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## **Title**

**Metabolic syndrome and prostate cancer in Afro-Caribbean men.**

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## ABSTRACT

### **Introduction and objectives**

Metabolic syndrome is a group of risk factors that increases the likelihood of developing cardiovascular diseases. Although suggested, the relationship between metabolic syndrome and prostate cancer is still inconclusive. Very few studies have addressed this question in populations of African descent, which are disproportionately affected by prostate cancer. This study aimed to assess the prevalence of metabolic syndrome among incident cases of Afro-Caribbean prostate cancer and estimate its association with adverse clinicopathological features and the risk of biochemical recurrence after radical prostatectomy.

### **Materials and methods**

We included 285 consecutive patients with incident cases of prostate cancer attending the University Hospital of Guadeloupe (French West Indies). Metabolic syndrome was evaluated at the time of diagnosis by collecting information on blood pressure, glycaemic status, triglyceride and HDL cholesterol levels, and obesity through various surrogates, including two waist circumference indicators ( $\leq 94$ cm,  $\geq 102$  cm), the waist-to-hip ratio ( $\geq 0.95$ ), and body mass index ( $\geq 30$  kg/m<sup>2</sup>). We followed 245 patients who underwent radical prostatectomy as primary treatment of localized prostate cancer.

### **Results**

The prevalence of metabolic syndrome varied greatly, from 31.6% to 16.4%, when a waist circumference  $\geq 94$ cm or body mass index were used as obesity surrogates, respectively. No significant associations were found between metabolic syndrome, regardless of the obesity criteria employed, and the risk of adverse pathological features or biochemical recurrence.

## **Conclusions**

The high variability in metabolic syndrome resulting from the diversity of obesity criteria used may explain the discordant associations reported in the literature. Further studies using strict and uniform criteria to define metabolic syndrome on homogeneous ethnic groups are encouraged to clarify the association, if any, between metabolic syndrome and prostate cancer outcomes.

**Key Words:** metabolic syndrome, prostate cancer, Afro-Caribbean, radical prostatectomy

## Introduction

Prostate cancer (PCa) is the leading non-cutaneous cancer in men from developed countries and the second most common such cancer in men worldwide.<sup>1</sup> It is disproportionately common among individuals of African descent, irrespective of the place where they live in the world, and less common in Caucasian and Asian populations.<sup>2</sup>

The etiology of prostate cancer is largely unknown, but probably involves a complex interplay between genetic, hormonal, and environmental factors.<sup>3</sup> The only established risk factors are advanced age, ethnic origin, and a family history of PCa.<sup>4</sup> Additional lifestyle-related factors, such as the westernization of eating habits and sedentarity, have been implicated but their true role in the etiology of PCa is still unclear.<sup>2,3</sup>

Metabolic syndrome (MetS) is a clustering of cardiovascular risk factors of which the components include insulin resistance/hyperglycemia, elevated blood pressure, obesity, and dyslipidemia (high serum triglyceride and low HDL-cholesterol). It is a major public health problem in countries with a westernized lifestyle and dietary habits, leading to a high incidence of obesity.<sup>5</sup>

There is evidence supporting the hypothesis that MetS could play a role in the development and/or progression of several cancers.<sup>6,7</sup> Metabolic syndrome has also been considered to be a possible risk factor for PCa but studies conducted to date are discordant and do not make it possible to draw a clear conclusion.<sup>8-11</sup> Moreover, divergences in the direction of associations have been reported depending on the PCa outcome under investigation, including incidence, tumor stage, aggressiveness, progression, and mortality.<sup>12-14</sup> This may be

explained by the wide heterogeneity in the design and quality of these studies, as well as the different MetS definitions and geographic origins and ethnicities of the populations studied.

