BJU International (2002), **89**, 699–702

Stromal and acinar components of the transition zone in normal and hyperplastic human prostate

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Objective To analyse the histological components of the transition zone in both normal human prostate and benign prostatic hyperplasia (BPH), and to determine the volumetric density (Vv) of the different elements (connective tissue, smooth muscle cells, acini and total stroma).

Materials and methods Samples of BPH tissue from the transition zone were obtained from 16 patients with clinical symptoms of bladder outlet obstruction who underwent open prostatectomy. The control samples comprised 16 transition zone samples from prostates obtained during necropsy of adults aged <30 years (killed in accidents). The Vv of these components was determined by stereological methods.

Results The mean (SD) Vv in the controls and BPH samples were, respectively: connective tissue 40.47 (5.16) and 46.71 (9.91)%; smooth muscle cells 24.86 (2.74) and 31.56 (5.49)%; acini 28.73 (6.25) and 17.78 (10.87)%; all differences were statistically significant.

Conclusions These results confirm the hypothesis that in BPH there is an increase in the stromal component, both smooth muscle fibres and connective tissue.

Keywords prostate, BPH, morphological analysis, quantitative morphometry, smooth muscle, connective tissue

Introduction

BPH is a cellular benign proliferation that results in the growth of the stroma or the glandular tissue, generally in a nodular arrangement. One result of this growth is a change in the cellular architecture at the histological or biochemical level in stromal organization [1–5]. In the vast majority of the cases, the hyperplastic nodules of BPH have their origin in the pre-prostatic and transition zone, compressing other prostatic regions, mainly the prostatic urethra [3,6,7].

The prostate stroma is basically composed of smooth muscle cells, with associated connective tissue (with a large proportion of collagen fibres, elastic fibres and undifferentiated fibroblasts), vessels and nerves [3,6–8]. Nevertheless, there is no agreement as to whether the main element involved in prostatic growth is epithelial in origin (duct or prostatic alveoli) or as stromal cell proliferation [1,6,8]. For the latter possibility there is no consensus on whether there is a predominance of smooth muscle cells or connective tissue (collagen/fibroblasts) [9,10]. In the present study we conducted a stereological analysis of the stromal and acinar histological components of the transition zone in normal and hyperplastic human prostate.

Accepted for publication 11 January 2002

Patients and methods

BPH tissue samples of the transition zone were obtained from 16 patients (mean age 72 years, range 63–79) with symptoms of BOO who had received no treatment for their symptomatic BPH and had undergone open prostatectomy (retropubic or transvesical). All had a histopathological diagnosis of BPH with no focus of prostatic carcinoma.

The control samples consisted of the transition zone from 16 prostates obtained from autopsies of young men (mean age 22 years, range 16–30) who had been killed in accidents and whose post mortem examination showed no changes in the urogenital system. A sagittal section from the anterior region to the lumen of the prostatic urethra exposed the verumontanum, and this anatomical landmark was used to accurately excise tissue from the transition zone. The time elapsed between death and fixation of the excised control samples was <6 h.

After the tissues were fixed in Bouin's solution, both the BPH and control samples were paraffin-embedded, sectioned at 5 μm thick and processed using routine histological methods. All samples were initially stained with haematoxylin and eosin, and then examined by a pathologist to detect any focus of carcinoma and to exclude samples with artefacts.

From each prostate, five samples were excised from the transition zone and from each, five different sections were selected; five random fields were then evaluated from each section, thus analysing 25 test areas from each prostate. For the stereological analysis the 5-μm sections were stained with Gomori trichrome to detect collagen fibres (stained green), creating a sharp contrast with smooth muscle fibres (stained red) [11]. The analysed fields were digitized to a final magnification of ×400 using a video camera coupled to a light microscope. The selected histological areas were the quantified using test-grid system on the digitized fields on the screen of a colour monitor (Fig. 1). From stereological principles in isotropic tissue, the area distribution of a given structure, as determined on a two-dimensional section of the structure, is proportional to the volume distribution of the structure. The volume density of the histological components was calculated as Vv = Pp/Pt, where Vv is the volume density, p is the tissue component under consideration, Pp is the number of test points associated with p, and Pt is the number of points of the test system. The stereological methods were described in detail elsewhere [12,13]. The two tissue groups were then compared using Student's *t*-test with $P < 0.05$ considered to indicate statistical significance.

Results

Table 1 lists the relative values of the three main histological components in the 32 prostates assessed. In the BPH samples there was more stroma and concomitantly less glandular component than in the control samples ($P < 0.05$). In normal prostate samples the stroma comprised ≈65% of the total tissue and the gland 29%; in BPH the stroma comprised 78% and the gland only 18%.

Discussion

Different studies have used various methods to quantify prostate components; frequently these studies compared samples obtained by different techniques and from different regions of the prostate [14,15] or they compared BPH with prostate cancer [16] or with fetal prostate [17]. Only Bartsch *et al.* [1] compared BPH with normal prostate but their control samples were obtained from different anatomical regions, including the peripheral zone.

