





The Correlation Between Body Mass Index and Prostate Volume: A Retrospective Analysis of Pre and Postoperative Measurements in Prostate Cancer Patients

Biagio Barone¹ | Ugo Amicuzi² | Matteo Massanova³ | Luigi Napolitano² | Pasquale Reccia⁴ | Benito Fabio Mirto² | Raffaele Balsamo⁴ | Francesco Del Giudice⁵ | Matteo Ferro⁶ | Gian Maria Busetto⁷ | Octavian Sabin Tataru⁸ | Giuseppe Lucarelli⁹ | Celeste Manfredi¹⁰ | Dario Del Biondo¹ | Vincenzo Francesco Caputo¹¹ | Roberto Falabella¹¹ | Ferdinando Fusco¹² | Ciro Imbimbo² | Felice Crocetto²

¹Department of Urology, Ospedale San Paolo, Naples, Italy | ²Department of Neurosciences and Reproductive Sciences and Odontostomatology, University of Naples Federico II, Naples, Italy | ³Urology Department, Southend-On-Sea University Hospital, Southend-On-Sea, UK | ⁴Urology Unit, AORN Ospedali dei Colli, Monaldi Hospital, Naples, Italy | ⁵Department of Urology, University Sapienza, Rome, Italy | ⁶2nd Unit of Urology, Department of Health Science, University of Milan, Milan, Italy | ⁷Department of Urology and Renal Transplantation, Policlinico Foggia, University of Foggia, Foggia, Italy | ⁸Department of Simulation Applied in Medicine, The Institution Organizing University Doctoral Studies (I.O.S.U.D.), George Emil Palade University of Medicine, Pharmacy, Sciences, and Technology from Târgu Mureş, Târgu Mureş, Romania | ⁹Urology, Andrology and Kidney Transplantation Unit, Department of Emergency and Organ Transplantation, University of Bari, Bari, Italy | ¹⁰Unit of Urology, Department of Woman, Child and General and Specialized Surgery, University of Campania "Luigi Vanvitelli", Naples, Italy | ¹¹Urology Unit, AO San Carlo, Potenza, Italy | ¹²Division of Urology, Department of Surgical Sciences, AORN Sant'Anna e San Sebastiano, Caserta, Italy

Correspondence: Felice Crocetto (felice.crocetto@unina.it)

Received: 28 October 2024 | Revised: 9 December 2024 | Accepted: 11 December 2024

Funding: The authors received no specific funding for this work.

Keywords: body mass index (BMI) | magnetic resonance imaging (MRI) | prostate measurement | prostate volume | radical prostatectomy

ABSTRACT

Background: This study aims to assess the relationship between body mass index (BMI) and prostate volume, utilizing pre and postoperative measurements.

Methods: A retrospective, observational study was conducted at a single site using data from an institutional database. Medical records of patients who underwent robot-assisted radical prostatectomy were reviewed. Data included age, BMI, and prostate volumes measured through digital rectal exam (DRE), transrectal ultrasound (TRUS), magnetic resonance imaging (MRI), and surgical specimen weight (SPW).

Results: A total of 168 patients were identified and included in the analysis. Spearman's correlation test revealed a significant association between BMI and prostate volume for all measurement methods, reporting r = 0.146 (p = 0.047) for DRE, r = 0.268 (p < 0.0001) for TRUS, r = 0.177 (p = 0.021) for MRI and r = 0.234 (p = 0.002) for SPW. Linear regression analysis confirmed the significant association between BMI and prostate volume, reporting, respectively, $R^2 = 0.026$ (p = 0.036) for DRE, $R^2 = 0.076$ (p < 0.0001) for TRUS, $R^2 = 0.038$ (p = 0.011) for MRI and $R^2 = 0.040$ (p = 0.009) for SPW. Notably, considering the SPW the best way to estimate prostate volume, for every increase in BMI, the predicted increase of prostate volume is 0.865gr.

Conclusions: This study demonstrates a positive linear correlation between BMI and prostate volume, highlighting the importance of considering BMI in prostate volume assessments.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2024 The Author(s). The Prostate published by Wiley Periodicals LLC.

1 | Introduction

Prostate cancer and benign prostatic hyperplasia (BPH), represent together two of the most commonly diagnosed conditions among men, particularly in those aged 50 years or older [1-3]. As the global population ages, there is an increasing interest in understanding the risk factors and associations that influence prostate health, and in particular, those that may predispose individuals to prostate cancer or BPH [4, 5]. Prostate volume represents indeed an important factor in BPH symptoms as well as in the detection of prostate cancer during MRI and prostate biopsy [6–8]. Several factors have been identified as influencers of prostate volume such as age, genetics, hormone levels and lifestyle factors such as diet and physical activity [9–12]. Among these, body mass index (BMI), due to the obesity epidemic and its influence on other pathologies, has garnered significant attention [13]. BMI is an essential clinical metric for assessing general health with obesity and overweight statuses associated with various health complications, including cardiovascular disease, diabetes and even certain cancers [14-17]. Understanding how excess body weight impacts specific organs such as the prostate, is critical for improving the detection of patients at risk of BPH and outlet obstruction and, therefore, providing specific treatments and prevention strategies. Several studies have explored the relationship between BMI and prostate health, with a particular focus on prostate cancer risk and the development of BPH [18, 19]. Prostate volume is a key parameter in diagnosing and managing BPH. The size of the prostate can influence clinical decisions regarding treatment options, including the necessity of surgical intervention, medications and active surveillance [20-22]. Prostate volume is indeed closely linked to symptoms of lower urinary tract dysfunction, a common issue in aging men. Larger prostate volumes are typically associated with greater obstruction of urinary flow, leading to a constellation of symptoms known as lower urinary tract symptoms (LUTS) which include frequent urination, difficulty in starting micturition and incomplete bladder emptying [23-25]. The measurement of prostate volume is commonly performed using various clinical methods which include, from the less to the highest reliable methods, digital rectal examination (DRE) to transrectal (TRUS) and suprapubic ultrasound, magnetic resonance imaging (MRI) [26, 27]. The most reliable method is associated, in surgical settings such as radical prostatectomy, with the assessment of surgical specimen weight (SPW). Given the clinical importance of assessing prostate volume for managing BPH, the possibility of identifying factors that may influence the prostate size, including patients' specific characteristics like BMI could represent a game changer in the prevention and management of BPH. Several mechanisms have been proposed to explain the relationship between increased BMI and prostate diseases. For instance, obesity is often associated with insulin resistance and increased levels of circulating insulin and insulin-like growth factors, both of which may promote prostatic tissue growth [28, 29]. Additionally, obese individuals often exhibit altered hormone levels, including reduced testosterone and increased estrogen, which could influence prostate cell proliferation and hypertrophy [30]. Adipose tissue, which is more abundant in individuals with higher BMI, is also known to produce inflammatory cytokines that may contribute to the development of prostate inflammation and enlargement [31]. Despite the well-established connection between obesity and prostate cancer risk, the specific impact of BMI on prostate volume has received less attention in the literature. Understanding this relationship is crucial because increased prostate volume can complicate surgical procedures like radical prostatectomy, affect the accuracy of prostate cancer screening tests such as prostate-specific antigen (PSA) levels, and influence the severity of LUTS [32]. As BMI increases, it may exert effects on different organs, including the prostate, potentially contributing to an increase in prostate volume. However, the extent of this influence and the mechanisms driving it are not yet fully understood. Given the rising prevalence of obesity worldwide and the established impact of BMI on various aspects of prostate health, further research into the relationship between BMI and prostate volume is warranted. Understanding this relationship has important clinical implications for the management of prostate conditions, particularly in terms of surgical planning and the assessment of disease severity.