Definitions of MetS have evolved since its introduction by the WHO in 1998.<sup>15</sup> At that time, the definition required that insulin resistance (impaired glucose tolerance, impaired fasting glucose, type 2 diabetes, or other evidence of insulin resistance) be present. Currently, most definitions do not require any specific component but at least 3 of the 5 features among the following: insulin resistance, elevated blood pressure, obesity, and high triglyceride and low HDL-cholesterol levels.<sup>16,17</sup> Central (abdominal) obesity, estimated by the waist circumference, was retained as an indicator of the obesity component, which has not prevented many authors from using alternative surrogates based on the body-mass index (BMI) or waist-to-hip ratio. In 2009, several major organizations (Joint Scientific Statement, JSS) attempted to unify the criteria, setting a single set of cut-offs, except waist circumference, for which the cut-off varied depending on the country or ethnicity of populations.<sup>5</sup> Thus, the prevalence of MetS may vary depending on the definition used and the cut-off for each criterion, particularly for that concerning obesity. Moreover, the prevalence of individual components that define MetS also differ according to ethnicity; for example, populations of African descent have lower prevalence rates of elevated serum triglyceride or reduced serum HDL-cholesterol and higher prevalence rates of hypertension and diabetes.<sup>18-21</sup> This has led certain authors to suggest that hypertension should be a mandatory criterion for populations of African descent and they have even raised questions about the cut-offs for triglyceride and HDL-cholesterol levels.<sup>22</sup>

Here, we aimed to determine the prevalence of MetS among incident cases of PCa in a population of African descent in the Caribbean (Afro-Caribbean, AC). We used the individual components unanimously used in the JSS definition of MetS and various surrogates for the obesity component. We also investigated the cross-sectional association between MetS and the clinicopathological features at the time of diagnosis and after surgery for those who underwent

radical prostatectomy (RP). Finally, we prospectively examined the association between MetS with the risk of biochemical recurrence (BCR) after RP.

## **Material and Methods**

### *Patients*

This study was conducted in Guadeloupe (French West Indies), a Caribbean archipelago where most of the 400,000 inhabitants are of African descent. Guadeloupe is a French overseas department for which the incidence rate of prostate cancer is one of the highest worldwide.<sup>23, 24</sup> The population benefits from free access to healthcare through the French universal social welfare system

We invited 300 consecutive patients with histologically-confirmed incident cases of PCa attending the University Hospital of Guadeloupe between November 2013 and December 2015. Fifteen of the 300 patients refused to participate, were too ill to participate, or underwent early treatment. We therefore included 285 patients. Patients were interviewed in-person within two months of diagnosis and before surgery. Information was collected concerning demographic characteristics, smoking (never, former, or current), alcohol consumption (never, former, or current), PCa screening history (prior PSA determination within the 5-year period before the PSA test preceding the histological diagnosis of PCa, never, ever), family history of PCa (first-degree relatives: no, yes, not known), and medical background, including the use of medication, in particular anti-hypertensive and hypoglycemic drugs. After the patients had rested at least 5 min, their blood pressure was measured in a sitting position from both arms. The arm with the higher blood pressure was used for three subsequent readings and the results averaged. Anthropometrics were assessed with the subject wearing a scrub suit and no shoes. Body weight was measured using a calibrated scale and standing height was measured with a vertical metal ruler. The BMI was calculated (weight in kilograms/height in meters squared). The

circumference of the waist (measured midway between the lowest ribs and the iliac crest) and hips (at the level of the greatest protrusion of the buttocks, maximum girth) were measured using an anthropometric tape<sup>25, 26</sup> and the waist-to-hip ratio (WHR) calculated. Participants were also asked to provide a fasting blood sample, allowing the measurement of glucose, triglyceride, and HDL-cholesterol concentrations using an automated Cobas 6000 analyzer (Roche Diagnostic, Switzerland). We collected information on the biopsy ISUP Gleason grade, clinical tumor stage, and PSA levels at the time of diagnosis.

Among the included patients, 245 with clinically organ-confined PCa subsequently underwent RP at the same University Hospital. After surgery, we collected data on the pathological tumor stage, pathological ISUP Gleason grade, surgical margins, and follow-up PSA levels. All patients were followed by serial PSA determinations and clinical visits every six months for the first three years after surgery and annually thereafter. BCR was defined as two consecutive (usually four weeks apart) PSA measurements above 0.2 ng/ml, with the date of the first increase after nadir as the recurrence date. Twelve patients were excluded because they were treated with neoadjuvant hormonal therapy or radiotherapy or because the PSA value did not return below 0.2 ng/ml within six weeks after surgery.

