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The correlation between obesity and prostate size in patients with benign prostatic hyperplasia at Charlotte Maxeke Johannesburg Academic Hospital

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2021
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THE CORRELATION BETWEEN OBESITY AND PROSTATE SIZE IN PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA AT CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

Dr. Eshely Mampa

18/07/2021

A research report submitted to the University of the Witwatersrand, Johannesburg in fulfilment for the requirement of the degree of Master of Medicine in Urology

DECLARATION

I, Dr Eshely Mampa declare that this research is of my own, unaided work. It is being submitted for the degree Master of Medicine in Urology at the University of the Witwatersrand, Johannesburg. It has not being submitted before for any degree or examination at any other University

Signature: 

18 day of July 2021 in Johannesburg

Presentation and publications from this research project

1. A presentation at Urology registrar forum
2. Publications: published by African Journal of Urology: Mampa E, Haffejee M, Fru P (2021) The correlation between obesity and prostate volume in patients with benign prostatic hyperplasia at Charlotte Maxeke Johannesburg Academic Hospital. Afri J Urol. 27(1):1-6

ABSTRACT

Background

Benign prostatic hyperplasia (BPH) is on the increase placing a substantial burden on health care systems including the Department of Urology at Charlotte Maxeke Johannesburg Hospital Academic (CMJAH). Recent studies have shown that men with high body mass index (BMI) and central obesity, as denoted by waist circumference (WC) have bigger prostate volumes (PV) with subsequent increase in lower urinary tract symptoms (LUTS) than men with normal BMI. The purpose of this research was to investigate the correlation between Obesity and PV in patients with BPH to appreciate the disease burden in our setting

Methodology

The study included 178 men aged between 50-75 years with BPH seen consecutively at CMJAH Urology Outpatient Department between September 2018 and February 2019. Weight and height measurements were obtained to calculate BMI. Furthermore, WC was measured using a measuring tape while a transrectal ultrasound (TRUS) was used to measure PV. Patient demographics, comorbid conditions such as hypertension, diabetes, smoking and prostate specific antigen (PSA) were also recorded

Results

Patients in the study had a mean age of 64.87 ± 6.53 years and the mean BMI was 27.31 ± 3.93 kg/m^2. The mean PV of each BMI group were 52.92± 38.49, 61.00± 33.10 and 64.86± 37.46 cm^3 for normal, overweight and obese groups respectively and the average PV score was 59.36 ± 36.50 cm^3. The mean PSA score was 4.30 ± 3.13 ng/ml, while the mean PV was 54.37 ± 35.25 cm^3 and 65.07 ± 37.29 cm^3 for WC < 94 cm and WC ≥ 94 cm respectively. The mean WC was 98.67 ± 11.50 cm. There was no correlation between BMI and PV (p-value = 0.195) as well as between PV and WC (p-value = 0.051), hypertension, diabetes or smoking. The results revealed that the relationship between PV with PSA level as well as age was significant (p-value = 0.001, p-value = 0.009 respectively)

Conclusion

The results showed no correlation between PV and BMI as well as WC. Diabetes and hypertension also had no positive correlation with PV. A follow-up study may be indicated to look at the correlation between obesity, lower urinary tract symptoms (LUTS) and urinary flow rates to establish whether aggressive management of obesity would have significant impact on the management of BPH.

ACKNOWLEDGEMENT

I would like to thank my supervisor and academic head, Professor M. Haffejee for his support, assistance and expertise in formulating the research topic and methodology. I would particularly like to single out my other supervisor Dr Pascaline Fru: I want to thank you for your excellent cooperation, untiring patience and understanding as you guided me throughout the writing of this project. You are indeed the greatest teacher and mentor. My sincere thanks to CMJAH management for allowing me to carry-out the study. Finally, I would like to thank Amitha Betchan (Urology secretary) and CMJAH staff for their assistance

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ABBREVIATIONS

BPH: benign prostatic hyperplasia

LUTS: lower urinary tract symptoms

PSA: prostate-specific antigen

WC: waist circumference

TRUS: transrectal ultrasound

CMJAH: Charlotte Maxeke Johannesburg Academic Hospital

BMI: body mass index

PV: prostate volume

HREC: Human research ethics committee

SUBMISSIBLE ARTICLE

Title: Correlation between Obesity and Prostate size in Patients with Benign Prostatic Hyperplasia at Charlotte Maxeke Johannesburg Academic Hospital

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INTRODUCTION

Benign prostatic hyperplasia (BPH) is a common condition in older men with an extensive burden on the health care system. Up to 75% of men over the age of 60 are affected and health care expenditure is consumed on outpatient medication [1]. The prevalence of obesity also increases with age and prostatic growth may be accentuated with obesity [2]

There are many mechanisms that have been postulated by which obesity exacerbates BPH. Obesity increases intra-abdominal pressure, which raises intravesical pressure, in turn worsening or causing BPH symptoms such as hesitancy, poor urine stream and nocturia [3]. The ensuing inflammatory activity and oxidative stress associated with obesity are other proposed mechanisms by which obesity worsens BPH [4].

