104

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Title: AGE-RELATED INCREASE OF COLLAGEN TYPE III IN THE ANTERIOR FIBROMUSCULAR
STROMA OF THE PROSTATE IN MEN WITHOUT BPH

Aims of study :

According to McNeal's zonal anatomy, the prostate has the anterior fibromuscular stroma AFMS as non-glandular tissue composed of smooth muscle and connective stroma surrounding the urethra. Although the AFMS comprises up to one-third of the total bulk of the prostate, its physiological function remains unknown. In our previous study, we reported the possible contribution of the AFMS to micturition in opening the prostatic urethra (1). Recently, we reported the peculiar innervation pattern between the AFMS and the other glandular tissue of the prostate using immunohistochemistry (2).   Additionally, we reported the age-related relative increase of the connective tissue in the AFMS (3). The aim of this study is to further reveal the histological changes in the AFMS caused by aging with special reference to the distribution of the types of collagen as well as elastic fibers.

Methods :

Human prostate specimens were obtained from 18 men 47±20 years, 18-76 years . Twelve elderly men (53-76 years) out of the 18 had undergone transrectal ultrasonography (TRUS) and the presumed circle area ratio (PCAR) was calculated on the horizontal sonogram with the maximum area. BPH was diagnosed based on transrectal ultrasonographic criteria as proposed originally by Watanabe et al (a value of PCAR more than 0.75) (4, 5). The prostate sections were processed with Azan stain, which dyed the connective tissue and the smooth muscle blue and red, respectively. Using a computer-assisted image analysis system (Mac Scope), the ratio of connective tissue-to-smooth muscle the C/S ratio   was obtained by dividing the sum of the connective tissue area by the sum of the smooth muscle area in the AFMS and the peripheral zone. Immunohistochemical stainings were also performed using the antiserum to collagen types 1 and 3. In addition, the sections were processed with Resorcin Fuchsin stain, which is a specific stain for elastic fibers. The density of the collagen fibers and elastic fibers in the AFMS was measured using a computer-assisted image analysis system. All values are expressed as the mean±standard deviation. An unpaired Student's t-test was used to compare the values between the groups.

Results :

Using a morphometric study, a significant correlation between age and the C/S ratio in the AFMS was noted among the 18 specimens (r=0.871, p<0.0001). We observed the AFMS compressed by the enlarged transition zone into a thin layer in BPH specimens. In the 12 elderly men who underwent TRUS, there was a significant correlation noted between the PCAR and the C/S ratio in the AFMS (r=0.817, p<0.001)). We further analyzed the 11 cases without BPH (including 6 younger men less than 45 years of age and 5 elderly men with a PCAR of less than 0.75). The C/S ratio in the AFMS was significantly higher (p<0.0001) in the elderly men than in the younger men (TABLE 1). In these 11 cases, there was a significant positive correlation noted between age and the C/S ratio in the AFMS r=0.889, p<0.0001 . Morphometric analysis revealed that while the density of

collagen type 1-immununoreactive (IR) area was not significantly different, the density of collagen type 3-IR area was significantly higher (p<0.05) in the elderly men without BPH than in the younger men (TABLE 2). Density of elastic fibers was observed in the AFMS by Resorcin Fuchsin stain. Although in elderly specimens some elastic fibers were observed as shortened or thickened fragments, quantitative analysis did not show a significant difference in the density of elastic fibers between the younger men and the elderly men without BPH (TABLE 2).

Table. 1 The connective tissue-to-smooth muscle ratio in younger and elderly men without BPH (%)

	Younger (n=6)	Elderly (n=5)
In the AFMS	28.8±6.1	65.1±26.8*
In the peripheral zone	53.9±5.9	48.6±18.6

*p<0.0001 Younger vs Elderly

Table. 2 The density of positive area to each specific stain (/100mm^2)

	Younger (n=6)	Elderly(n=5)
Elastic fiber	1.3±0.5	1.6±0.5
Collagen type 1	10.8±2.8	15.3±3.4
Collagen type 3	12.3±3.4	25.1±8.5*

* p<0.05 Younger vs Elderly

Conclusions :

This study suggested that collagen type   could be the main component of the significant relative increase of connective tissue in the AFMS with age. Many elastic fibers were observed as shortened or thickened fragments in the elderly specimens. These changes of the AFMS may account for the age-related disturbance of micturition.

References :

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