

## Bladder Drainage and Glandular Epithelial Morphometry of the Prostate in Benign Prostatic Hyperplasia with Severe Symptoms

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### ABSTRACT

*Objective:* Morphometrically analyze the cells nuclei of the basal layer of the prostatic glandular epithelium in 20 patients aged between 57 and 85 years presenting benign prostatic hyperplasia with severe symptoms, catheterized or not.

*Materials and Methods:* Patients with score of severe prostatic symptoms (with indication for transurethral resection of the prostate) were distributed according to the presence or absence of bladder drainage previous to the surgery, in the treated group (n = 10, catheter during 3 months) and in the control group (n = 10, without catheter). After obtaining prostate fragments through transurethral resection and the use of morphometric techniques, 100 nuclei of prostatic glands epithelium cells were studied (as to size and form), and compared to 500 nuclei from patients submitted to catheter drainage and 500 nuclei of non-catheterized patients.

*Results:* Significantly reduced values of the major, medium and minor nuclear diameters, volume, area and perimeter, contour index and nuclear volume-nuclear area ratio were observed in the treated group in relation to the control group. As to the form, eccentricity and coefficient of nuclear form, there were significant differences between treated and control groups.

*Conclusion:* Long-term catheter bladder drainage in patients presenting benign prostatic hyperplasia with severe symptoms is associated to the reduction of morphometric parameters of the nuclei of prostatic glands' epithelial cells, suggesting a likely decompressive duct effect.

*Key words:* prostate; BPH; morphometry; acini; adenoma

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### INTRODUCTION

Benign prostatic hyperplasia is the most common disease in older man, standing out in men over 50 years of age (1-3). At the age of 40, approximately 10% of the men present histological evidences of benign prostatic hyperplasia with a progressive increase of the condition according to the age, affecting 90% of the individuals at the age of 80 (4).

The increase of the survival rate exposes male population to the risk of being affected by benign prostatic hyperplasia that also increases the chances of urinary retention. This requires an immediate medical intervention, since men over 60 years old with life expectancy of more than 20 years will present chances of up to 23% to develop urinary retention. In these cases the immediate clinical treatment for urinary retention conditions is catheter bladder drainage (5).

The chronic use of catheter bladder drainage has awakened the interest regarding secondary alterations that the prostatic epithelium cells might develop due to hyperplasia (6) and through the constant contact of the epithelium of the prostatic urethra with the catheter. Histopathologic studies accomplished through transurethral biopsies of the prostatic urethral mucosa reveal inflammatory infiltration with proliferation of the prostatic urethra epithelial and connective tissues (7). However, morphometric studies on the prostatic cells in cases of urethral catheter are rare (8,9).

Therefore, this study aimed at morphometrically analyze nuclear alterations in prostatic gland cells on patients presenting benign prostatic hyperplasia with severe symptoms either catheterized or not, submitted to transurethral resection of the prostate .

## MATERIALS AND METHODS

After the approval of the Research Ethics Committee, 20 patients with symptomatic benign prostatic hyperplasia were studied, being 18 white and 2 black, aged between 57 and 85 years (mean of 70 years) seen during the year of 1998.

Clinical history was accomplished according to the International Symptom 7 questions Score index (10), counting on 7 questions with an option of answers with punctuations from 1 to 5 and classification of the symptoms as light (from 1 to 7 points), moderate (from 8 to 18 points) and severe (from 19 to 35 points). Only patients with a score of symptoms classified as severe were selected and those were divided into a treated group (10 patients with mean age of  $76 \pm 0.9$  years submitted to bladder drainage with a conventional 18F Foley catheter for 3 months due to urinary retention caused by benign prostatic hyperplasia, and a control group (10 patients with mean age of  $74 \pm 2.8$  years without bladder drainage presenting severe symptoms). Afterwards, both groups were assessed preoperatively and submitted to a single biopsy of prostatic tissue by the technique of transurethral endoscopic resection (11), with the size of the fragment varying from 0.5 to 1 cm length

by 2 to 3 mm thickness. Patients of both groups were not submitted to any other type of postoperative treatment.