#### *Assessment of metabolic syndrome*

We evaluated the individual components of MetS using those recommended for men of African descent in the 2009 JSS<sup>5</sup>: elevated blood pressure (systolic  $\geq 130$  and/or diastolic  $\geq 85$  mm Hg or antihypertensive drug treatment), elevated fasting glucose ( $\geq 1$  g/L [ $\geq 5.6$  mmol/L] or hypoglycemic drug treatment), elevated waist circumference ( $\geq 94$  cm), elevated triglycerides ( $> 1.50$  g/L [ $> 1.7$  mmol/L]), and reduced HDL-cholesterol ( $< 0.4$ g/L [ $< 1.0$  mmol/L]). The presence of MetS was defined as the presence of three or more of these individual components.<sup>5</sup> We also alternatively assessed MetS by changing the cut-off criteria for the waist circumference ( $\geq 102$  cm instead  $\geq 94$  cm) or substituting the waist component with a BMI  $\geq 30$  kg/m<sup>2</sup> or the

WHR ( $\geq 0.95$ ). We also used a challenging definition of MetS in which elevated blood pressure was mandatory with the presence of at least two other components.

### *Statistical analysis*

Prevalence values were calculated with their 95% confidence intervals (95%CI). The odds ratios (OR) and 95%CI for the association between MetS and adverse clinic-pathological features (defined as biopsy ISUP Gleason score  $\geq 3$ , clinical tumor stage T3 or T4, pathological ISUP Gleason score  $\geq 3$ , or pathological tumor stage pT3 or pT4 or N1) were estimated by logistic regression. Covariates (age at the time of diagnosis or surgery, education, smoking, alcohol consumption, PCa screening history, family history of PCa) were included in the models if they were found to change the main effect estimate by  $>10\%$ .<sup>27</sup> Multivariable Cox proportional hazards regression models and 95%CIs were used to estimate the hazard ratio (HR) of BCR associated with MetS prior to surgery. Time to event was defined as the duration between the date of surgery and the PSA value that defined the recurrence event. Patients who did not relapse or were lost to follow-up were censored at the last normal postoperative PSA measurement before May 31, 2020. Covariates (age at surgery, education, smoking, alcohol consumption, PCa screening history, family history of PCa, pathological Gleason grade, pathological tumor stage, surgical margins) were included in the models if they predicted ( $P < 0.05$ ) BCR status. In all regression models, missing data were handled using missing value indicator categories. Statistical analyses were carried out using MedCalc software version 20.010 (MedCalc Software Ltd, Ostend, Belgium). All tests were two-tailed and P values  $< 0.05$  were considered statistically significant unless otherwise indicated. The Holm-correction (step-down method) was used to adjust for multiple comparisons.<sup>28</sup>

The study was approved by the relevant ethical committee for studies involving human subjects (Comité de Protection des Personnes Sud-Ouest et Outremer III, n° 2012-A00556-37). Each participant received, completed, and signed a written informed consent form.

## Results

The baseline characteristics of the study population at the time of diagnosis are presented in Table 1.

The frequency of each individual MetS component at the time of diagnosis is presented in Table 2. Elevated blood pressure was the most frequent MetS component (63%). Among the anthropometric features that define obesity criteria, the prevalence varied widely, with extremes between 56.7% using a waist circumference  $\geq 94$  cm and 10.2% using BMI. Elevated fasting glucose was found for 35.1% of patients whereas elevated triglycerides and decreased HDL-cholesterol were found for only 20.3 and 13.9%, respectively. Using the JSS definition<sup>5</sup>, the prevalence of MetS was 31.6% (Table 2). Substitution of a waist circumference  $\geq 94$  cm with a waist circumference  $\geq 102$  cm, WHR, or BMI resulted in prevalence values for MetS of 23.8, 28.7, and 16.4%, respectively. Finally, making hypertension mandatory (and using a waist circumference  $\geq 94$  cm as the obesity criterion) resulted in a prevalence of MetS of 28.6%.

