Bladder Neck Muscle Degeneration in Patients with Prostatic Hyperplasia

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Abbreviations and Acronyms

ACNM = anterior CNM
AELM = anterior ELM
ASLM = anterior SLM
CNM = circular neck muscle
ELM = external longitudinal muscle
MIRP = minimally invasive radical prostatectomy
PCNM = posterior CNM
PELM = posterior ELM
PH = prostatic hyperplasia
PSLM = posterior SLM
PZ = prostate peripheral zone
SLM = submucosal longitudinal muscle
TZ = prostate transition zone

Accepted for publication July 11, 2015.

No direct or indirect commercial incentive associated with publishing this article.

The corresponding author certifies that, when applicable, a statement(s) has been included in the manuscript documenting institutional review board, ethics committee or ethical review board study approval; principles of Helsinki Declaration were followed in lieu of formal ethics committee approval; institutional animal care and use committee approval; all human subjects provided written informed consent with guarantees of confidentiality; IRB approved protocol number; animal approved project number.

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Purpose: To improve understanding of the variations of bladder neck musculature we investigated histological changes of the bladder neck associated with prostatic hyperplasia in adult male cadavers.

Materials and Methods: We examined histological sections from 24 donated male cadavers with a mean age of 74 years. Sections were subjected to Azan and immunohistochemical staining using desmin and S-100 antibodies. The collagen content per cross-sectional area was calculated and statistically compared.

Results: The existence of 3 muscle layers (submucosal longitudinal muscles, circular bladder neck muscles and external longitudinal muscles) was confirmed at the anterior and posterior regions of the bladder neck. Increased prostate volume significantly correlated with an increase in collagen fibers and thinning of muscle bundles in the anterior bladder neck. An increase in prostate volume and increasing age significantly correlated with degeneration of the posterior bladder neck muscles. As prostatic hyperplasia advanced the bladder neck muscles were progressively affected by fibrosis with the circular muscle fibers becoming thin and fragmented. In addition the severity of fibrosis associated with prostatic hyperplasia showed interindividual variation. We also devised a schematic classification of bladder neck morphology in men.

Conclusions: Degeneration of muscle bundles in the bladder neck of men with prostatic hyperplasia was confirmed. It was found that the bundles became thinner along with an increase in collagenous tissue. Our schematic classification of bladder neck morphology in men may be useful for further investigations.

Key Words: urinary bladder, prostatic hyperplasia, muscles, fibrosis, prostatectomy

BLADDER neck transection is one of the most challenging steps when MIRP is performed by the antegrade procedure.[1] Risks include incomplete removal of prostatic tissue or unnecessary resection of the bladder trigone, which can lead to bladder neck dysfunction. However, bladder neck transection is one of the least reproducible surgical steps in MIRP[2] due to marked interindividual variation in prostate size and shape, and bladder wall thickness. It is well known that the incidence of PH increases in men with aging[3] and male bladder neck morphology varies according to the location and extent of PH. However, to our knowledge

0022-5347/16/1951-0206/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2015.07.102
Vol. 195, 206-212, January 2016
Printed in U.S.A.

histological changes of the bladder neck caused by PH have not been elucidated. Also, the anatomy of the male bladder neck is still comprehended based on old drawings.[4,5]

The only relatively reliable anatomical landmark to use during posterior bladder neck transection in MIRP is the vesicoprostatic muscle.[6,7] However, there are few descriptions of whole bladder neck anatomy or interindividual variations in bladder neck morphology in patients with PH, although such information is required for reliable bladder neck transection during MIRP. To improve the understanding of bladder neck variation we determined histological changes and interindividual variations of bladder neck muscle morphology in men with PH.

MATERIALS AND METHODS

This study was performed in accordance with the provisions of the Declaration of Helsinki.[8] We examined 24 donated male cadavers ranging in age from 66 to 81 years. Cause of death was ischemic heart failure or intracranial bleeding. We confirmed that there was no history of bladder/prostate surgery in the records as well as by macroscopic observation after opening the abdominopelvic cavity. All cadavers were inspected to determine whether the urethral mucosa was affected by long-term catheterization. Macroscopic observation showed that the urethra of each cadaver was not dilated. These cadavers were donated to Tokyo Dental College for anatomical research and education, and use for research was approved by the university ethics committee.