The collected material was immediately fixed in 10% formalin, included in paraffin and sectioned with a thickness of 5  $\mu$ m. The slides were stained with hematoxylin-eosin (five slides per patient) and examined in a light microscope with 1.200X magnification for cariometric analysis. The cell nuclei of the basal layer of the prostate glandular epithelium were assessed, summing up to 500 nuclei per patient of the treated group (with catheter) and 500 nuclei per patient of the control group (without catheter), obtaining a mean value for each morphometric parameter in each patient, that allowed to calculate mean values for each parameter in the 2 groups.

Cariometric assess of the nuclei comprehended the study of major, medium and minor diameters, major/minor diameters ratio, nuclear volume, nuclear area, volume/area ratio, perimeter, contour index, eccentricity, and coefficient of form. For statistical analysis, the Student t test was used with the Welch correction for morphometric data comparison with arithmetic means and different standard deviations in 2 independent samples adopting an alpha error of 5%. The final results were expressed in a table containing the mean values and standard deviations for morphometric parameters of the cell nuclei of the basal layer of the prostate glandular epithelium for both the treated and the control groups.

Morphometric calculations (with conversion of the units in mm) were made by the GMC Basic Software Biologic Research®, 8.1. version, of the Faculty of Dentistry, Riberao Preto, University of Sao Paulo, available on the Internet (12). Statistical analysis was accomplished by means of the program MINITAB®, 12.21 version.

## RESULTS

Table-1 shows the mean values and standard deviations for the major, medium and minor diameters, nuclear volume, perimeter, eccentricity, contour index, volume/area ratio and coefficient of form

**Table 1** – Mean values and standard deviations for the major, medium and minor diameters, volume, perimeter, eccentricity, contour index, volume/area ratio, and coefficient of form of the cell nuclei of the basal layer of the prostate glandular epithelium in both the treated and the control groups.

Variable	Treated Group		Control Group		p Value
	Mean (mm)	Standard Deviation	Mean (mm)	Standard Deviation	
Major diameter	11.67	0.95	15.05	1.36	0.0000*
Minor diameter	7.09	0.91	8.38	0.90	0.0026*
Medium diameter	9.02	0.86	11.10	0.86	0.0001*
Major/Minor diameter	1.71	0.13	1.89	0.22	0.0550
Volume	4.21	1.21	7.74	1.76	0.0001*
Area	66.0	13.1	99.4	15.3	0.0001*
Perimeter	30.00	2.78	37.76	2.97	0.0026*
Eccentricity	0.76	0.03	0.78	0.52	0.1700
Contour Index	3.75	0.59	3.84	0.09	0.021*
Volume/Area ratio	6.01	0.61	7.40	0.57	0.00001*
Coefficient of form	0.89	0.02	0.86	0.04	0.0600

\* Significant difference for  $p < 0.05$ .

of the cell nuclei of the basal layer of the prostate glandular epithelium of both treated and control groups.

The mean of the major diameter of the prostatic gland cells in the treated group was significantly smaller ( $p = 0.0000$ ) in relation to the mean of the nuclei diameter in the control group, the same happening to the means of medium ( $p = 0.0001$ ) and minor ( $p = 0.0026$ ) diameters. The comparative study of the major diameter mean values ratio in relation to the minor diameter of both groups did not reveal a significant difference ( $p = 0.055$ ).

The mean value of the nuclear volume in the treated group was significantly smaller ( $p = 0.0001$ ) in relation to the control group, the same happening to the mean measurements of the nuclear area of the prostatic glands ( $p = 0.0001$ ), for the volume/area ratio ( $p = 0.00001$ ) and for the mean of the perimeters of prostatic cell nuclei ( $p = 0.0026$ ). In addition, the mean of the contour index of the nuclei of the treated group revealed to be significantly smaller ( $p = 0.021$ ) in relation to the control group.