The current study aims to address this gap in knowledge by systematically assessing the association between BMI and prostate volume using multiple measurement methods, including DRE, TRUS, MRI, and SPW, in a cohort of patients undergoing robot-assisted radical prostatectomy. By utilizing a retrospective, observational study design and a comprehensive institutional database, the study seeks to provide evidence regarding the influence of BMI on prostate volume and the potential clinical relevance of this association.

2 | Materials and Methods

This retrospective observational study was conducted at Queen Elizabeth University Hospital, Glasgow, United Kingdom, in adherence to the World Medical Association Declaration of Helsinki guidelines. Informed consent was obtained from all patients involved. The study population consisted of patients who underwent robot-assisted radical prostatectomy between June 2019 and June 2020. From an institutional database, 197 patients were identified for potential inclusion in the study. Of these, 29 patients were excluded due to prior neoadjuvant androgen deprivation therapy or treatment with 5-alpha reductase inhibitors (n = 19), or because the interval between magnetic resonance imaging (MRI) and surgery exceeded 6 months (n = 10). Ultimately, 168 patients were included in the final analysis. Clinical, radiological, and histological data were collected for each patient. These included patient age, BMI, serum prostate-specific antigen (PSA) levels at the time of prostate biopsy and prostate volumes measured by digital rectal examination (DRE), transrectal ultrasound (TRUS), MRI, and surgical specimen weight (SPW) and volume (SP). Prostate volumes from different measurement methods were obtained and recorded as follows:

- DRE: Estimated by a single operator who performed the DRE immediately before surgery.
- TRUS: Automatically calculated using the ellipsoid formula (length × width × height × 0.523) based on dimensions measured by the urologist performing the biopsy.

TRUS was performed contextually before the prostate biopsy.

- MRI: PVs were determined by the radiologist using the maximum diameter and tri-planar measurements of the prostate gland on high-resolution T2-weighted images. PVs were calculated using both the bullet formula (length \times width \times height \times 5 π /24) and the ellipsoid formula (length \times width \times height \times 0.52).
- Surgical Specimen: SPW and SP volume were obtained from pathology reports. SPW was recorded after removal of the seminal vesicles, vas deferens, and periprostatic fat. SP volume was calculated based on the specimen's recorded dimensions (length, width, and height), using both the bullet and ellipsoid formulae.

2.1 | Statistical Analysis

Descriptive statistics were used to summarize the data, with continuous variables reported as means and standard deviations, and categorical variables as frequencies and percentages. Spearman's correlation test was conducted to investigate the association of BMI with prostate volume for all measurement methods. Additionally, linear regression analyses were performed to assess the correlation between BMI and PV measurements. All statistical analyses were conducted using IBM SPSS software (version 29.0.1.0; IBM Corp., Armonk, NY, USA), with a significance threshold set at p < 0.05.

3 | Results

A total of 168 were identified and included in the analysis. The mean age of patients enrolled was 63.2 ± 6.5 years, while the mean BMI was 28 ± 3.5 . According to the BMI category, 82.2% of patients were overweight or obese. All patients underwent robotic radical prostatectomy. Table 1 reports descriptive data of patients involved in the study.

Spearman's correlation test revealed a significant association between BMI and prostate volume for all measurement methods, reporting $r\!=\!0.146$ ($p\!=\!0.047$) for DRE, $r\!=\!0.268$ ($p\!<\!0.0001$) for TRUS, $r\!=\!0.177$ ($p\!=\!0.021$) for MRI ellipse volume, $r\!=\!0.168$ ($p\!=\!0.030$) for MRI bullet volume while SP ellipse volume and SP bullet volume reported, respectively, $r\!=\!0.148$ ($p\!=\!0.035$) and $r\!=\!0.147$ ($p\!=\!0.048$). SPW reported, instead, $r\!=\!0.234$ ($p\!=\!0.002$) (Table 2).

Linear regression analysis confirmed the significant association between BMI and prostate volume, reporting, respectively, $R^2 = 0.026$ (p = 0.036) for DRE, $R^2 = 0.076$ (p < 0.0001) for TRUS, $R^2 = 0.038$ (p = 0.011) for MRI ellipse volume, $R^2 = 0.037$ (p = 0.013) for MRI bullet volume, $R^2 = 0.026$ (p = 0.037) for SP ellipse volume, $R^2 = 0.026$ (p = 0.036) for SP bullet volume and $R^2 = 0.040$ (p = 0.009) for SPW (Figures 1–5). Notably, considering the SPW the best way to estimate prostate volume, for every increase in BMI, the predicted increase of prostate volume is 0.865 gr.

TABLE 1 | Descriptive data of patients included in the study.