From the studies by McNeal [6,7] it is evident that the prostate is not anatomically homogeneous, but has regions with distinct embryological origins and of specific histological character. This may explain the different

Table 1 The volumetric density of the prostatic histological components in the transition zone of control and BPH samples

	Mean (SD, SEM) [range]	
Histological tissue	*Control*	*BPH*
Smooth muscle	24.86 (2.74, 0.68) [21.34–29.99]	31.56 (5.49, 1.37) [18.10–37.96]
Acini	28.73 (6.25, 1.56) [20.05–39.00]	17.78 (10.87, 2.71) [5.56–41.76]
Connective tissue	40.47 (5.16, 1.29) [30.36–47.47]	46.71 (9.91, 2.47) [28.33–60.72]

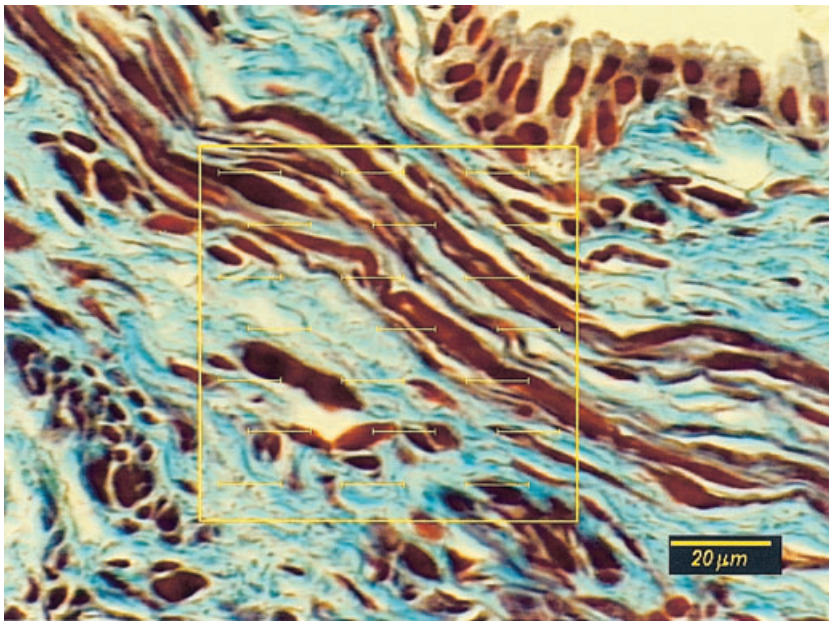

Fig. 1. The test grid system applied to a digitized image of a prostate section. Gomori trichrome, ×400.

results for normal and BPH histological components found by various authors. In many studies the samples analysed were obtained from transverse sections at the verumontanum or from transrectal biopsies. Although these methods are efficient for diagnosis, they are inappropriate for quantitative studies, because they may include material from other prostatic regions.

Deering *et al.* [8] considered that the histological composition of the prostate could modify the therapeutic response and consequently might influence the choice of pharmacotherapy for BPH. These authors analysed samples of BPH obtained by open prostatectomy, TURP or prostate needle biopsy (10 specimens from each). The proportion of stroma from the different sources of tissue were not statistically different and the authors concluded that the stromal component might be estimated from a needle biopsy. Overall, these authors reported the mean (SD, range) percentage of stroma in BPH to be 65.4 (7.4, 49.9–76.7). They showed that the largest component of BPH was stroma and that the increased percentage of stroma in some samples arose from non-muscular elements. These data agree with the present results showing a mean Vv of 78% for the stroma in BPH, with 15% more connective tissue and 27% more smooth muscle in BPH than in the control transition zone. Although smooth muscle was the stromal component most increased in BPH, the major stromal component was not muscular (Table 1).

Schuster and Schuster [18] measured the relative amount of epithelium, muscle, connective tissue and lumen in BPH obtained by TURP and correlated their findings with prostate size. In specimens of BPH, as prostate size increased there was significantly more epithelium and lumen, and less muscle tissue. These findings disagree with those of Deering *et al.* [8] who found no relationship between percentage stroma and specimen weight. In the present study the weight of the BPH specimens was not considered but all patients had undergone open prostatectomy, which in our institution is indicated only for prostates of >40 g.

In the present study there was 20% more stroma and concomitantly 38% less acinar tissue in BPH samples than in the transition zone of the control samples. These findings seem to confirm the hypothesis that the increased Vv of smooth muscle fibres in BPH arises by cellular proliferation. In cellular cultures of stroma the proportion of smooth muscle cells is greater in BPH than in normal prostate [19]; this may be clinically important.

In patients with BPH there is a close correlation between smooth muscle fibre density and the urethral resistance factor [20], as previously proposed by Caine [21]. However, to establish a relationship with obstructive symptoms it is necessary to confirm a simultaneous interaction between the quantitative changes in the stromal components (relatively small) with a qualitative change. This involves both the cellular (smooth muscle) and extracellular matrix components. In a recent study [5] there was statistically significantly more (62%) glycosaminoglycan in BPH tissue than in normal prostate. Perhaps changes in the composition of the extracellular matrix could modify the biological properties of prostate tissue and influence the elasticity or resistance [5,22].

In conclusion, to our knowledge this is the first report of the comparative morphology of BPH stromal components and the transition zone of control samples; the results confirm that in BPH tissue there is significantly more stroma (both smooth muscle cells and connective tissue). These changes in the normal histological composition, mainly in the muscular component, may alter the morphological and functional properties of the prostate and must be considered when evaluating and treating BOO.

Acknowledgements

This work was supported by Grants no. 52.0312/96.1 from the National Council of Scientific and Technological Development (CNPq-Brazil), and No. E-26/151.500/99 from the Foundation for Research Support of Rio de Janeiro (FAPERJ).

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