Mean eccentricity of the nuclei in both the treated and control groups did not present any significant difference ( $p = 0.17$ ); the same occurred to mean values of the coefficient of form ( $p = 0.06$ ).

## COMMENTS

Even though the benefits obtained with bladder drainage are defined, physiopathological aspects related to voiding improvement under the influence of catheterism are still obscure (13-15). The dynamics of the prostatic function seems to be under the effect of 2 stimuli, the nervous (16,17) and the hormonal, being that the acute obstruction is consequent to the occlusion of the bladder neck (18).

The decrease in the volume of prostatic tissue seems to occur by the installation of a nervous reflex that determines the relaxation of smooth muscles and allow the drainage of the prostatic secretion. Facts that stimulate the sympathetic activity can augment the prostate muscles tonus, the bladder neck and the prostatic urethra, determining not only prostatic congestion but also urinary retention (19,20).

Morphologic alterations in prostatic congestion are characterized by a stasis of various degrees of secretion at the acinar lumen, including corpora amylacea (21). Considering morphologic criteria, the reduction in some dimensions of the nuclei of the epithelial cells in the treated group (with vesical catheter) can suggest the reduction of congestive alterations in

the benign prostatic hyperplasia, be it a phenomenon concomitant to the reduction of nuclear dimensions on the prostatic epithelium, possibly explained by the mechanical compression and the blockage of the ducts that drain the glandular acina and the veins (21).

Nuclear augmentation has been established as one of the criteria used for the diagnosis of prostate adenocarcinoma. Nuclear parameters have been used in computerized morphometric studies for differential diagnosis of the prostate, revealing nuclear area values of 32.5  $\mu\text{m}$  and 39.6  $\mu\text{m}$  in both benign and malignant hyperplasia, respectively (22). The computerized analysis of the image with adaptation to the morphometric grid has been used to quantify relative stroma and epithelium quantities in benign prostatic hyperplasia in patients submitted to transurethral prostatic resection, open prostatectomy or cystoprostatectomy (23,24).

Morphometric image analysis has also been used to help determine the expression of the receptors for epithelial growth factors in benign prostatic hyperplasia (25), besides contributing for the study of the metabolism of satellite hyperplastic epithelial cells affected by growth factors produced by cancerous prostatic cells (26). However, it is fundamental in morphometric studies of the nuclei of prostatic epithelial cells, that there is an initial immediate fixation of the material (27), as it occurred in the present study.

Effects of mechanic tissue deformation over the morphology of intracellular organelles involved in cellular biosynthesis and metabolism have been assessed (28,29), supplying a theoretical basis for the performance of prostatic studies. Nuclear reduction consequent to the application of strengths or mechanic devices over tissues (such as in the passage of a catheter) has been verified. The compression of cartilaginous tissue results in reduction of chondrocytes' volume and its nuclei indicating that a balance between osmotic and mechanic intracellular gradients tends to govern the organelles' alterations of form and volume in case of tissular compression (28). In human hearts, the implant of a left ventricular assistance equipment in cases of severe dilated cardiomyopathy occasioned reduction of cardiac work, reduction in the size and content of the DNA of the cardiac myocytes nuclei and consequently, reversion of cellular hypertrophy (29).

This study compared the influence of bladder drainage on the morphometry of prostatic glandular epithelial cells nuclei aiming at explaining, in an original way, why certain patients presenting benign prostatic hyperplasia develop urinary retention. We can notice that the presence of bladder drainage was concomitant to the reduction of prostatic epithelial cells nuclei that suggests an association of alterations of nuclear morphometric parameters with the presence of vesical catheter.

## CONCLUSION

The use of long-term bladder drainage in patients presenting severe symptoms of benign prostatic hyperplasia is associated to the reduction of morphometric parameters of the nuclei of the prostatic glandular epithelial cells, suggesting a possible decompressive duct effect.

## CONFLICT OF INTEREST

None declared.

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