	Mean	Standard deviation
Age, years	63.2	6.5
BMI	28	3.5
PSA, ng/mL	10.43	6.5
PSA density, ng/mL ²	0.28	0.18
DRE volume, cc	51.9	19
TRUS volume, cc	37.4	15.2
MRI ellipse volume, cc	39.3	13.7
MRI bullet volume, cc	48.9	17.1
SPW, gr	43.6	15.2
SP ellipse volume, cc	41.2	16.7
SP bullet volume, cc	51.4	20.8
	Frequency	Percentage
BMI categories		
Underweight	2	1.2
Healthy weight	28	16.7
Overweight	90	53.6
Obesity	48	28.6

TABLE 2 | Spearman's correlations related to BMI.

	Correlation coefficient	p value
Age	-0.212	0.006
PSA	0.101	0.192
PSA density	-0.011	0.889
DRE volume	0.146	0.047
TRUS volume	0.268	< 0.0001
MRI ellipse volume	0.177	0.021
MRI bullet volume	0.168	0.030
SPW	0.234	0.002
SP ellipse volume	0.148	0.035
SP bullet volume	0.147	0.048

4 | Discussion

The relationship between BMI and prostate volume is a subject of considerable clinical interest, particularly in the context of conditions such as BPH and prostate cancer. Both conditions are indeed highly prevalent in older male populations, with prostate volume being a critical factor in diagnosis, symptom severity and management decisions of BPH [33]. Prostate volume plays indeed a pivotal role in the management of BPH, which is characterized by an enlarged prostate leading to LUTS [34]. Larger prostate volumes are typically associated with more

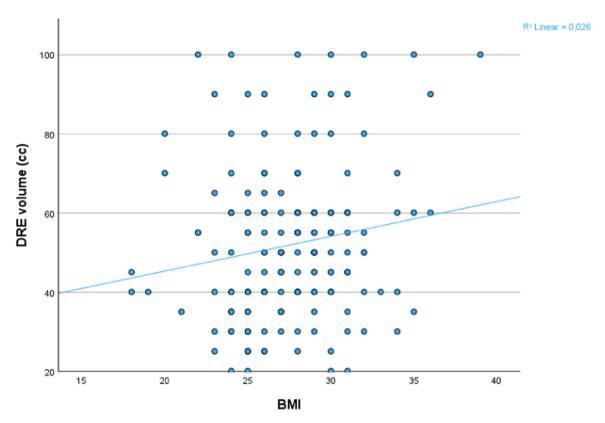


FIGURE 1 | Linear regression plot for BMI and DRE. [Color figure can be viewed at wileyonlinelibrary.com]

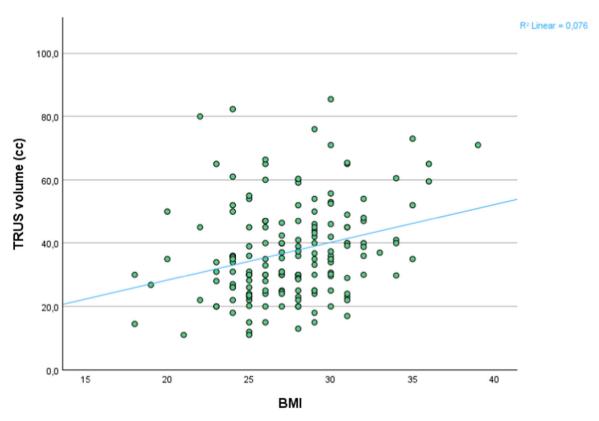


FIGURE 2 | Linear regression plot for BMI and TRUS volume. [Color figure can be viewed at wileyonlinelibrary.com]

severe LUTS, which can significantly affect a patient's quality of life [35]. Accurate measurement of prostate volume is, therefore, essential in the clinical decision-making process regarding BPH treatment options. Previous studies have established a link

between obesity and BPH. This link however is not limited to benign conditions but has been generalized to other prostatic diseases, from prostatitis to prostate cancer [36–38]. One of the first studies to suggest this association was the one by Wallner

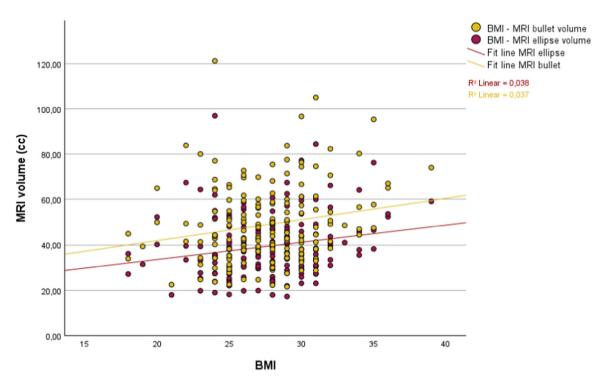


FIGURE 3 | Linear regression plot for BMI and MRI (ellipse and bullet) volume. [Color figure can be viewed at wileyonlinelibrary.com]

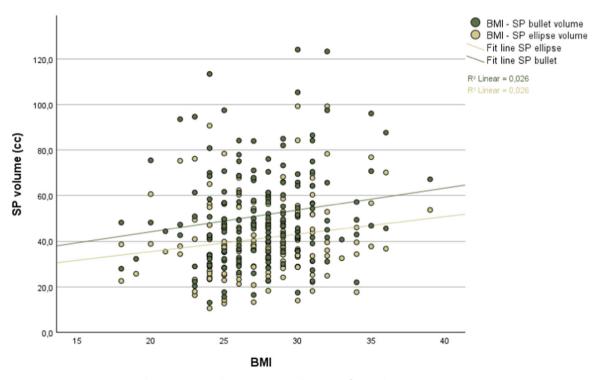


FIGURE 4 | Linear regression plot for BMI and SP (ellipse and bullet) volume. [Color figure can be viewed at wileyonlinelibrary.com]

et al. which assessed a linear correlation between baseline obesity and prostate volume in 2011, based on data from patients randomly selected aged 40 to 79 years [39]. Similarly, Bhindi et al., in 2014, examined the association between BMI, prostate volume and LUTS in a multiethnic cohort of 1613 men reporting a significantly higher prostate volume in patients with higher BMI, albeit no association was reported with worsened LUTS [40]. In a more recent study, Li et al. assessed a

significant link between higher BMI and prostate volume in a cohort of 788 patients. Also in this case, however, no association was found between BMI and worsened LUTS [41]. Analogous results were reported by Yue et al., Zaza et al., and Negi et al. [42–44]. In particular, in these last studies, an interesting association between BMI and LUTS was also assessed, highlighting the aforementioned considerations on prostate volume and BPH management. Prostate volume has undoubtedly



