

Evaluation of the influence of body mass index (BMI) and preoperative prostate specific antigen (PSA) concentration on carcinoma of prostate progression, continence, and erection disorders in men after radical retropubic prostatectomy

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KEY WORDS

prostate ► carcinoma of prostate ► radical retropubic prostatectomy ► BMI ► PSA ► cancer progression ► continence and erectile disorders

ABSTRACT

Introduction. Lower testosterone (T) and higher estrogen (E) concentrations in obese men associated with aggravation, delay of detection, and adequate treatment of prostate carcinoma (PCa) make BMI an independent factor influencing the outcomes of its treatment. The aim of this study was the clinical assessment of the influence of BMI depending on preoperative PSA concentration on PCa progression, continence, and erectile dysfunction in 214 patients after radical retropubic prostatectomy.

Material and methods. The group of 214 patients after radical suprapubic prostatectomy was divided into 3 subgroups depending on increasing PSA concentration and into 2 subgroups depending on nerve sparing surgery. The group of 168 patients was divided into 3 subgroups depending on BMI and progression continence and erectile dysfunction were also assessed.

Results. Preoperative PSA concentration significantly influences the postoperative Gleason score and PCa progression. BMI does not influence PCa progression. Neither BMI nor preoperative PSA concentration influenced continence and erectile dysfunction in patients after radical suprapubic prostatectomy.

Conclusions. 1. Preoperative PSA concentration affects postoperative Gleason score, biochemical recurrence, and metastases, but does not influence continence or erectile function. 2. BMI does not correlate with preoperative PSA concentration, postoperative Gleason score, progression, continence, or erectile function. 3. Radical retropubic prostatectomy with nerve sparing impacts on decreased percentage of continence and erectile dysfunction, but it is not proportional improvement.

evaluate risk factors they may influence in order to reduce adverse tendencies. These factors may be: biological, environmental and associated with inappropriate behavioral patterns. Therefore, it may be a genetic polymorphism, obesity, diet, socioeconomic conditions or other unexplored factors [1].

Obesity is such a factor, which incidence has been rising for the last two decades at an alarming pace, particularly in civilized societies [2].

Scientific evidences gathered in the last few years indicate that obesity may increase the risk of death in patients with diabetes, heart diseases and with metabolic disorders. At the same time, countless evidence proves that the risk of neoplastic diseases is increased in obese individuals [3, 4]. The influence of obesity on prostate cancer is currently ambiguous and experts' opinions are often radically different [5, 6].

The aim of the study is to evaluate the influence of BMI on preoperative total PSA, Gleason scale, and progression of prostate cancer after radical retropubic prostatectomy. At the same time the influence of BMI and PSA on the level and rate of continence and erection disorders was evaluated.

MATERIAL AND METHODS

214 subjects participated in the study evaluating the influence of PSA on the progression of prostate cancer and the influence of radical retropubic prostatectomy with nerve sparing surgery. 168 patients responded to a survey on continence and erection disorders with evaluation of the influence of BMI. These patients were aged 49–73 years (mean 60.9 years). All patients were operated in 1997–2007. Only the patients with radical retropubic prostatectomy were followed-up.

The patients were divided into 2 groups on the basis of nerve sparing surgery: 1 (n = 157) with sparing and 2 (n = 57) without sparing. The patients were divided into 3 groups on the basis of total PSA levels before surgery treatment: 1. (n = 97) the patients with PSA ≤10 ng/ml, 2. (n = 80) with PSA 10.1–20.0 ng/ml, and 3. (n = 37) patients with PSA ≥20.1 ng/ml.

The majority of patients were followed-up because control evaluations of PSA were carried out every 6 months, while ultrasonographic examination of the urinary system and chest X-ray were performed every 6–12 months. Biochemical relapse was defined as the level of total PSA >0.2 ng/ml in two consecutive evaluations. Real relapse was diagnosed on the basis of a positive result of histopathological examination of a biopsy specimen taken from the suspected location, for example from urethrocystostomy.

BMI was calculated on the basis of the formula: body weight (in kilograms) divided by body height (in meters) squared. According to

INTRODUCTION

In the process of searching for causes of increased incidence and mortality in men with prostate cancer, researchers began to

Table 1. Modified continence and erectile dysfunction scale.

Continence		Erection
O ⁰	No incontinence	No erection disorders
1 ⁰	Little stress urinary incontinence. Incontinence of 1–10 g of urine. Sanitary pads 1–2 usually only wet.	Erections infrequent or not full/difficulties in penetration or premature ejaculation
2 ⁰	Stress urinary incontinence after little effort, sanitary pads 1–4 usually wet. Incontinence of 10–50 ml of urine. Improvement after pharmacological treatment. Bed wetting.	Erection and penetration possible only after pharmacological treatment
3 ⁰	Severe urinary incontinence, even without effort, more than 4 sanitary pads wet. Incontinence of more than 50 ml of urine per day. No effect after pharmacotherapy.	No erection even after pharmacotherapy.

