may originate from the residual tumor.[12,27]

Our findings suggest that not all patients with advanced prostate cancer can undergo pTURP. Only patients who have symptoms, such as urinary retention, bladder stone,

haematuria, and/or hydronephrosis, are candidates for pTURP on the patient. Apart from that, other data from this study show that complications that occur after pTURP are hematuria, acute urinary retention, febrile, azotemia, diarrhea, leg or scrotal edema, and perioperative transfusion. In this study, the most common complications that occurred within 90 days after pTURP surgery were hematuria (12.5%) and acute urinary retention (7.5%). It is true that prostate cancer can cause hematuria; however, if there was no blood clots causing urinary retention prior to pTURP, but a blood clot appears after pTURP, so that the patient cannot urinate spontaneously, the blood clots are a complication of pTURP, and action must be taken to restore the patient's ability to urinate spontaneously as before the pTURP operation. Acute urine retention develops as a result of post-operative edema in the urinary system, and the recovery time varies by individual.[6,12] These complication after pTURP can be still acceptable. The patients with advanced prostate cancer can safely undergo pTURP, and the procedure's risks and effectiveness seem to be the same in the modern era of medicine and consistent with earlier research. Zhang et al (2023) reported that intermittent ADT in conjunction with pTURP is a successful treatment for elderly patients with localized prostate cancer in stages T1 and T2 with prostatic hyperplasia.[25] It can effectively address dysuria as soon as possible. The research published in 2020 by Thomsen FB, et al, pTURP was determined to be a safe technique for treating advanced prostate cancer patients' LUTS. Low rates of postoperative urine retention, urethral stricture, and urinary incontinence were noted, along with low rates of morbidity and mortality.[20]

In this study, the average preoperative tPSA level was 68.10 ng/ml, dropping to 39.28 ng/ml after pTURP. This reduction was statistically significant ($p < 0.05$), indicating a notable decrease in PSA levels following. In addition, the results of this study also show the correlation between delta tPSA and resection weight. It is known that a linear and positive relationship exists between delta tPSA and resection weight, indicating that as delta tPSA increases, so does the weight of the resection (R^2 linear = 0.244). Despite the clear association between high PSA levels and poor prognosis, there is a lack of specific classification models or scoring systems that reliably predict survival outcomes based solely on PSA levels. Prognosis in advanced prostate cancer is influenced by multiple factors beyond PSA, including overall health, tumor characteristics, and response to treatment.[23-25] Rising PSA levels over time can indicate disease progression or treatment resistance, increased risks complications, and reduced overall survival. Treatment decisions should consider the balance between potential benefits and harms, focusing on optimizing quality of life and symptom management. Regular monitoring of PSA levels is essential in assessing treatment response and disease progression.[5-7]

Wu et al (2021) demonstrated that in localized prostate cancer, conservative management is considered for patients at low or intermediate risk who have greater PSA reduction following TURP and low post-TURP PSA. The findings suggest the pathologic finding of TURP and changes in PSA could be used as adjuvant markers to guide a risk-adaptive strategy for patients with localized prostate cancer.[7] Previous studies have demonstrated that PSA levels obtained before and after TURP can help predict the amount of residual tumor left in the prostate post-surgery.[27-28] The magnitude of PSA decline post-TURP may reflect changes in the prostate tissue composition, such as reduction in hyperplasia (benign tissue growth), inflammation, or abnormal cells (including cancerous cells).[27] A greater volume of tissue removal during TURP is typically associated with a greater PSA decline—consistent with our finding.[26-28]

To our knowledge, this study represents one of the largest analyses in current literature examining the effect of pTURP on serum tPSA level in advanced prostate cancer. A similar study by Onuigbo et al (2023) involved only 22 patients and was conducted in a different setting.[8] Our study is also an attempt to identify which advanced prostate cancer patients may benefit or not from pTURP. Based on our findings, patients should be counseled that pTURP may not yield outcomes as favorable as in those without advanced disease, due to potential complications. We recommend that patients should be routinely assessed by standard flow studies, symptom scores, and, where necessary, by urodynamic assessment, so that the quality of life remains good. pTURP can be conducted safely even in cases when prostate cancer has progressed,

despite showing worse clinical outcomes than patients who did not require intervention. This is associated with post-operative complications that occur. Therefore, pTURP should only be performed on patients who have strong indications and should be done with careful.

This study has several limitations. The most significant is the limited sample size. Additionally, the retrospective nature of the study introduces potential bias. The true oncological impact of pTURP warrants investigation through prospective, randomized controlled trials. Nevertheless, our results provide useful local insights for patients and urologists in Indonesia. This may have important clinical implications, particularly at the UGM Academic Hospital. This hospital was chosen due to its status as a major academic and referral center in Yogyakarta, where a wide range of urological cases are managed.

CONCLUSION

The serum PSA level showed a significant change in patients with advanced prostate cancer who underwent pTURP. pTURP reduced prostate volume, which in turn caused a decline in tPSA levels. It is an effective treatment for bladder outlet obstruction in carefully selected patients with local symptoms of advanced prostate cancer. The theoretical benefits of this research is its contribution to the advancement of science and technology, particularly in the medical field, by highlighting the potential of pTURP in managing advanced prostate cancer. This may assist the medical community, especially those involved in making therapeutic decision to provide effective and efficient treatment for patients with advanced prostate cancer.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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DATA AVALABILITY

Data derived from the medical records of RSA UGM. Data were obtained following the approval of ethical clearance. Subsequently, it was submitted to the director of RSA UGM. The presentation of raw data in this journal is restricted due to ethical clearance limitations..

SUPPLEMENTAL DATA

No supplemental data.

AUTHOR CONTRIBUTIONS

WK planned and designed the study, participated to data collection, analysis, and interpretation, and wrote and critically revised the report. HPH helped to analyze and interpret the data and wrote the manuscript.

DECLARATION OF USING AI IN THE WRITING PROCESS

To create better words, employ AI (Google Translate).

LIST OF ABBREVIATIONS

tPSA: total prostate specific antigen; PSA: prostate specific antigen; pTURP: palliative transurethral resection of the prostate; UTI: urinary tract infection; SD: standard deviation; Cl: confidence interval; GS: gleason score; ISUP: international society for urological pathology.

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