The method of preparing sections from blocks was described previously.[9,10] The tissue block was bisected along the mid sagittal line and 12 mm slices were made from each resulting hemiblock. After routine embedding in paraffin 6 sagittal sections 70 × 50 mm were prepared for azan staining from each slice at 2 mm intervals. Prostate volume was estimated as the product of the width, depth and height of each specimen. We also examined the horizontal plane in 1 cadaver with a normal size prostate for reference.

For immunohistochemistry mouse monoclonal anti-human desmin antibody (dilution 1:50, N1526) and mouse monoclonal anti-human S-100 protein antibody (dilution 1:200, Z0311, Dako, Glostrup, Denmark) were used as the primary antibodies. The secondary antibody was labeled with horseradish peroxidase and antigen-antibody complexes were detected by the horseradish peroxidase catalyzed reaction with diaminobenzidine. Counterstaining with hematoxylin was also performed. A negative control without primary antibody was created for each specimen. Observation and photography were performed with an Eclipse 80 microscope (Nikon®).

Calculating Cross-Sectional Image Collagen Component

Digitized images obtained under a 20× objective lens were processed and a scale bar was set for each image using ImageJ, version 1.45 (http://imagej.nih.gov/ij/). Collagen fibers were identified manually as blue areas. Collagen fiber density was calculated as the percent area of a tissue rectangle (0.6 × 0.3 mm) occupied by blue fibers. Mean collagen fiber density was determined by calculating the average density of 10 randomly selected areas in each muscle region.

Statistical Analysis

All analyses were performed with JMP®, version 10.0. To investigate whether estimated prostate volume or patient age correlated with degenerative changes we performed simple linear regression analysis to assess the relation between these continuous variables and collagen fiber density. Multiple linear regression analysis was then done to control for confounding effects. Estimated prostate volume and age were used as potential predictors of increased collagen fiber density in the model building process. Partial regression coefficients were calculated for each variable. Results are shown as the mean ± SD with $p < 0.05$ considered statistically significant.

RESULTS

Mean estimated prostate volume was 46.4 ± 23.2 ml and mean patient age was 74.4 ± 4.5 years.

Bladder Neck Anatomy

The large sections covered a wide area, including 1) the detrusor muscle in the anterior and posterior walls of the bladder, 2) the entire bladder neck, 3) the full anteroposterior length of the prostate in the mid sagittal plane and 4) the proximal urethra including the upper part of the rhabdosphincter. The detrusor was composed of muscle bundles. The bundles were thick and round in the posterior wall but thin and irregular in the anterior wall. In the anterior and posterior regions of the bladder neck we identified 3 muscle layers, including 1) SLMs continuous with the urethral wall, 2) CNMs as a distal continuation of the detrusor and 3) ELMs.

In the mid portion of the bladder neck the CNMs were composed of abundant thin muscle bundles. These bundles were thinner and almost round in the posterior bladder neck (figs. 1, *D*, 2, *F* and 3, *E*). They were thicker and irregular in the anterior bladder neck (figs. 1, *F*, 2, *E* and 3, *D*). ELMs were more evident in the posterior wall of the bladder neck than in the anterior wall (figs. 1, *A*, 2, *A* and 3, *A*). In contrast SLM fibers were thicker and more abundant in the anterior wall (figs. 1, *C* and *E*, and 2, *B* and *D*). Similar to the SLM the AELM passed superior to the CNM to join the urethral muscles in 9 specimens (37.5%) (fig. 3, *A*). It did not do so in the majority of cadavers. Rather the AELM ran downward and was dispersed along and into the rhabdosphincter area. Despite the close topographical relation whether the AELM did or did not join the urethra was unrelated to ACNM morphology (figs. 2, *F* and 3, *E*).