At the time of diagnosis, no significant cross-sectional associations were found between individual MetS components or MetS, regardless of the obesity surrogate or the mandatory presence of hypertension, and adverse tumor grade or tumor stage (Table 3). Although elevated blood pressure appeared to be associated with a reduced risk of adverse clinical tumor stage ( $P = 0.03$ ), the association was no longer significant after applying a corrected significance level ( $\alpha = 0.006$ ) for multiple comparison.

In total, 245 patients presenting with localized PCa underwent RP and their characteristics are presented in Table 4. Among them, the frequency of each individual MetS component, as well the prevalence of MetS, irrespective of the obesity surrogate or the mandatory presence of hypertension, did not differ from that observed among all incident cases (Supplemental Table 1).

The cross-sectional associations between individual MetS components and the various MetS definitions and adverse clinical and pathological features after RP are presented in Supplemental Table 2. There were no significant associations, except for a waist circumference  $\geq 94$  cm, as an individual MetS component, and pathological ISUP Gleason score  $\geq 3$  (OR = 2.51, IC95% = 1.35-4.68, P = 0.004). The associations remained significant even after applying a corrected significance level ( $\alpha = 0.006$ ) for multiple comparisons.

During 741 person-years of follow-up after surgery, 65 men (27.9 %) experienced BCR. The median follow-up time was 3.6 years and that among men without progression 4.0 years. No significant prospective associations were found between the presence of any individual MetS component or the various MetS definitions, and the risk of BCR (Table 5).

## Discussion

Here, we examined the prevalence of MetS and the individual components that comprise it among an incident AC population of PCa and their association with adverse clinico-pathological features and the risk of BCR for those who underwent RP.

As expected for a population of African descent, the prevalence of elevated blood pressure and fasting glucose were particularly high, affecting almost two thirds and more than one third of PCa patients, respectively. The obesity component applied to populations of African descent, as recommended by the JSS definition of MetS (waist circumference  $\geq 94$  cm)<sup>5</sup>, was the second most frequent individual feature and affected more than half of the patients. By contrast, the prevalence of alternative obesity criteria (waist circumference  $\geq 102$  cm, WHR, BMI) was lower and only present for one tenth of the patients when the BMI criterion was used. Thus, the prevalence of MetS at the time of diagnosis varied greatly, by a factor of two, depending on the obesity criteria used: from 31.6% using a waist circumference  $>94$  cm to 16.4% using BMI. A similar range in the prevalence of MetS was observed for

patients who underwent RP: from 32.6% using the waist circumference  $\geq 94$  cm criterion to 17.3% using BMI. One study that addressed the question of MetS in 139 African-Americans (AA) with PCa at the time of diagnosis did not properly determine the prevalence of MetS because the lipid profile was not collected<sup>29</sup>. In another study that included 274 AA with PCa, the authors reported a prevalence of MetS at the time of diagnosis of 24.4% using BMI as the obesity surrogate. However, this figure is not comparable with our results because this prevalence estimate included 104 AA controls<sup>30</sup>. A third study that included 168 AA with PCa treated by RP reported a prevalence of MetS of 27.4% using a waist circumference  $\geq 102$ cm<sup>31</sup>, which does not differ from that observed in our patients who underwent RP (25.4%, 95%CI = 19.9-31.7) using the same obesity surrogate.

We observed no cross-sectional associations between most individual components of MetS or the various definitions of MetS and adverse PCa features at the time of diagnosis (using biopsy data) or after RP (using the prostate specimen). A positive association was only observed between an elevated waist circumference ( $\geq 94$ cm) and pathological ISUP Gleason score  $\geq 3$ . Although this association remained significant after correction for multiple comparisons, it should be interpreted with caution because of the obvious limited causal inference of our cross-sectional approach. Moreover, the significance of this association is yet to be established, given the absence of an association between this obesity surrogate and the risk of BCR (see below).