Table 2. The influence of preoperative PSA concentration on prostate carcinoma progression in men after radical prostatectomy.

	Group I PSA ≤10 ng/ml (n = 97)	Group II PSA 10.1 – 20 ng/ml (n = 80)	Group III PSA >20 ng/ml (n = 37)	Together (n = 214)	Statistical differences
Patient age (years) ^a	61.6	58.3	61.7	60.8	0.96
PSA T ng/ml ^a	6.52	13.2	33.4	13.7	0.000
Gleason Scale (total)	4.82	5.81	6.83	5.53	0.001
pT3	10 ^b – 10.5% ^c	33 – 41.2%	24 – 64.9%	67 – 31.3%	0.001
Mortality	6 – 6.2%	9 – 11.2%	2 – 5.4%	17 – 7.3%	0.07
Biological relapse	10 – 10.3%	21 – 26.2%	17 – 45.9%	48 – 22.4%	0.005
Actual relapse	6 – 6.2%	8 – 10.0%	3 – 8.1%	17 – 7.9%	0.3
Metastasis	5 – 5.1%	6 – 7.5%	1 – 2.7%	12 – 5.6%	0.47
Observation time (months)	58.5	59.1	66.9	60.3	

a – average, b – number of patients with a given disease, c – percent of patients with a given disease

Table 3. The influence of Body Mass Index (BMI) on prostate carcinoma progression in men after radical prostatectomy.

BMI	Group I BMI <25 kg/m ² (n = 52)	Group II BMI 25 – 29.9 kg/m ² (n = 74)	Group I BMI ≥30 kg/m ² (n = 42)	Total (n = 16.8)	Statistical difference
Age of patients (years) ^a	62.5	60.7	61.5	61.5	0.53
PSA T (ng/ml) ^a	13.3	14.3	11.5	13.4	0.67
Gleason scale ^a (total score)	5.27	5.35	5.65	5.41	0.51
pT ₃	8 ^b – 15.4% ^c	25 – 33.8%	18 – 30.3%	51 – 30.3%	0.015
Death	4 – 7.7%	4 – 5.4%	3 – 7.1%	11 – 6.6%	0.49
Biological relapse	12 – 23%	12 – 16.2%	10 – 23.8%	34 – 20.2%	0.66
Real relapse	4 – 7.7%	8 – 10.8%	3 – 7.1%	15 – 8.9%	0.83
Metastasis	–	4 – 5.4%	2 – 4.8%	6 – 3.6%	0.27
Time of follow-up (months)	54.2	56.5	61.4	56.8	

a – mean values of a parameter, b – number of patients with an event, c – percentage of patients with an event

WHO recommendations, the following limit values were accepted: below 18.5 kg/m² – underweight, up to 24.99 kg/m² – norm, up to 29.9 kg/m² – overweight, above 30 kg/m² – obesity, and above 35 kg/m² – pathological obesity. The patients were divided into 3 groups on the basis of these norms: 1. (n = 52) norm, 2. (n = 74) overweight, 3. (n = 42) obese.

The degree of continence and erection disorders was evaluated on the basis of a three-degree scale based on the recommendations of the International Continence Study. Modified Mac Gair [7] scale, which included both continence and erection, was filled in by patients (Table 1).

Before surgical treatment 9 (4.2%) patients had urinary incontinence, while 46 (21.5%) did not have sexual intercourse for ap-

proximately one year. There were 58 (27.1%) patients treated with hormone therapy after surgery and 21 (9.8%) before surgery. Radiotherapy was used in 11 (5.1%) patients. Statistical analysis was carried out using Statistica v. 6.0 software using Chi2 and ANOVA tests with the confidence level equaling p <0.05.

RESULTS

16 of 214 (7.5%) patients treated surgically died during the study, 13 (6.1%) of them died due to neoplastic causes. Follow-up duration ranged from 6 to 143 months (mean 57.8 months).

As seen in the results from Table 2, the differences in mean PSA levels, Gleason scale, the rate of pT3, and biochemical relapses

Table 4. The influence of Body Mass Index (BMI) on prostate carcinoma progression in men after radical prostatectomy depending on preoperative PSA concentration.