Central obesity accentuates microvascular disease and inflammation, leading to ischemia and oxidative stress favourable to BPH [5]. Chronic inflammation causes the release of pro-growth cytokines and various other growth factors [6]. Another hypothesis is alteration of endocrine status. Increased adipose tissue increases aromatase activity and the conversion of androgen to estrogen resulting in an increase estrogen to androgen ratio. Increased production estrogen by adipose tissue causes suppression of gonadotropins, leading to reduction in testosterone levels, this favours the development of BPH [4].

Body mass index (BMI) is the most commonly used parameter to assess obesity, however, recent guidelines have shown that alternative measurements such as waist circumference (WC) are superior to BMI to assess central obesity [7]. Even though it is easy to calculate, BMI has its drawbacks, including its inability to differentiate between muscle and fat, especially in the elderly. Central obesity is shown to be more detrimental than general obesity and tends to correlate more with BPH than BMI due to its ability to accelerate hormonal and systemic changes that result in inflammation [6]. Although both BMI and WC are important indices required to make the diagnosis of obesity, literature has shown similar outcomes, that obesity increases the risk of BPH while worsening lower urinary tract symptoms (LUTS) [7,8,9,10,11,12].

The Department of Urology at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) treats a considerable number of patients with BPH both medically and

surgically and the incidence is growing as the population ages. This continues to place a substantial burden on the health care system, in this otherwise manageable condition if obesity is reduced [1]. Recent Literature has shown that the impact of obesity on prostate size may also make detection of prostate cancer difficult, leading to under-diagnosis of prostate cancer amongst men with obesity who have large prostate size [13]. In addition, declining PSA levels with rising BMI could affect early detection of prostate cancer since PSA is used as a screening tool and trigger point for prostate biopsy [14]. This study aimed to understand the correlation between obesity and prostatic enlargement and detect a potentially modifiable risk factor for LUTS that could contribute to the epidemiologic investigation of obesity and BPH. The correlation between obesity and PSA levels as well as prostate volume (PV) with diabetes, hypertension and smoking was also investigated.

METHODOLOGY

The study was a prospective cohort analytical study. Ethics approval to conduct the study was obtained from the Human Research Ethics Committee (HREC) of the University of the Witwatersrand (ethics no: M180641). In total, 178 patients between the ages of 50-75 with BPH seen consecutively at CMJAH outpatient department between September 2018 and February 2019 were recruited following informed consent. Patients with prostate cancer**,** on 5 alpha-reductase inhibitors for the treatment of BPH**,** with previous prostate surgery or with BMI <18.5 kg/m2 were excluded from the study.

Measurements

Measurement of body weight and height were done by one trained nurse using standardised protocols. Consenting participants were required to take off their shoes and only wear light clothing. WC was also measured by one trained nurse using a tape measure with the participants in a standing position. To accurately measure WC anterior superior iliac spine (ASIS) was located, measuring tape was placed circumferentially around bare stomach just above the ASIS with participants in quite respiration.

Transrectal ultrasound (TRUS) was used to measure PV by the primary researcher. The patient were required to lie on the left lateral position. The prostate was imaged in the sagittal and axial views. Volume was measured with the TRUS machine settings using length, width and height. In addition, patient age, comorbid conditions such as hypertension, diabetes, smoking and PSA were also recorded.

Classification of overall and central obesity

BMI was derived by dividing weight in kilograms(kg) by height in metres square (m^2). The patients were divided into three subgroups according to their BMI (normal BMI 18.5-24.9 kg/m2, overweight BMI 25-29.9 kg/m2 and obese BMI > 30 kg/m2) in accordance with WHO classification. They were also classified into two groups by WC: normal (<94 cm) and central obesity (>94 cm) using WHO classification

Statistical Analysis

The results were summarised by percentages and frequencies (categorical variables) and means, percentiles, or standard deviations (numerical variables). Associations between variables and outcome were investigated using contingency tables with relative risks and appropriate hypothesis testing. A one-way analysis of variance (ANOVA) was used to assess the relationship between BMI and PV. The relationship between variables was considered positive when the Pearson correlation (r) was greater than zero. A p value of <0.05 was considered significant.

RESULTS

Patients characteristics

The sample was made up of 178 men aged between 50-75 years with BPH seen consecutively at CMJAH Urology Outpatient Department. Patients in the study had a mean age of 64.87 ± 6.53 years and the mean BMI was 27.31 ± 3.93 kg/m^2 with the average PV score of 59.36 ± 36.51 cm^3. The mean PSA score was 4.30 ± 3.13 ng/ml while the mean WC was 98.67 ± 11.50 cm. Baseline characteristics of the participants is shown in Table 1

Table 1: Baseline characteristics of the subjects.