After a median follow-up of 3.6 years, we did not observe any association between individual components of MetS, irrespective of the definition, and the risk of BCR. These results are in accordance with those observed among 168 AA patients after a median follow-up of 4.1 years after RP<sup>31</sup>.

Although limited by the relatively small number of cases, this study shows that the use of different obesity surrogate criteria, even if they are measured - and not reported - as in our study, may result in high variability of the value for the prevalence of MetS. In turn, such

variability obviously affects the estimated associations with any outcome under study and may explain the discordances observed in studies related to MetS and PCa.<sup>8-14</sup>

In conclusion, we did not find any significant association between MetS at the time of diagnosis and clinicopathological features of PCa or the risk of BCR after RP in our population of AC men. Further studies with a larger number of patients, using strict and uniform criteria to define MetS, with homogeneous ethnic groups are necessary to clarify the link, if any, between MetS and PCa outcomes.

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There is no particular acknowledgement for this work.

## **Data availability statement**

Due to ethical concerns, supporting data cannot be made openly available. Data can be provided on request, subject to appropriate approvals. Contact the corresponding author for application

## **Ethic statement**

The study was approved by the relevant ethical committee for studies involving human subjects (Comité de Protection des Personnes Sud-Ouest et Outremer III; n° 2012-A00556-37). Each participant provided written informed consent.

## **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## **Author contribution**

ABD, PB, LMu, and LB contributed to conception and design of the study. FL, ABD, LMi, PB, and LB contributed to acquisition of data. LMu and LMi organized the database, and LM realized the statistical analyses. FL and LM wrote the first draft of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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**Table 1****Baseline characteristics of the study population at the time of prostate cancer diagnosis.**

Characteristics	N° (%)
Number of patients	285
Age (years). [median (interquartile range)]	64.6 (59.1-69.9)
Education	
Primary	99 (36.0)
Secondary	122 (44.4)
High school and higher	54 (19.6)
Body mass index (kg/m <sup>2</sup> ) [median (interquartile range)]	25.0 (22.9-28.0)
Body mass index (kg/m <sup>2</sup> )	
< 25	137 (48.2)
25 to 30	118 (41.5)
≥ 30	29 (10.2)
Waist circumference (cm), [median (interquartile range)]	96.0 (88.0-102.0)
Hip circumference (cm), [median (interquartile range)]	102.0 (95.0-108.0)
Smoking	
Never	183 (65.8)
Former or current	95 (34.2)
Alcohol consumption	
Never	43 (15.5)
Former or current	235 (84.5)
PCa screening history	
Never	131 (46.0)
Ever	154 (54.0)
Family history of prostate cancer	
No	152 (55.7)
Yes	84 (30.8)
Do not known	37 (13.5)
PSA (ng/mL) [median (interquartile range)]	7.9 (5.6-12.6)
Clinical stage	
T1c or T2	269 (94.4)
T3 or T4	16 (5.6)
Biopsy Gleason grade	
ISUP Gleason grade 2 or lower	194 (68.1)
ISUP Gleason grade 3 or higher	91 (31.9)

Missing data: Education (n=10), body mass index (n=1), waist circumference (n=8), hip circumference (n=7), smoking (n=7), alcohol (n=7), family history of prostate cancer (n=12)

**Table 2**

**Prevalence of individual metabolic syndrome components and metabolic syndrome at the time of prostate cancer diagnosis**

