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ORIGINAL RESEARCH

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A novel nomogram using PSA mass for predicting BPH

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Abstract

In 2019, there were 94 million cases of benign prostatic hyperplasia globally among men aged 40 years and older. Assessment of prostate volume (PV) is important in evaluating lower urinary tract symptoms and risks in asymptomatic individuals. Serum prostate-specific antigen (PSA) levels have been suggested as a convenient and useful biomarker for benign prostate hyperplasia (BPH). However, studies suggest that using PSA as a biomarker for BPH and prostate cancer can lead to underestimation of disease severity in patients with a high body mass index (BMI). PSA mass has been proposed as a potentially superior predictor compared to total PSA levels. This retrospective study recruited the male patients visiting Kuang Tien General Hospital who had serum PSA level test, underwent transrectal ultrasonography (TRUS) for evaluation of prostate volume between January 2009 and December 2019. PSA mass was obtained by calculating body surface area (BSA) and plasma volume. The data were proved to build a nomogram, to predict the volume of the prostate, and its accuracy was evaluated using internal validation techniques. Statistical analyses were performed using SAS and R. A total of 417 men were included in this study, with a mean age of 67.3 years, mean BMI of 24.9 kg/m^2, mean prostate volume of 43.87 mL, mean PSA level of 2.94 ng/mL, and mean PSA mass of 8.68 ng/mL. The results showed that PSA mass had a higher accuracy than PSA in predicting prostate volume, as evidenced by a higher area under curve (AUC) value of 0.8271 for the PSA mass model compared to 0.8218 for the PSA model. Our nomogram showed a satisfying prediction accuracy. PSA mass may be a superior predictor of prostate volume compared to total PSA levels, although only slight improvement was shown.

Keywords

BPH; PSA; PSA mass; LUTS

1. Introduction

In 2019, there were 94 million cases of benign prostatic hyperplasia (BPH) globally among men aged 40 years and older [1]. Accurate assessment of prostate volume (PV) is a crucial clinical tool for evaluating the progression and severity of lower urinary tract symptoms (LUTS) and the potential risks in asymptomatic individuals [2, 3].

According to the American Urological Association (AUA), clinicians should give consideration to using transrectal or abdominal ultrasound, cystoscopy or cross-sectional imaging studies (such as magnetic resonance imaging or computed tomography) to assess prostate size [4]. Nonetheless, due to their high cost, these measurement techniques are not economically feasible for large-scale studies or routine health checkups.

A quick and convenient alternative for prostate volume assessment is the measurement of serum prostate-specific antigen (PSA) levels [5]. Although traditionally used as a biomarker for prostate cancer progression, PSA can also serve as a useful biomarker for BPH [6]. Studies have examined the relationship between PSA and total prostate volume (TPV) in both Asian and European populations, demonstrating a correlation between PSA levels and prostate volume [7, 8].

Several studies have suggested that utilizing PSA as a biomarker for diagnosing prostate cancer and BPH tends to result in an underestimation of the disease severity in patients with a high body mass index (BMI) [9, 10]. One of the most popular hypotheses is that patients with higher BMI have larger plasma volume, which leads to hemodilution [11]. As a result, PSA mass, which refers to the absolute amount of PSA protein secreted into circulation, has been suggested as a potentially superior predictor compared to total PSA levels.

The purpose of this study is to compare the predictive performance of PSA and PSA mass for prostate volume and to evaluate whether PSA mass is a more accurate predictor of prostate volume in the Taiwanese population.

2. Materials and methods

This retrospective study focused on male patients attending the urology outpatient department at Kuang Tien General Hospital. The study encompassed individuals who had undergone serum

PSA level testing and transrectal ultrasonography (TRUS) to assess prostate volume. The data collection period spanned from January 2009 to December 2019. All patients had their age, gender and physical measurements taken, which included the calculation of Body Mass Index (BMI) by dividing their weight in kilograms by the square of their height in meters (kg/m^2). To be eligible for inclusion in the analysis, each patient had to have undergone a serum PSA level test. Additionally, complete demographic data was required for each patient in order to be included in the selected group. We exclude the patients with either of the following condition: (1) diagnosed with prostate cancer, (2) serum PSA >10 ng/mL, (3) undergoing 5-alpha reductase therapy, (4) diagnosed with other types of cancer.