BMI	Group I PSA 10.0	Group II PSA 10.1–20.0	Group III PSA >20.1	Observation time	Total	Statistical difference
<25.0	5 ^a /26 ^b – 11.2% ^c	6/17 – 35.3%	5/9 – 55.5%	54.2	16/52 – 30.8%	<0.05
25–29.9	8/39 – 20.5%	9/21 – 42.8%	9/14 – 64.3%	55.5	26/74 – 35.1%	<0.01
≥30.0	6/21 – 28.6%	5/13 – 38.5%	5/8 – 62.5%	61.4	16/42 – 38.0	<0.05
Total	19/87 – 21.8%	20/50 – 40.0%	19/31 – 61.3%	57.0	58/168 – 34.9%	<0.01
Statistical differences	0.64	0.8	0.75			

a – mean values of a parameter, b – number of patients with an event, c – percentage of patients with an event

Table 5. The influence of Body Mass Index (BMI) on continence and erectile dysfunction in men after radical prostatectomy.

BMI	Continence			Erection disorders		
	0+1 ^o	2 ^o	3 ^o	0+1 ^o	2 ^o	3 ^o
<25.0 (n – 52)	38 ^a – 73% ^b	4 – 7.7%	10 – 19.3%	41 – 78.8%	11 – 21.2%	–
25–29.9 (n – 74)	61 – 82.4%	3 – 4%	10 – 13.6%	64 – 86.4%	10 – 13.6%	–
≥30.0 (n – 42)	30 – 71.4%	4 – 9.5%	8 – 19.1%	34 – 80.9%	8 – 19.1%	–
Statistical differences	0,86			0,56		

a – number of patients in a group, b – percentage of patients in a group

Table 6. The influence of preoperative PSA concentration on continence and erectile dysfunction in men after radical prostatectomy.

PSA–T	Continence			Erection disorders		
	0+10	20	30	0+10	20	30
Group I (n=97)	73 ^a – 75.2% ^b	5 – 5.1%	19 – 19.7%	38 39.1%	5–5.1%	54 – 55.8%
Group II (n=80)	63 – 78.7%	5 – 6.3%	12 – 15%	27 – 33.7%	8–10%	45 – 56.3%
Group III (n=37)	31 – 83.7%	2 – 5.4%	4 – 10.9%	11 – 29.7%	3–8.1%	23 – 62.2%
Statistical differences	0.34			0.53		

a – number of patients in a group, b – percentage of patients in a group

are statistically significant in the studied groups. Such differences were also demonstrated with reference to progression of prostate cancer ($p = 0.002$), where the following variables were summed: biochemical and real relapses, deaths, and metastases. Progression was as follows: 27.8%, 54.9%, and 62.1% respectively; 5-year survival depending on the level of PSA T was: 93.8%, 88.8%, and 94.6% respectively, and relapse-free survival: 83.5%, 63.8%, and 46% ($p = 0.002$) respectively.

Table 3 shows that BMI level had no statistically significant influence on mean total PSA level before surgery, Gleason score, or prostate cancer progression. Only the rate of advanced (pT3) prostate cancers was significantly higher in the consecutive groups ($p = 0.016$). This table demonstrates that 5-year total survival was: 92.3%, 94.6%, and 92.9% respectively, while relapse-free survival was: 69.5%, 72.0%, and 69.1% respectively, the differences are not significant.

As Table 4 shows, progression of prostate cancer is significantly different in groups of patients with different PSA levels. Such differences were not shown in case of groups of patients with different BMI values within the groups of patients with different PSA levels.

Table 5 shows that both continence and erection disorders, irrespective of their magnitude, are independent on BMI value.

Table 6 shows that preoperative total PSA levels had no significant influence on the degree and rate of continence and erection disorders.

Comparing two groups of patients, with and without nerve sparing surgery, it was found that continence 0–20 was maintained

in group I in 143 (91.1%) patients and in group II in 44 (77.2%) patients ($p = 0.03$). Erection disorders 0–20 were present in 77 (49.0%) and 15 (26.3%) patients, respectively ($p = 0.001$). This difference with reference to group I equaled 42.2% and with reference to group II equaled 50.9%. This indicates disproportionate improvement of both complications after radical retropubic prostatectomy with or without nerve sparing surgery.

DISCUSSION

In the last few years, papers demonstrating the influence of obesity on the risk of stress urinary incontinence, BPH, nephrolithiasis (particularly cast-like), erection disorders, and metabolic syndrome were published in urological literature. The risk of deaths in patients with kidney and prostate cancers is also increased [8, 9, 10].

It is emphasized in numerous publications that obesity may influence the results of prostate cancer treatment by the influence of excessive fatty tissue on hormone (mainly sexual hormones) metabolism. It is probable that aggressive forms of prostate cancer may develop as a result of decreased concentration of T because of its conversion to E catalyzed by aromatase contained in adipocytes [11, 12].