Features <sup>a</sup>	N°/total N°	% (IC95%)
<b>Metabolic syndrome components</b>		
Elevated blood pressure	179/284	63.0 (57 - 68.7)
Elevated fasting glucose	100/285	35.1 (29.6 - 40.9)
<b>Obesity</b>		
Elevated waist circumference ( $\geq 94$ cm)	157/277	56.7 (50.6 - 62.6)
Elevated waist circumference ( $\geq 102$ cm)	66/277	23.8 (18.9 - 29.3)
Elevated waist-to-hip ratio ( $\geq 0.95$ )	113/276	40.9 (35.1 - 47.0)
Elevated Body Mass Index ( $\geq 30$ kg/m <sup>2</sup> )	29/284	10.2 (6.7 - 14.3)
Elevated triglycerides	52/256	20.3 (15.6 - 25.8)
Reduced HDL-Cholesterol	35/254	13.9 (9.9 - 18.8)
<b>Metabolic syndrome</b>		
With waist circumference ( $\geq 94$ cm)	83/263	31.6 (25.9 - 37.2)
With waist circumference ( $\geq 102$ cm)	62/260	23.8 (19.1 - 29.4)
With waist-to-hip ratio ( $\geq 0.95$ )	75/261	28.7 (23.3 - 34.2)
With body mass index ( $\geq 30$ kg/m <sup>2</sup> )	43/262	16.4 (11.9 - 20.9)
With mandatory hypertension <sup>b</sup>	75/262	28.6 (23.2 - 34.1)

<sup>a</sup> Missing data: Blood pressure (n=1), waist circumference (n=8), waist-to-hip circumference (n=9), body mass index (n=1), triglycerides (n=29), HDL-Cholesterol (n=33).

<sup>b</sup> With waist circumference  $\geq 94$ cm

**Table 3**

**Individual metabolic syndrome components and metabolic syndrome according to ISUP biopsy Gleason score and clinical stage at the time of prostate cancer diagnosis**

Features	ISUP				Clinical tumor stage			
	ISUP < 3 N° (%)	ISUP $\geq 3$ N° (%)	Adjusted OR (IC95%) <sup>a</sup>	P-value	T1c or T2	T3 or T4	Adjusted OR (IC95%) <sup>a</sup>	P-value
<b>Metabolic components</b>								
Elevated blood pressure	121 (62.7)	58 (63.7)	0.93 (0.54-1.59)	0.93	173 (64.2)	7 (43.8)	0.27 (0.08-0.87)	0.03
Elevated fasting glucose	66 (34.0)	34 (37.4)	1.17 (0.68-2.01)	0.57	96 (35.7)	4 (25.0)	0.31 (0.07-1.28)	0.11
Elevated waist circumference ( $\geq 94$ cm)	104 (55.6)	53 (58.9)	1.09 (0.65-1.85)	0.74	149 (57.1)	8 (50.0)	0.75 (0.25-2.29)	0.61

Elevated waist circumference ( $\geq 102$ cm)	45 (24.1)	21 (23.3)	1.06 (0.58-1.96)	0.85	61 (23.4)	5 (31.3)	2.56 (0.74-8.80)	0.14
Elevated waist-to-hip ratio ( $\geq 0.95$ )	73 (39.2)	40 (44.4)	1.18 (0.70-2.00)	0.54	106 (40.8)	7 (43.8)	0.91 (0.30-2.81)	0.87
Elevated Body Mass Index ( $\geq 30$ kg/m <sup>2</sup> )	20 (10.4)	9 (9.9)	1.27 (0.53-3.02)	0.59	28 (10.4)	1 (6.3)	1.96 (0.22-17.7)	0.55
Elevated triglycerides	38 (21.7)	14 (17.3)	0.95 (0.47-1.93)	0.89	51 (21.0)	1 (7.7)	0.82 (0.09-7.78)	0.86
Reduced HDL-Cholesterol	25 (14.5)	10 (12.5)	0.85 (0.38-1.89)	0.69	34 (14.2)	1 (7.7)	0.68 (0.08-5.97)	0.73
<b>Metabolic syndrome</b>								
With waist circumference ( $\geq 94$ cm)	63 (34.8)	20 (24.4)	0.66 (0.36-1.21)	0.18	82 (32.8)	1 (7.7)	0.16 (0.02-1.60)	0.12
With waist circumference ( $\geq 102$ cm)	48 (26.8)	14 (17.3)	0.67 (0.34-1.33)	0.25	61 (24.7)	1 (7.7)	0.60 (0.07-5.29)	0.65
With waist-to-hip ratio ( $\geq 0.95$ )	53 (29.8)	22 (26.5)	0.89 (0.49-1.63)	0.70	74 (30.0)	1 (7.1)	0.17 (0.02-1.52)	0.11
With body mass index ( $\geq 30$ kg/m <sup>2</sup> )	32 (17.9)	11 (13.3)	0.82 (0.38-1.77)	0.62	42 (16.9)	1 (7.1)	0.82 (0.10-7.06)	0.85
With mandatory hypertension <sup>b</sup>	57 (31.7)	18 (22.0)	0.65 (0.35-1.21)	0.17	74 (29.7)	1 (7.7)	0.17 (0.02-1.73)	0.14