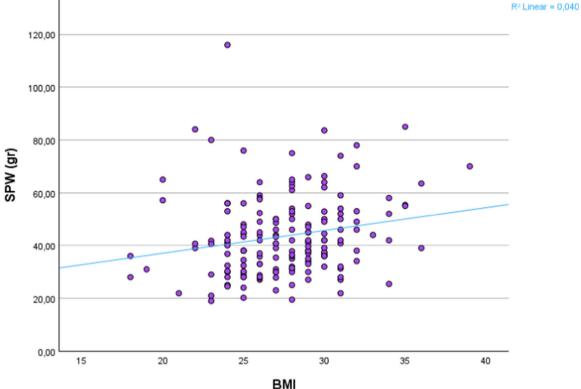


FIGURE 5 | Linear regression plot for BMI and SPW. [Color figure can be viewed at wileyonlinelibrary.com]

implications also for prostate cancer screening although this affirmation is still debated. Elevated prostate-specific antigen (PSA) levels, which are utilized as the first diagnostic marker for prostate cancer, could be also elevated in patients with larger prostate volumes due to BPH [45-47]. As a result, understanding factors such as BMI that may influence prostate volume can enhance the accuracy of PSA-based cancer screening and prevent unnecessary biopsies or overtreatment [48-54]. Recent studies have provided compelling evidence of an inverse correlation between prostate volume and the incidence of biopsy-proven prostate cancer. A systematic review and meta-analysis by Moolupuri et al. in 2021 revealed that 90% of included studies support the hypothesis that larger prostate size is protective against prostate cancer, with no studies demonstrating a positive correlation [55]. Similarly, Al-Khalil et al. found that smaller prostates were associated with higher biopsy rates and a greater proportion of aggressive cancers (Gleason score ≥ 8), supporting the protective role of larger prostate volumes [56]. Related to this issue, PSA density, a wellknown volume-dependent marker, is still a valuable tool to refine prostate cancer risk assessment. Yusim et al. demonstrated that PSAD outperformed PSA alone in predicting clinically significant prostate cancer, with a significant diagnostic advantage in men with smaller prostate volumes (< 33 mL) and PSAD in the gray zone (0.09-0.19 ng/mL²) [57]. Similarly, Nordström et al. highlighted that using PSA density to guide biopsy decisions could reduce unnecessary biopsies and overdiagnosis while maintaining high sensitivity for clinically significant cancers [58]. The results of this study demonstrate a positive linear correlation between BMI and prostate volume across all measurement modalities. Notably, the strongest correlation was observed with TRUS (r = 0.268, p < 0.0001) and

SPW (r = 0.234, p = 0.002). These findings suggest that TRUS may provide reliable prostate volume measurements within the specific parameters of this study. However, this does not imply that TRUS is universally more reliable than MRI, as each method has its own advantages and limitations. Linear regression analysis further confirmed the significant association between BMI and prostate volume. These findings suggest that as BMI increases, so does prostate volume, with a predicted increase of 0.865 grams in prostate weight for each unit increase in BMI. Several biological mechanisms may explain the observed association between increased BMI and larger prostate volumes. Obesity is often characterized by insulin resistance and hyperinsulinemia, which can lead to increased circulating levels of insulin and insulin-like growth factors (IGFs) [59, 60]. Both insulin and IGFs have been shown to promote cellular proliferation, including in prostatic tissue, potentially contributing to prostate enlargement [61]. Additionally, obesity is associated with hormonal changes, including lower levels of testosterone and higher levels of estrogen [62, 63]. Testosterone plays a key role in maintaining prostate homeostasis, and reduced levels of testosterone, along with increased estrogen, may promote prostatic hypertrophy [64]. This hormonal imbalance could be a contributing factor to the increased prostate volume observed in individuals with higher BMI. Adipose tissue, which is more abundant in individuals with higher BMI, also secretes various inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α) interleukin-6 (IL-6) [65, 66]. Chronic inflammation has been implicated in the development of BPH and may contribute to prostate enlargement by promoting prostatic cell proliferation and fibrosis [67]. The findings of this study have several important implications for clinical practice. First, the positive

correlation between BMI and prostate volume suggests that clinicians should consider BMI when assessing prostate volume in patients with BPH or prostate cancer. Overweight and obese patients are more likely to have larger prostate volumes, which could influence their treatment options. For example, patients with larger prostates may be less suitable candidates for certain minimally invasive procedures and may require more aggressive interventions. Furthermore, the association between BMI and prostate volume highlights the importance of weight management in preventing and managing BPH. Weight loss interventions, including dietary changes and increased physical activity, may not only reduce the risk of cardiovascular and metabolic diseases but also help to mitigate prostate enlargement and its associated symptoms. In addition, the study's findings may have implications for prostate cancer screening and diagnosis. Given that larger prostate volumes are associated with higher PSA levels, clinicians should take into account a patient's BMI when interpreting PSA results. Obese patients may have larger prostates and therefore higher PSA levels, which could lead to false-positive results if BMI is not considered. Adjusting PSA thresholds based on BMI may improve the accuracy of prostate cancer screening in overweight and obese individuals.

Despite its strengths, this study has several limitations that should be acknowledged. First, it is a retrospective observational study conducted at a single institution, which may limit the generalizability of the findings. Future studies should aim to replicate these results in larger, multicenter cohorts with more diverse populations. Second, while the study demonstrates a correlation between BMI and prostate volume, it does not establish a causal relationship. Longitudinal studies are needed to determine whether changes in BMI over time are associated with changes in prostate volume. Additionally, future research should explore the underlying mechanisms linking obesity to prostate enlargement, including the role of insulin resistance, hormonal changes, and inflammation. Thirdly, while the study utilizes multiple methods for measuring prostate volume, including DRE, TRUS, MRI, and SPW, each method has its limitations. DRE, for example, is highly operator-dependent and may not provide accurate volume estimates, while MRI is expensive and not always available in routine clinical practice. TRUS and SPW are somewhat reliable, but the former is subject to variability based on the operator's experience, and the latter can only be obtained postoperatively. Fourthly, it is also important to note that the majority of patients in our study had prostate volumes less than 70 cc, with limited representation of patients with larger prostates. As such, the study results are primarily applicable to patients with prostate volumes under 70 cc, and further research is needed to assess the relevance of these findings in patients with larger prostate volumes. Lastly, while this study was conducted exclusively in a PCa cohort, limiting direct extrapolation to BPH patients, it is noteworthy that radical prostatectomy provides the most accurate and reliable measurements of prostate volume and weight. In contrast, surgeries for BPH typically remove only portions of the prostate, resulting in incomplete volume assessment. Furthermore, imaging-based estimates commonly used in BPH studies are subject to variability. Therefore, our findings, based on comprehensive and precise measurements, provide robust insights into the association between BMI and prostate volume.