The increased levels of leptin, insulin or insulin-like growth factor observed in these patients correlates with the degree of obesity and may be a mitotic factor for prostate tissue [8]. On the other hand, increased level of E should inhibit the development of prostate cancer and have a positive effect on the treatment of existing prostate cancer [13].

Spangler et al. found that the fivefold increase in the frequency of biochemical relapses and significantly increased advancement of prostate cancer after radical retropubic prostatectomy in Afro-Americans comparing to Euro-Americans may be caused, among others, by obesity. The incidence of overweight individuals and obesity is three times higher comparing to Caucasian patients [1].

Freedland et al. on the basis of studying more than 3000 patients after radical retropubic prostatectomy estimated the risk of prostate cancer of high histopathological malignancy and clinical advancement (positive surgical margin, infiltration of the capsule, often positive lymph nodes) as increasing, together with increasing BMI value. These changes are accompanied by a significant increase of biochemical progression, particularly in the patients with BMI above 35 kg/m². They also found that obesity is present in younger patients, whose physiological values of PSA are already lower [14].

Amling and Freedman on the basis of clinical studies of 4,000 patients after radical retropubic prostatectomy demonstrated that increased value of BMI is associated with a statistically significant increase of biochemical progression risk [15]. These observations were confirmed by Freedland et al. in a study in which 3,000 patients from one center participated. They also stated that this progression was observed in shorter time after radical retropubic prostatectomy and increased BMI value correlates with increasing risk of metastases, which was particularly noticeable in the last 10 years [5].

Numerous authors do not agree with the assessment of obesity as an unambiguous predictor of poor outcome. In two large clinical studies Montgomery and Halabi found a positive effect of obesity on the rate of relapses and metastases, as well as on total survival in patients treated with LHRH analogues with hormone-sensitive prostate cancer [13]. Some authors explain the observations mentioned above by the fact that these patients were in better condition comparing to patients with underweight or cachexic [9, 14].

On the basis of the current state of knowledge it has to be objectively stated that not only an increased share of the fatty tissue in total body weight, but also other factors increase the risk of progression. The following facts are listed to prove this thesis:

Difficulties in per-rectum examination in obese patients.

Relatively low values of PSA in laboratory tests due to hemodilution in obese patients.

Increased levels of estrogens, insulin, leptin, and a low level of T require further diagnostics, which delays adequate treatment.

Increased rate of diseases coexisting with obesity delays radical retropubic prostatectomy, which often translates to greater advancement of prostate cancer in these patients [2, 10, 12].

Three clinical studies cited in the introduction, in which 10,000 patients after radical retropubic prostatectomy were included, seem to be statistically strong enough to prove that obesity is an independent risk factor for biochemical relapse and increased advancement of prostate cancer [5, 14, 15].

Our study, in which a significantly lower number of patients were enrolled, did not confirm a statistically significant influence of BMI on the progression of prostate cancer, contrary to baseline PSA.

Continence and erection disorders are the most frequent complications of radical retropubic prostatectomy, which significantly affects postoperative quality of life [16]. Since the introduction of radical retropubic prostatectomy with nerve sparing surgery the rate of these complications has been significantly reduced. Further improvement followed the introduction of laparoscopic and robotic surgery. In spite of considerable advancement in this area, the quality of life of numerous patients is significantly decreased because of these complications [17].

Castilles et al. evaluated the rate of continence and erection disorders after radical retropubic prostatectomy in 428 patients

and found that in patients without nerve sparing surgery the rate of good results was 37% compared to 7% in patients with nerve sparing surgery. Only age, but not the value of BMI, had an effect on worse results [16]. Similar observations were reported by other authors, but for example Ahlgren et al. noted that improved continence does not go hand in hand with improved erection and vice versa. These authors explain this fact by the existence of different nerve fibers for these two functions [18].

Similar conclusions result from our observation. Radical retropubic prostatectomy with nerve sparing surgery significantly decreases the rate of these complications, but this improvement is not the same in terms of their incidence, as well as their advancement. The results obtained after radical retropubic prostatectomy with nerve sparing surgery are comparable to those reported by other authors [19, 20]. Slightly worse results in maintaining erection may result from the fact that impotence is present before radical retropubic prostatectomy in more than 21% of patients.

CONCLUSIONS

Preoperative levels of PSA have a statistically significant effect on: Gleason score, rate of biochemical relapses, and cancer progression, but not on the rate and degree of continence and erection disorders in the patients after radical prostatectomy.

An increased level of BMI value does not affect increased level of PSA, Gleason score, or cancer progression, but has no effect on the rate and degree of continence and erection disorders.

Nerve sparing radical retropubic prostatectomy in patients decreases the rate of incontinence and erection disorders, but the improvement is not proportional for both complications.

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