Variable (n=178)	Minimum	Maximum	Mean ± SD
Age (years)	50	75	64.87 ± 6.53
PV (cm^3)	19	230	59.36 ± 36.51
PSA (ng/ml)	1.3	6.4	4.30 ± 3.13
BMI (kg/m^2)	20	38	27.31 ± 3.93
WC (cm)	66	122	98.67 ± 11.50

Of the 178 patients, 49% (n=88/178) had hypertension, 29% (n=51/178) had diabetes and 21% (n=37/178) were smokers as shown on Figure 1

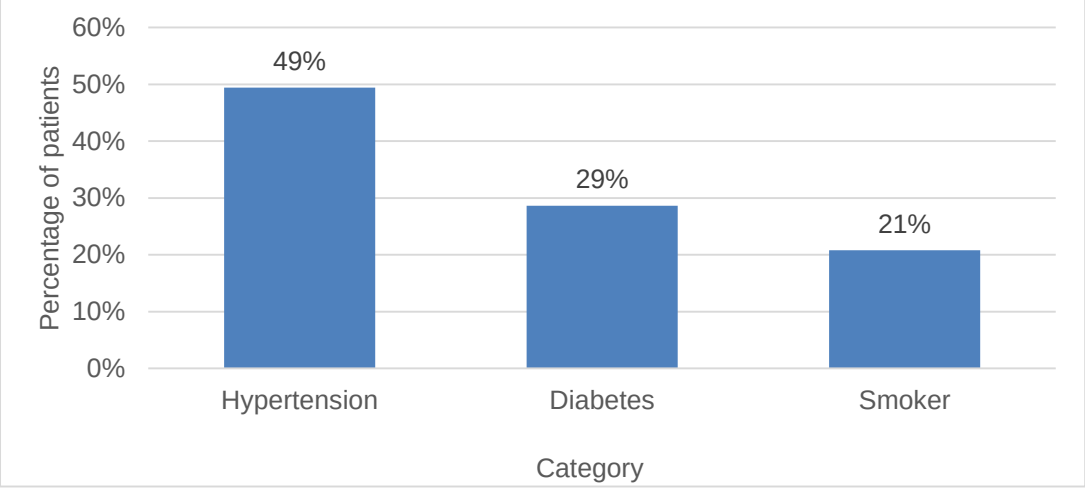

Figure 3: Proportion of patients with hypertension, diabetes and smoking habits

It was noted that 35% (n=62/178) of the patients had a normal BMI, another 35% (n=62/178) were overweight and 30% (n=54/178) were obese indicating an approximate 1:1:1 ratio (Fig. 2).

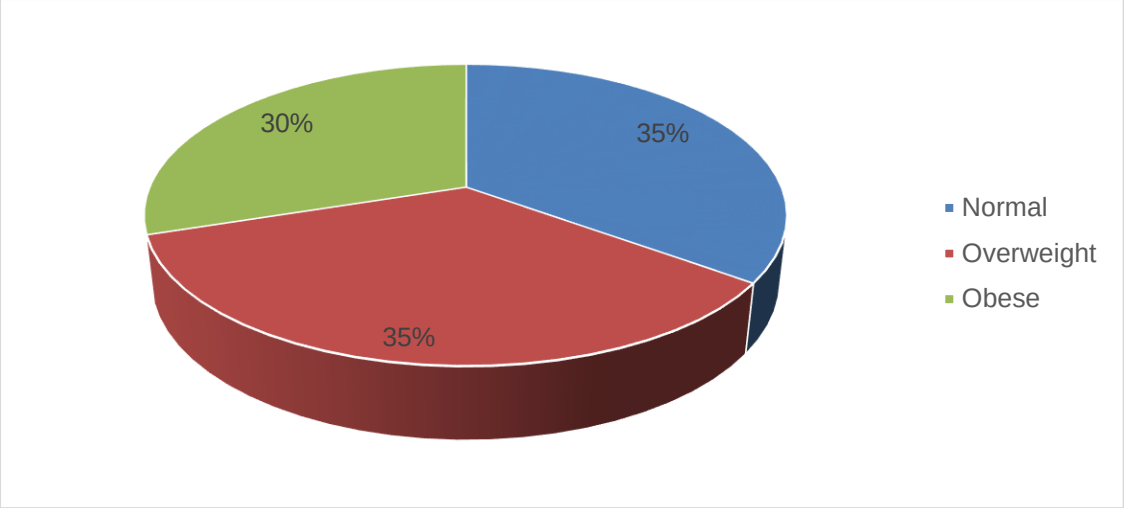

Figure 4: Body mass index categories.

Relationships among variables

BMI and prostate volume

The mean PV of each BMI group were 52.92± 38.49, 61.00± 33.10 and 64.86± 37.46 cm^3 for normal, overweight and obese groups respectively and the average PV score was 59.36 ± 36.51cm^3. Although the PV values were increasing with an increase in the BMI category, these were not statistically significant (p= 0.195) (Table 2)

Table 2: Descriptive statistics for PV (cm^3) for each BMI category

PV (cm^3)

BMI range (kg/m^2)	N	Mean± SD	95% CI Mean		Minimum	Maximum
			Lower Bound	Upper Bound		
Normal(18.5-24.9)	62	52.92± 38.49	43.15	62.69	20.0	205.0
Overweight(25-29.9)	62	61.00± 33.10	52.60	69.40	19.0	193.0
Obese (>30)	54	64.86± 37.46	54.63	75.08	20.0	230.0
Total	178	59.36± 36.50	53.96	64.75	19.0	230.0