PSA mass was obtained by first estimating body surface area (BSA) and plasma volume using the following established formula: BSA (m^2) = body weight $(kg)^{0.425}$ × height $(cm)^{0.725}$ × 0.007184 and then determining the plasma volume (l) by multiplying BSA (m^2) by 1.670. PSA mass was represented by PSA times plasma volume. The prostate transverse (width), craniocaudal (length) and anteroposterior (height) dimensions were measured by TRUS, and the TPV was calculated by using the ellipsoid formula (multiplication of the three dimensions × 0.542). The data were proved to build a nomogram, which was created to predict the volume of the prostate, and its accuracy was evaluated using internal validation techniques.

All continuous data are expressed as the mean ± standard deviation (SD). Multiple logistic regression for predictive parameters of TPV, BSA and BMI in predicting the serum PSA levels was calculated. All statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA) and R (R Core Team 2017, Vienna, Austria).

3. Results

A total of 417 male individuals were included in this study, with a mean age of 67.3 years (SD: 9.1). The mean BMI of the group was 24.9 kg/m^2 (SD: 4.1), and the mean prostate volume was 43.87 mL (SD: 22.3). The mean PSA level of the group was 2.94 ng/mL (SD: 2.6), and the mean PSA mass was 8.68 ng/mL (SD: 8.1). The data was shown in Table 1.

TABLE 1. patient characteristics.

Variables	Value, mean (IQR)	Unit
Age	67.32 (62.00–73.00)	yr
BMI	24.96 (21.96–27.89)	
PV	43.87 (28.00–53.00)	mL
PSA	2.94 (0.80–4.40)	ng/mL
PSA mass	8.68 (2.32–12.84)	ng

BMI, body mass index; PV, prostate volume; PSA, prostate specific antigen; IQR, interquartile range.

A nomogram (Fig. 1) was created to predict the likelihood of benign prostatic hyperplasia (BPH) based on three factors: age, BMI and PSA. The accuracy of the model was evaluated using the area under the curve (AUC) of the receiver operating characteristic (ROC) curve. The analysis with PSA, age and BMI resulted in an AUC of 0.8218 (Fig. 2A). When PSA was replaced with PSA mass, the AUC increased slightly to 0.8271 (Fig. 2B). This indicates that the predictive accuracy of the model improved marginally when using PSA mass instead of PSA.

4. Discussion

The prevalence of BPH is high in aging men. Serum PSA is a convenient screening tool for total prostate volume (TPV). Many studies showed serum PSA concentration has its importance in predicting TPV and clinical symptoms. However, lower serum PSA in obese men was found in a number of studies [10, 12, 13]. The accuracy of serum PSA might be due to hemodilution owing to increased plasma volume [10, 13]. Correcting PSA with body weight helps to improve the precision of predicting TPV [14]. Currently, TRUS is still the most accurate tool of evaluating actual volume of prostate. However, TRUS is more invasive and costly than simple blood test, and the procedure brings discomfort to patients receiving the exam. Using corrected PSA mass surely brings benefits to clinical management in approaching BPH patients.

In the present study, PSA was corrected by BMI to create PSA mass instead of body weight solely. While the presence of a substantial amount of adipose tissue in men is known to diminish androgen levels through their conversion to estradiol, the relationship between adipose tissue and PSA levels might not be direct. Conversely, emerging research proposes a stronger correlation between elevating lean body mass and the reduction of PSA levels [15]. Despite body size elevation in life course was associated with incidence of BPH [16], BMI has been regarded as an independent risk factor of BPH and lower urinary tract symptoms (LUTS) [17–19]. Positive correlation between BMI, prostate volume and BPH-related outcome was demonstrated [20]. Hence, the effect of rectification by BMI should be stronger than by body weight solely, to prove more precise outcome of TPV prediction.

Masuda *et al*. [14] previously reported that PSA mass is a superior parameter to serum PSA for estimating TPV due to its resistance to the hemodilution effect. However, in our study, we found that the improvement in TPV prediction using PSA mass compared to serum PSA was minimal. These results are consistent with previous studies reporting only modest improvements in TPV prediction with the use of PSA mass [21]. It is possible that the effect of PSA mass on TPV estimation may differ between regions, and further studies are needed to explore this potential variability. Therefore, additional research is required to better understand the effect of PSA mass on TPV prediction and its clinical utility.