<sup>a</sup> Adjusted to age and prior PSA testing

<sup>b</sup> With waist circumference  $\geq 94$ cm

**Table 4**

**Characteristics of patients undergoing radical prostatectomy**

Characteristics	N° (%)
Number of patients	245
Age at surgery (years), [median (interquartile range)]	63.5 (57.9-68.4)
Pathological Gleason grade	
ISUP Gleason grade 2 or lower	175 (71.4)
ISUP Gleason grade 3 or higher	70 (28.6)
Pathological stage	
pT2 and N0	200 (81.6)
pT3 or pT4 or N1	45 (18.4)
Surgical margins	
Negative	150 (61.2)
Positive	95 (38.8)
Biochemical recurrence status <sup>a</sup>	
No	168 (72.1)
Yes	65 (27.9)
Follow-up time (years) [median (interquartile range)]	3.6 (1.6-4.7)

<sup>a</sup> Twelve patients excluded

**Table 5**

**Biochemical recurrence of prostate cancer according to the presence of individual metabolic syndrome components and metabolic syndrome**

<b>Features</b>	<b>Without biochemical recurrence N° (%)</b>	<b>With biochemical recurrence N° (%)</b>	<b>Adjusted HR (IC95%)<sup>a</sup></b>	<b>P-value</b>
<b>Metabolic components</b>				
Elevated blood pressure	103 (61.7)	40 (61.5)	0.79 (0.47-1.32)	0.36
Elevated fasting glucose	51 (30.4)	22 (33.8)	1.22 (0.72-2.07)	0.46
Elevated waist circumference ( $\geq 94$ cm)	91 (56.2)	41 (65.1)	0.96 (0.55-1.68)	0.89
Elevated waist circumference ( $\geq 102$ cm)	41 (25.3)	15 (23.8)	0.61 (0.33-1.15)	0.13
Elevated waist-to-hip ratio ( $\geq 0.95$ )	64 (39.8)	28 (44.4)	1.23 (0.74-2.05)	0.41
Elevated Body Mass Index ( $\geq 30$ kg/m <sup>2</sup> )	19 (11.4)	8 (12.3)	0.60 (0.27-1.34)	0.21
Elevated triglycerides	30 (19.7)	15 (26.3)	1.71 (0.93-3.14)	0.08
Reduced HDL-Cholesterol	15 (10.0)	13 (23.2)	1.15 (0.60-2.20)	0.68
<b>Metabolic syndrome</b>				
With waist circumference criteria ( $\geq 94$ cm)	45 (28.8)	22 (36.7)	1.38 (0.80-2.41)	0.25
With waist circumference criteria ( $\geq 102$ cm)	34 (21.9)	18 (31.0)	1.41 (0.78-2.51)	0.25
With waist-to-hip ratio criteria ( $\geq 0.95$ )	39 (25.5)	20 (33.3)	1.32 (0.75-2.31)	0.34
With body mass index criteria ( $\geq 30$ kg/m <sup>2</sup> )	20 (12.7)	16 (28.1)	1.72 (0.94-3.14)	0.08
With mandatory hypertension criteria <sup>b</sup>	39 (25.0)	20 (33.9)	1.53 (0.86-2.69)	0.15

<sup>a</sup> Adjusted for age at surgery, pathological Gleason grade, pathological stage, and surgical margins

<sup>b</sup> With waist circumference criteria  $\geq 94$ cm