Correlation between PV and WC

The mean PV was 54.37 ± 35.25 and 65.07 ± 37.29 cm^3 for WC < 94 and WC ≥ 94 respectively and the average PV was 59.36 ± 36.51 cm^3. These showed no correlation between PV and WC (p-value = 0.051) (Table 3)

Table 3: Correlation between PV and WC

WC	N	PV (cm3) (mean ± SD)	p-value
< 94 (normal)	95	54.37 ± 35.25	
≥ 94 (central obesity	83	65.06 ± 37.29	
Total	168	59.36 ± 36.51	0.051

Correlation between PV with PSA and age

Correlation between PV and each of PSA and age was conducted using Pearson correlation statistics for all 178 participants. Pearson's correlation coefficient showed positive correlation between PV and PSA level (r= 0.247, p-value = 0.001) as well as PV and age (r= 0.195, p-value = 0.009).

Correlation between PV with Hypertension, Diabetes, and smoking independently

The relationship between PV and hypertension, diabetes or smoking is shown in Table 4. The average PV values and p values are shown. There were no significant differences in PV in patients with or without hypertension, diabetes or those who were smokers versus non-smokers (p>0.05)

Table 4: Relationship between PV and hypertension, diabetes or smoking

	Yes	**No**	**Total**	**P-value**
Hypertension				
N(%)	88 (49.4%)	90 (50.6%)	178	
PV (cm^3)	57.28±33.47	61.39±39.33	59.36±36.51	0.45
Diabetes				
N (%)	51 (28.7%)	127 (71.3%)	178	
PV (cm^3)	60.28±28.67	58.99±39.31	59.36±36.51	0.83
Smokers				
N (%)	37 (20.8%)	141 (79.2%)	178	
PV (cm^3)	52.21±26.09	61.23±38.64	59.36±36.51	0.18

DISCUSSION

BPH is a prevalent condition with an estimated 90% of men in their 80s demonstrating histologic evidence of the disease [15]. Previous studies have established a link between obesity and BPH [3,7,9,16,17]. Worldwide, obesity is on the rise even in countries with low socio-economic index implying it is no longer a disease of the affluent [18,19]. This necessitated further research into the effects of obesity on PV, PSA levels and LUTS. A recent systematic review re-affirmed the aggravating effects of obesity on BPH [16].

BMI and central obesity, as determined by the WC, are modifiable risk factors to the development of prostate disease - including BPH, prostatitis and prostate cancer [3 ,10,12,20,21]. Other studies have gone further and demonstrated that central obesity was the most significant predictor of PV than overall obesity [15,22]. Our data suggest that there is no correlation between BMI and PV, whereby obese patients generally had larger PV but the results were not statistically significant (5% CI, P=0.195).

Lee et al and Kim et al arrived at a similar conclusion, that there was no link between BMI and PV, leading to the conclusion that central obesity as denoted by WC> 90cm rather than overall obesity is a predictor of prostate growth and LUTS. These findings were a result of a multicentre, prospective, cross-sectional study at four urology centres in Korea from July 2007 to May 2008 recruiting 602 patients with BPH. Men with waist circumference > 90 cm had increased prostate volume, however, they had lower PSA values than men with WC < 90cm [22,23]. This is in contrast to our study which showed no correlation between WC and PV (p-value= 0.051).

Lee et al showed that prostate volume was bigger in obese and central obesity patients than in those with normal BMI. The authors analysed 146 men over the age of 40 and separated them into three groups according to their BMI and into two groups according to their WC. Significantly increased prostate size was noticeable in the obesity group than in the normal group as well as in the central obesity group than in the group with normal waist size [7]. Similarly to this Matsuda et al and Kim et al showed a positive correlation between BMI and prostate size, however in both these studies there was a negative correlation between BMI and prostate specific antigen (PSA) levels, whereby men with high BMI had low PSA [8,9].

The study showed that hypertension, diabetes and smoking were quite prevalent in our population. There was no statistically significant difference in PV between the hypertensive and the non-hypertensive (P=0.454). similarly to our study, Xie et al showed no correlation between BPH and hypertension [11]. This is in contrast to the findings of a 2013 South Korean study in which men with hypertension had a higher International Prostate Symptom Score as well as larger PV putting them at an increased risk of LUTS compared to the non-hypertensive [24].

Our data showed that diabetic patients had slightly higher mean PV. However, the results were not statistically significant at 5% CI (P=0.832). This finding differs with Ahmed Elabbady's study findings in which diabetes was significantly associated with lower serum PSA and testosterone levels, but larger PV [25]. We did not include the correlation with ethnicity and testosterone levels as an endpoint in our study, which could explain the findings in Elabbady's study.

Smoking is a known trigger of prostate inflammation - a mechanism contributing to BPH [26]. However, previous studies have shown conflicting results on the effects of smoking on PV [24,27]. This study demonstrated that smoking had no statistically significant effect on PV (5% CI, P=0182) despite smokers having minimally larger prostates than non-smokers. This was corroborated by a study done by Platz et al which showed that smoking had no correlation with PV, and that it may in fact reduce PV, thus protecting against BPH [28].