While these insights may hold relevance for BPH, further validation in a dedicated BPH cohort is warranted.

5 | Conclusions

This study provides evidence for a positive linear association between BMI and prostate volume, highlighting the importance of considering BMI in prostate volume assessments. The findings suggest that increased BMI is associated with larger prostate volumes, which may have significant implications for the diagnosis, management, and treatment of BPH and prostate cancer. Understanding the relationship between BMI and prostate volume can help clinicians improve patient outcomes by tailoring treatment strategies to individual patient characteristics, including body weight. Furthermore, weight management strategies may represent a valuable approach to reducing the risk of prostate enlargement and its associated symptoms, thereby improving the quality of life for patients with BPH.

Author Contributions

Conceptualization: Biagio Barone, Ugo Amicuzi, Matteo Massanova. Methodology: Biagio Barone, Luigi Napolitano, Pasquale Reccia, Benito Fabio Mirto, Software: Benito Fabio Mirto, Raffaele Balsamo, Francesco Del Giudice. Validation: Matteo Ferro, Gian Maria Busetto, Octavian Sabin Tataru. Formal analysis: Biagio Barone, Matteo Massanova, Luigi Napolitano. Investigation: Biagio Barone, Ugo Amicuzi, Luigi Napolitano, Pasquale Reccia, Giuseppe Lucarelli, Celeste Manfredi, Vincenzo Francesco Caputo. Resources: Pasquale Reccia, Benito Fabio Mirto, Raffaele Balsamo, Francesco Del Giudice, Dario Del Biondo, Vincenzo Francesco Caputo, Roberto Falabella. Data curation: Biagio Barone, Dario Del Biondo, Raffaele Balsamo, Ferdinando Fusco. Writing-original draft preparation: Biagio Barone, Ugo Amicuzi, Matteo Massanova, Luigi Napolitano, Pasquale Reccia. Writing-review and editing: Biagio Barone, Benito Fabio Mirto, Felice Crocetto. Visualization: Matteo Ferro, Gian Maria Busetto, Octavian Sabin Tataru, Giuseppe Lucarelli, Celeste Manfredi, Roberto Falabella. Supervision: Dario Del Biondo, Ferdinando Fusco, Ciro Imbimbo, Felice Crocetto. All authors have read and agreed to the published version of the manuscript.

Acknowledgments

The authors have nothing to report. Open access publishing facilitated by Universita degli Studi di Napoli Federico II, as part of the Wiley - CRUI-CARE agreement.

Ethics Statement

The study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The study was approved by the Ethical Committee of the Queen Elizabeth University Hospital, Glasgow, United Kingdom.

Consent

The patients involved in the study have given their written informed consent.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data available on request.

References

- 1. P. Rawla, "Epidemiology of Prostate Cancer," World Journal of Oncology 10 (2019): 63–89, https://doi.org/10.14740/wjon1191.
- 2. K. B. Lim, "Epidemiology of Clinical Benign Prostatic Hyperplasia," *Asian Journal of Urology* 4 (2017): 148–151, https://doi.org/10.1016/j.ajur.2017.06.004.
- 3. F. Crocetto, C. Buonerba, V. Caputo, et al., "Urologic Malignancies: Advances in the Analysis and Interpretation of Clinical Findings," *Future Science OA* 7 (2021): 7, https://doi.org/10.2144/fsoa-2020-0210.
- 4. Z. Ye, J. Wang, Y. Xiao, J. Luo, L. Xu, and Z. Chen, "Global Burden of Benign Prostatic Hyperplasia in Males Aged 60–90 Years From 1990 to 2019: Results From the Global Burden of Disease Study 2019," *BMC Urology* 24 (2024): 193, https://doi.org/10.1186/s12894-024-01582-w.
- 5. W. Zhang, G. Cao, F. Wu, et al., "Global Burden of Prostate Cancer and Association With Socioeconomic Status, 1990–2019: A Systematic Analysis From the Global Burden of Disease Study," *Journal of Epidemiology and Global Health* 13 (2023): 407–421, https://doi.org/10.1007/s44197-023-00103-6.
- 6. A. Loghin, O. Preda, V. Bacârea, et al., "Predictive Preoperatory Variables of the Prostate Tumor Volume," *Romanian Journal of Morphology and Embryology = Revue Roumaine de Morphologie et Embryologie* 52 (2011): 363–368.
- 7. M. Massanova, S. Robertson, B. Barone, et al., "The Comparison of Imaging and Clinical Methods to Estimate Prostate Volume: A Single-Centre Retrospective Study," *Urologia Internationalis* 105 (2021): 804–810, https://doi.org/10.1159/000516681.
- 8. M. Amenta, F. Oliva, B. Barone, et al., "Minimally Invasive Simple Prostatectomy: Robotic-Assisted Versus Laparoscopy. A Comparative Study," *Archivio Italiano di Urologia e Andrologia* 94 (2022): 37–40, https://doi.org/10.4081/aiua.2022.1.37.
- 9. G. W. K. Duarsa, D. O. Dau, I. B. P. Pramana, et al., "Risk Factors for Prostate Volume Progression After Prostate-Transurethral Resection," *Research and Reports in Urology* 12 (2020): 175–178, https://doi.org/10.2147/RRU.S249734.
- 10. J. R. Yamashiro and W. T. de Riese, "Any Correlation Between Prostate Volume and Incidence of Prostate Cancer: A Review of Reported Data for the Last Thirty Years," *Research and Reports in Urology* 13 (2021): 749–757, https://doi.org/10.2147/RRU.S331506.
- 11. Y. Hirasawa, Y. Kato, and K. Fujita, "Age and Prostate Volume Are Risk Factors for Transient Urinary Incontinence After Transurethral Enucleation With Bipolar for Benign Prostatic Hyperplasia," *International Journal of Urology* 25 (2018): 76–80, https://doi.org/10.1111/iju.13472.
- 12. B.-W. Xia, S.-C. Zhao, Z.-P. Chen, et al., "Relationship Between Serum Total Testosterone and Prostate Volume in Aging Men," *Scientific Reports* 11 (2021): 14122, https://doi.org/10.1038/s41598-021-93728-1.
- 13. S. C. Larsson and S. Burgess, "Causal Role of High Body Mass Index in Multiple Chronic Diseases: A Systematic Review and Meta-Analysis of Mendelian Randomization Studies," *BMC Medicine* 19 (2021): 320, https://doi.org/10.1186/s12916-021-02188-x.
- 14. S. Pati, W. Irfan, A. Jameel, S. Ahmed, and R. K. Shahid, "Obesity and Cancer: A Current Overview of Epidemiology, Pathogenesis, Outcomes, and Management," *Cancers* 15 (2023): 485, https://doi.org/10.3390/cancers15020485.
- 15. National Academies of Sciences. "The Science, Strengths, and Limitations of Body Mass Index." *Translating Knowledge of Foundational Drivers of Obesity into Practice: Proceedings of a Workshop Series*; (National Academies Press (US), 2023).