The precise estimation of TPV cannot be reached only by a single factor. In the process of building our nomogram, a combined model including PSA, BMI and age were considered. As the baseline of prostate volume as well as serum PSA increased with age [22], the correlation of age and TPV was significantly positive [18, 22]. Moreover, independent positive relation between age and PSA was still shown after controlling for prostate volume [23]. A study in Netherlands even concluded the future prostate volume can be predicted by age and previous prostate volume history [24]. Age-related

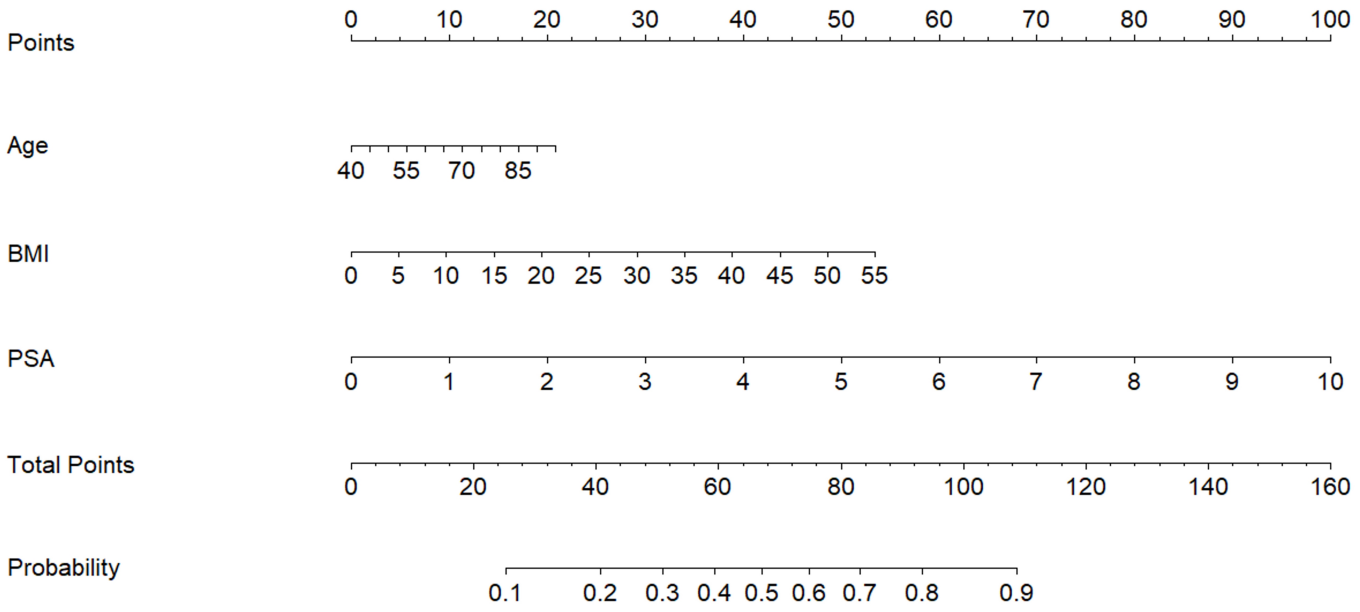

FIGURE 1. Nomogram prediction of benign prostate hyperplasia. BMI, body mass index; PSA, prostate specific antigen.