The current evidence trends towards the level of both total and free PSA being directly proportional to PV [29,30,31,32]. This study confirms this relationship as our data showed a direct correlation between the level of PSA and PV (r=0.247, P=0001). Our findings further suggest that increasing age was associated with increased PV (r=0.195, P=0.009) which was in keeping with evidence from previous studies [30]. However not all previous studies agree with these findings. Loeb et al found that PV was highly variable in men with BPH and a good number of aging men had stable or decreasing prostate size [33].

Currently, the medical management of BPH related LUTS is hugely reliant on the prostatic smooth muscle relaxation effects of alpha-adrenergic receptor blockers [18,34]. This has led to a hunt for alternate therapies that may aid LUTS improvement. With the previously established link between obesity and BPH, there have been

proposals to promote and incorporate lifestyle modifications and appropriate medical management as an adjunct to diseases prevention, diagnosis and therapy [11,18,34].

The findings of this study suggest that the routine/aggressive medical management of obesity would be of little to no benefit with regard to BPH/LUTS as there was no correlation between PV and any of hypertension, diabetes, BMI, and WC. This is supported by another study which showed that modest weight loss might not prevent the onset or progression of LUTS [35].

Study limitations

Like many other previous studies, some limitations of this study were a small sample size as well as the fact that it was a single centre study. Larger multicentre studies are required to establish the true effects of obesity on BPH as related to PV and LUTS.

CONCLUSION

The urology department at CMJAH treats a significant number of patients with BPH annually. Obesity has been cited as one of the risk factors for the development of BPH/LUTS. In our study, there was no correlation between PV and BMI, as well as with diabetes, hypertension and smoking. It must be noted though that the size of the prostate does not always correlate with the severity of LUTS. Obesity has the potential to increase intra-abdominal pressure and intravesical pressure, in turn worsening BPH symptoms independent of the PV [3]. A follow-up study is warranted to look at the correlation between obesity, LUTS and urinary flow rates to establish whether aggressive management of obesity would have significant impact on the management of BPH.

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APPENDIX I: Participant information sheet



DEPARTMENT OF UROLOGY

Re: THE CORRELATION BETWEEN OBESITY AND PROSTATE VOLUME IN PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA

Hello, I am Dr E. Mampa, a Urology registrar at Wits University. I would like to invite you to take part in a research study

The purpose of this research is to look at the correlation between obesity and prostate volume in patients with BPH, and identify a potentially modifiable risk factor. Benign prostatic hyperplasia is a highly prevalent disease in older men with substantial burden on public health care system. Recent studies have shown that men with high BMI have large prostate volumes and experience more lower urinary tract symptoms than men with normal BMI. Approval to conduct this study has been obtained from Postgraduate Committee and the Human Research Ethics of the University of the Witwatersrand.

I would like you to partake in this study by undergoing the following measurements: weight, height, BMI, waist circumference, hip circumference and prostate volume. Completion of the measurements will take approximately 15 mins and will be done concurrently with your consultation. You may feel uncomfortable with some of these measurements, but none are harmful. The likely benefit to you are minimal, but, the overall impact on the community will be significant.

Participation in this study is voluntary and will have no impact on your consultation or care. All completed data will remain confidential and anonymity is ensured. The result of the study will be made available to you on your request. The results of the study may be published in a medical journal or presented at a congress.

If you have any queries you contact me on 071 122 6676 or send an email on kastro.kasi@yahoo.com. Further queries may be directed to the WITS Human Research Ethics Committee (Medical)

- Chairperson: Prof Cleaton-Jones @ peter.cleaton-jones@wits.ac.za
- Administrators: Ms Zanele Ndlovu/ Mr. Rhulani Mkansi/ Mr. Lebo Moeng Tel: 011 717 2700/2656/1234

Thank you for your time

Regards
Dr. E Mampa

APPENDIX II: Participant informed consent

INFORMED CONSENT FOR PARTICIPATION IN RESEARCH STUDY			
The correlation between Obesity and prostate volume in patients with benign prostatic hyperplasia			
Participant copy			
HOSPITAL NO		**STUDY ID**	