- 16. D. Rendina, L. D'Elia, M. Evangelista, et al., "Metabolic Syndrome Is Associated to an Increased Risk of Low Bone Mineral Density in Free-Living Women With Suspected Osteoporosis," *Journal of Endocrinological Investigation* 44 (2021): 1321–1326, https://doi.org/10.1007/s40618-020-01428-w.
- 17. D. Rendina, L. D'Elia, G. De Filippo, et al., "Metabolic Syndrome Is Not Associated to an Increased Risk of Low Bone Mineral Density in Men at Risk for Osteoporosis," *Journal of Endocrinological Investigation* 45 (2022): 309–315, https://doi.org/10.1007/s40618-021-01638-w.
- 18. S. H. J. Jochems, P. Stattin, C. Häggström, et al., "Height, Body Mass Index and Prostate Cancer Risk and Mortality by Way of Detection and Cancer Risk Category," *International Journal of Cancer* 147 (2020): 3328–3338, https://doi.org/10.1002/ijc.33150.
- 19. N. Tzenios, M. E. Tazanios, and M. Chahine, "The Impact of Body Mass Index on Prostate Cancer: An Updated Systematic Review and Meta-Analysis," *Medicine* 101 (2022): e30191, https://doi.org/10.1097/MD.0000000000030191.
- 20. A. Lee, H. J. Lee, and K. T. Foo, "Can Men With Prostates Sized 80 mL or Larger Be Managed Conservatively," *Investigative and Clinical Urology* 58 (2017): 359, https://doi.org/10.4111/icu.2017.58.5.359.
- 21. J. E. Tallman, C. J. D. Wallis, Z. Zhao, et al., "Prostate Volume, Baseline Urinary Function, and Their Association With Treatment Choice and Post-Treatment Urinary Function in Men Treated for Localized Prostate Cancer," *Prostate Cancer and Prostatic Diseases* 26 (2023): 787–794, https://doi.org/10.1038/s41391-022-00627-1.
- 22. F. Trama, G. D. Lauro, E. Illiano, et al., "Ejaculation Sparing Thulium Laser Enucleation of the Prostate: An Observational Prospective Study," *Journal of Clinical Medicine* 11 (2022): 6365, https://doi.org/10.3390/jcm11216365.
- 23. D. Trumbeckas, D. Milonas, M. Jievaltas, et al., "BPH Importance of Prostate Volume and Urinary Flow Rate in Prediction of Bladder Outlet Obstruction in Men With Symptomatic Benign Prostatic Hyperplasia," *Central European Journal of Urology* 64 (2011): 75–79, https://doi.org/10.5173/ceju.2011.02.art5.
- 24. M. El-Adawy, A. Abdelaziz, A. Salem, et al., "Relation of Baseline Prostate Volume to Improvement of Lower Urinary Tract Symptoms Due to Tamsulosin Monotherapy in Benign Prostatic Hyperplasia: An Exploratory, Multicenter, Prospective Study," *Urology Annals* 12 (2020): 271, https://doi.org/10.4103/UA.UA_91_19.
- 25. B. Barone, L. De Luca, L. Napolitano, et al., "Lower Urinary Tract Symptoms and Mental Health during COVID-19 Pandemic," *Archivio Italiano di Urologia e Andrologia* 94 (2022): 46–50, https://doi.org/10.4081/aiua.2022.1.46.
- 26. T. Martins, T. C. Mussi, and R. H. Baroni, "Prostate Volume Measurement by Multiparametric Magnetic Resonance and Transrectal Ultrasound: Comparison With Surgical Specimen Weight," *Einstein (São Paulo)* 18 (2020): eAO4662, https://doi.org/10.31744/einstein_journal/2020AO4662.
- 27. S. B. Kim, I.-C. Cho, and S. K. Min, "Prostate Volume Measurement by Transrectal Ultrasonography: Comparison of Height Obtained by Use of Transaxial and Midsagittal Scanning," *Korean Journal of Urology* 55 (2014): 470, https://doi.org/10.4111/kju.2014.55.7.470.
- 28. D. Parikesit, C. A. Mochtar, R. Umbas, and A. R. A. H. Hamid, "The Impact of Obesity Towards Prostate Diseases," *Prostate International* 4 (2016): 1–6, https://doi.org/10.1016/j.prnil.2015.08.001.
- 29. J. H. Han, Y. T. Lee, K. W. Kwak, et al., "Relationship Between Insulin Resistance, Obesity and Serum Prostate-Specific Antigen Levels in Healthy Men," *Asian Journal of Andrology* 12 (2010): 400–404, https://doi.org/10.1038/aja.2009.90.
- 30. T. Jarvis, B. Chughtai, and S. Kaplan, "Testosterone and Benign Prostatic Hyperplasia," *Asian Journal of Andrology* 17 (2015): 212, https://doi.org/10.4103/1008-682X.140966.