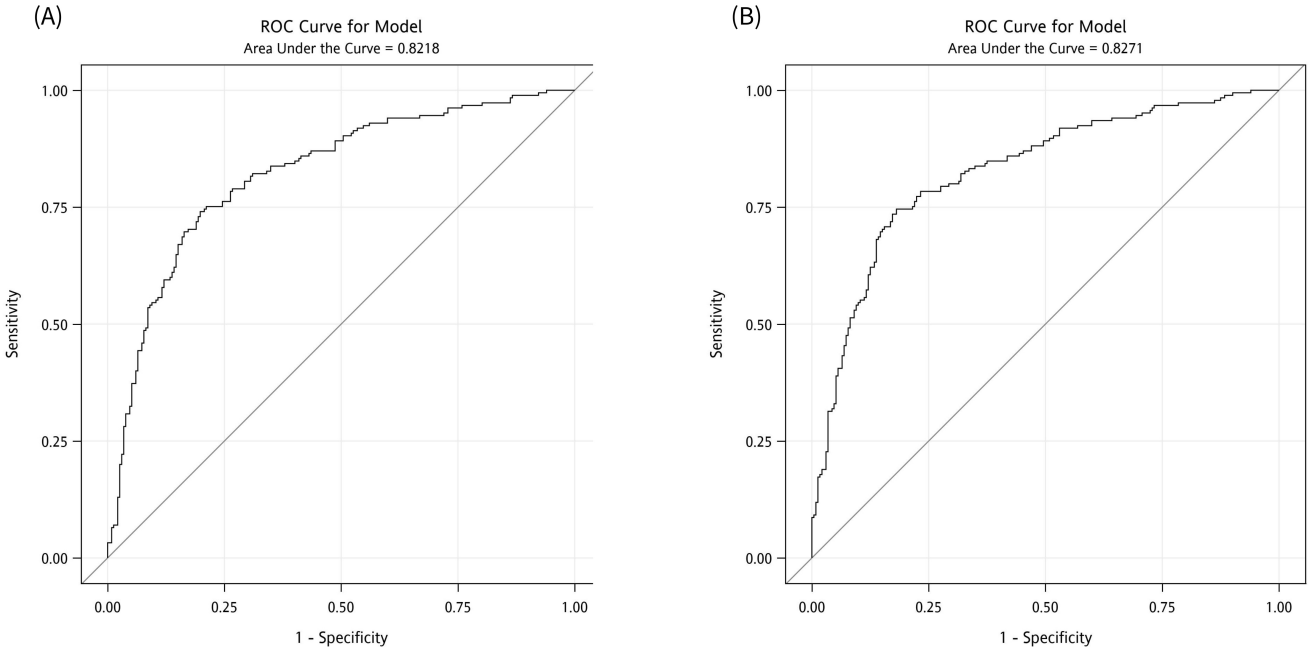

FIGURE 2. ROC curve of the nomogram prediction of benign prostate hyperplasia. (A) Using PSA as variable, AUC = 0.8218; (B) Using PSA mass as variable, AUC = 0.8271. ROC, receiver operating characteristic.

prostate enlargement was also observed in Asian population [25]. The mechanism of prostate volume increase due to aging was widely discussed and yet not a single factor was confirmed [26]. However, age was found to be the main contributor of growth of transient zone more than in peripheral zone [27, 28], leading to BPH-related lower urinary tract symptoms [22]. As a strong risk factor for BPH, age was reasonably adopted in our nomogram.

The prostate volume does not necessarily indicate the clinical symptoms of outlet obstruction. However, the volume of prostate gives a holistic prospective of the situation, including symptoms and prognosis. The nomogram functions as a graphical tool, simplifying complex statistics and assisting clinicians in making informed decisions by estimating probabilities. In our healthcare system, serum PSA tests are frequently used in health examinations. Utilizing available data, healthcare providers can quickly screen patients for BPH risk and decide if specialist evaluation is necessary. The nomogram was designed for patients averse to or unable to undergo transrectal ultrasonography (TRUS). This is especially crucial when patient queues for TRUS are long, potentially leading to loss of follow-up or patient refusal due to the invasiveness of TRUS. The nomogram provides a novel method for assessing BPH risk and considering further examination. Its clear visuals help

to improve patient-clinician communication. To sum up, our nomogram combines several independent risk factors, providing reliable prediction of TPV, and a step forward, a useful tool to approach BPH in Taiwanese population. While the PSA mass nomogram did not yield a significant enhancement in predictive capability, it does provide a refined level of prediction accuracy. Given the influence of BMI on serum PSA levels, our confidence remains in the potential of PSA mass to offer heightened precision in TPV estimation. However, it is evident that a broader spectrum of variables and a larger dataset will be essential to fully realize the potential of PSA mass nomograms in optimizing precision.

Limitation: our study exhibits several limitations. Primarily, the retrospective nature of our research and the non-routine nature of free form PSA assessments at our hospital posed challenges in data collection. The absence of free form PSA information may have its potential influence on the nomogram. Secondly, our dataset's case count might be deemed insufficient. More cases might be needed to further elaborate the nomogram. Additionally, our patient cohort predominantly originates from a confined geographic region, potentially introducing regional bias and limiting the generalizability of our findings to a broader population. These limitations collectively underscore the need for cautious interpretation of our results within these outlined contexts.

5. Conclusions

In this study, a nomogram was developed to accurately predict total prostate volume (TPV) using BPH-related factors. This tool helps the clinicians to decide if the patient needs to be further evaluated by a specialist. The results demonstrated that the nomogram was a reliable tool for predicting TPV. While PSA mass may initially seem like a viable alternative to serum PSA in predicting TPV since it is not subject to potential hemodilution effects, the study found that using PSA mass only slightly improved clinical determination of TPV. Therefore, further research is needed to determine if PSA mass provide clinically meaningful improvements for predicting TPV in a real-world setting.

AVAILABILITY OF DATA AND MATERIALS

The dataset in this study is available from the first author or the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS

CCL—study design. HKH and YLT—data analysis and writing original draft. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This retrospective study was reviewed and approved by Kuang Tien General Hospital institutional review board. IRB Reference number: 11049. The study adhered to the principles of the Declaration of Helsinki and relevant local regulations. Informed consent from individual participants was deemed unnecessary by the Kuang Tien General Hospital IRB/Ethics Committee. This decision was based on the fact that the data analyzed were anonymized and did not contain any identifiable personal information.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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