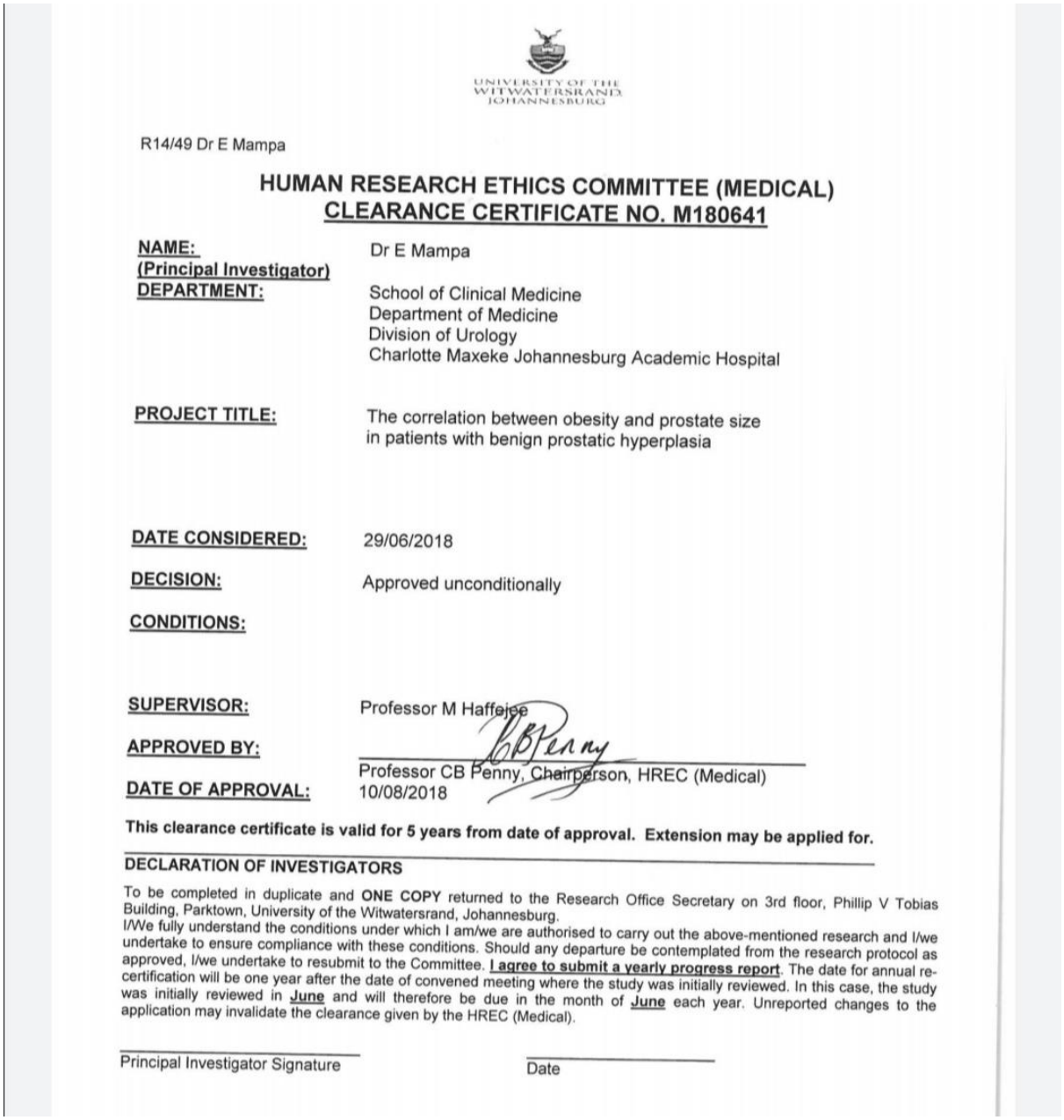
Dear participant

We are conducting a study on the correlation between obesity and prostate volume in patients with benign prostatic hyperplasia. You have been identified as a potential participant in this study

Please read the following information thoroughly

- Benign prostatic hyperplasia is a highly prevalent disease in older men with substantial burden on public health care system.
- Recent studies have shown that men with high BMI have large prostate volumes and experience more lower urinary tract symptoms than men with normal BMI.
- The purpose of this research is to look at the correlation between obesity and prostate volume in patients with BPH, and identify a potentially modifiable risk factor
- The participants will undergo the following measurements: weight, height, BMI, waist circumference, hip circumference and prostate volume
- Subjects will be divided into three subgroups according to BMI (normal BMI 20-25, overweight BMI 26-30 and obese BMI> 30
- You may feel uncomfortable with some of these measurements, but none are harmful
- The likely benefit to you are minimal, but, the overall impact on the community will be significant
- Even though this form contains your hospital number, it will remain private and confidential
- The result of the study will be made available to you on your request
- The results of the study may be published in a medical journal or presented at a congress
- It is emphasised that your participation is voluntary
- You have the right to withdraw participation in the study without the fear of any repercussions, or it affecting your treatmemt.

APPENDIX III: Ethics approval certificate



UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr E Mampa

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M180641

NAME: (Principal Investigator)	Dr E Mampa
DEPARTMENT:	School of Clinical Medicine Department of Medicine Division of Urology Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	The correlation between obesity and prostate size in patients with benign prostatic hyperplasia
DATE CONSIDERED:	29/06/2018
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Professor M Haffejee
APPROVED BY:	Professor CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	10/08/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on 3rd floor, Phillip V Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/We fully understand the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to resubmit to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **June** and will therefore be due in the month of **June** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

Date

APPENDIX IV: Turnitin report



ORIGINALITY REPORT

5%	4%	3%	1%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Seung Hwan Lee. "Effects of obesity on lower urinary tract symptoms in Korean BPH patients", Asian Journal of Andrology, 09/21/2009 Publication	1%
2	hdl.handle.net Internet Source	1%
3	www.diabetovalens.com Internet Source	1%
4	sajcd.org.za Internet Source	1%
5	www.sportmedicine.ru Internet Source	<1%
6	journals.lww.com Internet Source	<1%
7	worldwidescience.org Internet Source	<1%
8	Ozaifa Kareem, Masood Tanvir, Ghulam Nabi Bader. "Prevalence of Obstructive Sleep Apnoea in Patients with Hypertension: Study from a Tertiary Care Hospital", Research Square, 2020 Publication	<1%
9	www.elsevier.es Internet Source	<1%
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APPENDIX V: PROPOSAL