- 31. J. H. Fowke, T. Koyama, O. Fadare, and P. E. Clark, "Does Inflammation Mediate the Obesity and BPH Relationship? An Epidemiologic Analysis of Body Composition and Inflammatory Markers in Blood, Urine, and Prostate Tissue, and the Relationship With Prostate Enlargement and Lower Urinary Tract Symptoms," *PLoS One* 11 (2016): e0156918, https://doi.org/10.1371/journal.pone.0156918.
- 32. J. Coric, J. Mujic, E. Kucukalic, and D. Ler, "Prostate-Specific Antigen (PSA) and Prostate Volume: Better Predictor of Prostate Cancer for Bosnian and Herzegovina Men," *The Open Biochemistry Journal* 9 (2015): 34–36, https://doi.org/10.2174/1874091X01509010034.
- 33. A. F. Awedew, H. Han, B. Abbasi, et al., "The Global, Regional, and National Burden of Benign Prostatic Hyperplasia in 204 Countries and Territories From 2000 to 2019: A Systematic Analysis for the Global Burden of Disease Study 2019," *The Lancet Healthy Longevity* 3 (2022): e754–e776, https://doi.org/10.1016/S2666-7568(22)00213-6.
- 34. R. M. Simon, L. E. Howard, D. M. Moreira, et al., "Does Prostate Size Predict the Development of Incident Lower Urinary Tract Symptoms in Men With Mild to No Current Symptoms? Results From the REDUCE Trial," *European Urology* 69 (2016): 885–891, https://doi.org/10.1016/j.eururo.2015.12.002.
- 35. J. E. Batista-Miranda, B. Molinuevo, and Y. Pardo, "Impact of Lower Urinary Tract Symptoms on Quality of Life Using Functional Assessment Cancer Therapy Scale," *Urology* 69 (2007): 285–288, https://doi.org/10.1016/j.urology.2006.09.054.
- 36. M. Rivera-Izquierdo, J. Pérez de Rojas, V. Martínez-Ruiz, et al., "Obesity As a Risk Factor for Prostate Cancer Mortality: A Systematic Review and Dose-Response Meta-Analysis of 280, 199 Patients," *Cancers* 13 (2021): 4169, https://doi.org/10.3390/cancers13164169.
- 37. K. Yelsel, E. Alma, A. Eken, M. Gülüm, H. Erçil, and A. Ayyildiz, "Effect of Obesity on International Prostate Symptom Score and Prostate Volume," *Urology Annals* 7 (2015): 371, https://doi.org/10.4103/0974-7796.152056.
- 38. J. Baillargeon, B. H. Pollock, A. R. Kristal, et al., "The Association of Body Mass Index and Prostate-Specific Antigen in a Population-Based Study," *Cancer* 103 (2005): 1092–1095, https://doi.org/10.1002/cncr. 20856.
- 39. L. P. Wallner, H. Morgenstern, M. E. McGree, et al., "The Effects of Body Mass Index on Changes in Prostate-Specific Antigen Levels and Prostate Volume over 15 Years of Follow-Up: Implications for Prostate Cancer Detection," *Cancer Epidemiology, Biomarkers & Prevention* 20 (2011): 501–508, https://doi.org/10.1158/1055-9965.EPI-10-1006.
- 40. B. Bhindi, D. Margel, G. Trottier, et al., "Obesity Is Associated With Larger Prostate Volume But Not With Worse Urinary Symptoms: Analysis of a Large Multiethnic Cohort," *Urology* 83 (2014): 81–87, https://doi.org/10.1016/j.urology.2013.07.039.
- 41. B.-H. Li, T. Deng, Q. Huang, H. Zi, H. Weng, and X.-T. Zeng, "Body Mass Index and Risk of Prostate Volume, International Prostate Symptom Score, Maximum Urinary Flow Rate, and Post-Void Residual in Benign Prostatic Hyperplasia Patients," *American Journal of Men's Health* 13 (2019): 1557988319870382, https://doi.org/10.1177/1557988319870382.
- 42. L. Yue, Y. Ge, T. Wang, M. Ge, C. Zhang, and W. Zhang, "The Correlation Between Body Mass Index and Prostatic-Related Parameters in Men 40 Years or Older in Zhengzhou," *The Aging Male* 23 (2020): 483–488, https://doi.org/10.1080/13685538.2018.1530754.
- 43. M. M. Zaza, T. A.-M. Salem, I. S. F. Hassanin, and M. H. A. Soliman, "Effect of Body Mass Index on Prostate Volume and Prostate-Specific Antigen in Men over 50: A Cross-Sectional Study," *Urologia Journal* 90 (2023): 224–229, https://doi.org/10.1177/03915603231163349.
- 44. S. K. Negi, S. Desai, G. Faujdar, et al., "The Correlation Between Obesity and Prostate Volume in Patients With Benign Prostatic Hyperplasia: A Prospective Cohort Study," *Urologia Journal* 91 (2024): 512–517, https://doi.org/10.1177/03915603241240645.