INTRODUCTION

BPH is an exceedingly common condition in older men with extensive unfavourable outcomes on health care system. Up to 75% of men over the age of 60 are affected and health care expenditure are consumed on outpatient medication (Wei et. al, 2005). The prevalence of obesity also increases with age and prostatic growth may be accentuated with obesity (Flegal et. al, 2002)

There are many mechanisms that have been postulated by which obesity exacerbates BPH. Obesity increases intra-abdominal pressure, which raises intravesical pressure, in turn worsening or causing BPH symptoms such as hesitancy, poor urine stream and nocturia (Wang et. al, 2012). The inflammatory activity and oxidative stress is another proposed mechanisms by which obesity worsens BPH. Central obesity accentuates microvascular disease and inflammation, leading to ischemia and oxidative stress favourable to BPH (Chughtai et. al, 2011). Chronic inflammation causes the release of pro-growth cytokines and various other growth factors (Penna et. al, 2009). Another hypothesis is alteration of endocrine status, with raised estrogen to androgen ratio. Increased adipose tissue increases aromatase activity and the conversion of androgen to estrogen. Increased estrogen by adipose tissue causes suppression of gonadotropins, leading to reduction in testosterone levels, a mechanisms favoured in the development of BPH (Williams, 2012)

Generally, prostate size was bigger in obese and central obesity patients than in normal BMI group in a study by Sangyeoup et. al, (2006). The authors analysed 146 men over the age of 40 and were separated into three groups according to their BMI

and two groups according to their WC. Increased prostate size was noticeable in the obesity group than in the normal group (p= 0.03) as well as in the central obesity group than in the group with normal waist size (p=0.002). Similarly to this Rinsho et. al (2004) and Kim et al (2011) showed a positive correlation between BMI and prostate size, however in both studies there was a negative correlation between BMI and PSA levels, whereby men with high BMI had low PSA.

Lee et. al (2009) and Kim et al (2011) arrived at a similar conclusion that , there was no link between BMI and prostate volume, leading to the conclusion that central obesity as denoted by WC> 90cm rather than overall obesity is a predictor of prostate growth and LUTS. This after Lee et al (2009) did a multicentre, prospective, cross-sectional study at four urology centres in Korea from July 2007 to May 2008 which recruiting 602 patients with BPH. Men with waist circumference > 90cm had increased prostate volume, however, they had lower PSA values than men with WC < 90cm.

Fowke et al (2007) did a prospective study to identify the association between BMI, hip and waist circumferences, waist-hip-ratio and height on prostate size, PSA density and PSA levels. After 753 men referred for prostate biopsy were reviewed, men with negative biopsy had increased prostate size by 25% from lowest to highest BMI, Waist or Hip circumferences or height categories. These findings correlate with those of a study done by Li-Ping et al (2007) in China. A total of 649 participants were recruited to undergo transrectal ultrasound (TRUS) prostate volume measurement. BMI and blood pressure were also evaluated by multivariate linear and logistic regression analysis. There was 1cm3 rise in prostate volume for each 0.37 kg/m2 increase in BMI, However there was no association between BPH and hypertension.

In another study by Fowke et al(2016), the authors analysed the correlation between the body composition, prostate tissue inflammation, and systemic inflammation against BPH outcomes, including prostate size and LUTS. A total of 191 patients were reviewed, whereby, anthropometric parameters were measured and systemic inflammation was assessed by serum IL-6, IL-8, IL-1β and TNFα; and by urinary prostaglandin E2 metabolites. The authors found that prostrate volume was 5-9 ml larger in obese men. There was a strong link between the degree of prostate tissue inflammation and LUTS

Although there are many criteria in classifying patient's BMI and WC required to make the diagnosis of obesity, literature has shown similar outcomes, that obesity increases the risk of BPH and while worsening LUTS (Wang et al, 2012). Even though it is easy to calculate, BMI has its drawbacks, including its inability to differentiate between muscle and fat, especially in the elderly. Central obesity is shown to be more detrimental than general obesity and tends to correlate more with BPH than BMI due to its ability to accelerate hormonal and systemic changes leading to inflammation (Penn et al, 2009).

Motivation for Study

The Department of Urology at Charlotte Maxeke Hospital treats a considerable number of patients with BPH both medically and surgically and the incidence is growing as the population ages. This continues to place substantial burden on the health care system, and hours of productivity are lost annually. Recent literature has shown that the impact of obesity on prostate size may also make detection of

prostate cancer difficult, leading to under-diagnosis of prostate cancer amongst men with obesity who have large prostate size (Presti et. al, 2004)

We, therefore, seek to understand the correlation between obesity and prostatic enlargement and detect a potentially modifiable risk factor for LUTS that could potentially contribute to the epidemiologic investigation of obesity and prostate cancer

STUDY OBJECTIVES AND AIMS

Primary Objective

- To investigate the correlation between obesity and prostate size in men with BPH at Charlotte Maxeke Academic Hospital

Secondary Objectives

- To determine the correlation between obesity and PSA levels
- To determine the association between prostate size and patient demographics
- To determine the correlation between prostate volume and other components of metabolic syndrome

METHODOLOGY

Study Design

- Prospective cohort analytical study

Sample Population

This study will include all men aged between 50-75 years with benign prostatic hyperplasia seen conservatively at CMJAH Urology Outpatient Department. A minimum of 200 patients will be recruited in the study based on prevalence of BPH, and will be divided into three subgroups according to their BMI

The following patients will be excluded from the study

- Patients with prostate cancer or suspected prostate cancer
- Patients on 5α-reductase inhibitors for the treatment of BPH
- Patients with previous prostate surgery
- Patients with of BMI <20

Measurements

All patients will be required to provide informed consent before any measurements are undertaken.

Measurement of body weight and height will be measured by one trained nurse using standardised protocols. Consenting participants will be required to take off their shoes and only wear light clothing. The scales will be zeroed before the patient steps onto them. Height measurements will be taken using a drop down tape measure fixed to a wall at 2 metres. Patients will be required to take off their shoes before height measurements are taken. Patients will stand with their back to the wall and look forward. Measuring device will be lowered until it rests on top of the head and height will be recorded. BMI will then be calculated.

Waist and hip circumferences will be measured in standardised protocol by a trained nurse using a tape measure. To accurately measure waist circumference anterior superior iliac spine (ASIS) will be located, measuring tape will be placed circumferentially around bare stomach just above the ASIS. The tape will be tightly in contact with the stomach, but not tight enough to cause compression.

Hip circumference will be measured by identifying the widest part of the buttocks. The tape will be placed at this point and circumferential measurement of hips will be taken. Waist-to-hip ratio will then be calculated

TRUS prostate volume will be measured by the primary researcher. The patient will be required to lie on the left lateral position. The prostate will be imaged in the sagittal and axial views. Volume will be measured with the transrectal ultrasound machine settings using length, width and height

Data Collection

The data collection form is appended as appendix I and will be used for collection of patient demographics, clinical characteristics and for the recording of anthropometry measurements

DATA ANALYSIS

Subjects will be divided into three subgroups according to BMI (normal BMI 20-25, overweight BMI 25-30 and Obese BMI > 30) with a minimum of 50 patients in each category. The data will be entered into an excel spreadsheet and analysis will be done through the assistance of the Department of Biostatistics. Results will be summarised by percentages and frequencies (categorical variables) and means, percentiles, or standard deviations (numerical variables). Associations between variables and outcome will be investigated using contingency tables with relative risks and appropriate hypothesis testing.

IMPLEMENTATION OF FINDINGS

The urology department at CMJAH treats a significant number of patients with BPH annually. Obesity has been cited as one of the risk factors for the development of

BPH, and no study has been done locally to look at the association between obesity and BPH.

Physical activity has been shown to decrease the risk of BPH. This study hopes to develop prevention strategies and treatment directed towards lifestyle changes and weight loss, thereby identifying patients who may benefit from these intervention strategies.

ETHICAL CONSIDERATIONS

The study will be conducted in accordance with the ethical standards as laid down in the 2013 Declaration of Helsinki.

- Prior to initiation of the study the following will be obtained:
  - Approval from the Health Sciences Research Ethics Committee of Wits University
  - Permission from the Head, Department of Urology at CMJAH
  - Permission from the Gauteng Department of Health
- All patients will be required to provide informed consent before any measurements are taken
- Patient identification will be kept confidential, only the primary researcher will have access to the patients' names
- Data analysis will be conducted separate from patient identifiers
- The project is not funded by any industry or organisation
- The study will remain faithful to the study protocol and will respect the opinions, beliefs, and traditions of all the participants and their respective families
- Patients are not chosen to participate in the study based on their ethnicity, age, religion or social class so discrimination will, therefore, be of no concern.
- There are no conflicts of interest that require declaration

TIME SCHEDULE

PHASE	TIME PERIOD
Literature study	1 January 2018 – 31 January 2018
Planning and drafting of research protocol	1 February 2018 – 31 March 2018
Finalisation of research protocol	1 April 2018 – 31 May 2018
Ethics committee submission	June 2018
Data collection and verification	September 2018
Statistical analysis	October 2018 – November 2018
Compilation of research report	December 2018 - January 2019
Completion of project	February 2019
TOTAL TIMESPAN OF STUDY	**± 14 months**

BUDGET

Funding for the study is minimum and will be covered by the principal researcher.

BUDGET			
Forms			R300.00
	Data collection sheets (200 @ 50 cent/form) Participants information sheets (200@ 50 cent/form) Participants consent forms (200@ 50 cent/form)		
TOTAL EXPENSES			**R300.00**

PROBLEMS

There is potential for measurement and methodological errors in the study. Measures to limit errors will be undertaken as follows: One trained Nurse to do all the anthropometric measurements, same calibrated weighing scale will be used for all patients, no heavy clothing when doing measurements, shoes to be taken off, measurements will be repeated when there is doubt

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