- 45. A. Erdogan, S. Polat, E. Keskin, and A. Turan, "Is Prostate Volume Better Than PSA Density and Free/Total PSA Ratio in Predicting Prostate Cancer in Patients With PSA 2.5-10 Ng/Ml and 10.1-30 Ng/mL," *The Aging Male* 23 (2020): 59–65, https://doi.org/10.1080/13685538.2019.1578741.
- 46. E. Aigbe, E. Irekpita, F. Ogbetere, and U. Alili, "Correlation Between Prostate Volume and Prostate-Specific Antigen in Nigerian Men With Symptomatic Histologically-Diagnosed Benign Prostatic Hyperplasia," *Nigerian Journal of Clinical Practice* 25 (2022): 1523–1528, https://doi.org/10.4103/njcp.njcp_67_22.
- 47. F. Gentile, E. La Civita, B. Della Ventura, et al., "A Combinatorial Neural Network Analysis Reveals a Synergistic Behaviour of Multiparametric Magnetic Resonance and Prostate Health Index in the Identification of Clinically Significant Prostate Cancer," *Clinical Genitourinary Cancer* 20 (2022): e406–e410, https://doi.org/10.1016/j.clgc.2022.04.013.
- 48. E. Kandirali, M. Z. Temiz, A. Colakerol, E. Yuruk, A. Semercioz, and A. Y. Muslumanoglu, "Does the Prostate Volume Always Effect Cancer Detection Rate in Prostate Biopsy? Additional Role of Prostate-Specific Antigen Levels: A Retrospective Analysis of 2079 Patients," *Türk Üroloji Dergisi/Turkish Journal of Urology* 45 (2019): 103–107, https://doi.org/10.5152/tud.2018.66909.
- 49. T. Kobayashi, K. Mitsumori, T. Kawahara, K. Nishizawa, K. Ogura, and Y. Ide, "Prostate Gland Volume is a Strong Predictor of Biopsy Results in Men 70 Years or Older With Prostate-Specific Antigen Levels of 2.0–10.0 ng/mL," *International Journal of Urology* 12 (2005): 969–975, https://doi.org/10.1111/j.1442-2042.2005.01189.x.
- 50. B. Barone, L. Napolitano, F. P. Calace, et al., "Reliability of Multi-parametric Magnetic Resonance Imaging in Patients With a Previous Negative Biopsy: Comparison With Biopsy-Naïve Patients in the Detection of Clinically Significant Prostate Cancer," *Diagnostics* 13 (2023): 1939, https://doi.org/10.3390/diagnostics13111939.
- 51. M. Massanova, R. Vere, S. Robertson, et al., "Clinical and Prostate Multiparametric Magnetic Resonance Imaging Findings as Predictors of General and Clinically Significant Prostate Cancer Risk: A Retrospective Single-Center Study," *Current Urology* 17 (2023): 147–152, https://doi.org/10.1097/CU9.0000000000000173.
- 52. M. Massanova, B. Barone, V. F. Caputo, et al., "The Detection Rate for Prostate Cancer in Systematic and Targeted Prostate Biopsy in Biopsy-Naive Patients, According to the Localization of the Lesion at the mpMRI: A Single-Center Retrospective Observational Study," *The Prostate* 84 (2024): 1234–1243, https://doi.org/10.1002/pros.24761.
- 53. S. Rapisarda, M. Bada, F. Crocetto, et al., "The Role of Multiparametric Resonance and Biopsy in Prostate Cancer Detection: Comparison With Definitive Histological Report after Laparoscopic/Robotic Radical Prostatectomy," *Abdominal Radiology* 45 (2020): 4178–4184, https://doi.org/10.1007/s00261-020-02798-8.
- 54. D. Terracciano, E. La Civita, A. Athanasiou, et al., "New Strategy for the Identification of Prostate Cancer: The Combination of Proclarix and the Prostate Health Index," *The Prostate* 82 (2022): 1469–1476, https://doi.org/10.1002/pros.24422.
- 55. A. Moolupuri, J. Camacho, and W. T. de Riese, "Association Between Prostate Size and the Incidence of Prostate Cancer: A Meta-Analysis and Review for Urologists and Clinicians," *International Urology and Nephrology* 53 (2021): 1955–1961, https://doi.org/10.1007/s11255-021-02892-w.
- 56. S. Al-Khalil, C. Ibilibor, J. Cammack, and W. de Riese, "Association of Prostate Volume With Incidence and Aggressiveness of Prostate Cancer," *Research and Reports in Urology* 8 (2016): 201–205, https://doi.org/10.2147/RRU.S117963.
- 57. I. Yusim, M. Krenawi, E. Mazor, V. Novack, and N. J. Mabjeesh, "The Use of Prostate Specific Antigen Density to Predict Clinically Significant Prostate Cancer," *Scientific Reports* 10 (2020): 20015, https://doi.org/10.1038/s41598-020-76786-9.

- 58. T. Nordström, O. Akre, M. Aly, H. Grönberg, and M. Eklund, "Prostate-Specific Antigen (PSA) Density in the Diagnostic Algorithm of Prostate Cancer," *Prostate Cancer and Prostatic Diseases* 21 (2018): 57–63, https://doi.org/10.1038/s41391-017-0024-7.
- 59. M. Matsushita, K. Fujita, K. Hatano, M. A. De Velasco, H. Uemura, and N. Nonomura, "Connecting the Dots Between the Gut-IGF1-Prostate Axis: A Role of IGF-1 in Prostate Carcinogenesis," *Frontiers in Endocrinology* 13 (2022): 852382, https://doi.org/10.3389/fendo.2022.852382.
- 60. W. Zhong, X. Wang, Y. Wang, G. Sun, J. Zhang, and Z. Li, "Obesity and Endocrine-Related Cancer: The Important Role of IGF-1," *Frontiers in Endocrinology* 14 (2023): 1093257, https://doi.org/10.3389/fendo. 2023.1093257.
- 61. A. P. Chokkalingam, Y.-T. Gao, J. Deng, et al., "Insulin-Like Growth Factors and Risk of Benign Prostatic Hyperplasia," *The Prostate* 52 (2002): 98–105, https://doi.org/10.1002/pros.10096.
- 62. E. Mazza, E. Troiano, Y. Ferro, et al., "Obesity, Dietary Patterns, and Hormonal Balance Modulation: Gender-Specific Impacts," *Nutrients* 16 (2024): 1629, https://doi.org/10.3390/nu16111629.
- 63. S. Ding, C. O. Madu, and Y. Lu, "The Impact of Hormonal Imbalances Associated With Obesity on the Incidence of Endometrial Cancer in Postmenopausal Women," *Journal of Cancer* 11 (2020): 5456–5465, https://doi.org/10.7150/jca.47580.
- 64. G. Rastrelli, L. Vignozzi, G. Corona, and M. Maggi, "Testosterone and Benign Prostatic Hyperplasia," *Sexual Medicine Reviews* 7 (2019): 259–271, https://doi.org/10.1016/j.sxmr.2018.10.006.
- 65. M. S. Han, A. White, R. J. Perry, et al., "Regulation of Adipose Tissue Inflammation by Interleukin 6," *Proceedings of the National Academy of Sciences* 117 (2020): 2751–2760, https://doi.org/10.1073/pnas.1920004117.
- 66. J. N. Fain, "Release of Interleukins and Other Inflammatory Cytokines by Human Adipose Tissue Is Enhanced in Obesity and Primarily Due to the Nonfat Cells," *Vitamins and Hormones* 74 (2006): 443–477, https://doi.org/10.1016/S0083-6729(06)74018-3.
- 67. S. O. Oseni, C. Naar, M. Pavlović, et al., "The Molecular Basis and Clinical Consequences of Chronic Inflammation in Prostatic Diseases: Prostatitis, Benign Prostatic Hyperplasia, and Prostate Cancer," *Cancers* 15 (2023): 3110, https://doi.org/10.3390/cancers15123110.