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PERI-URETHRAL FIBROSIS RELATED WITH LOWER URINARY TRACT SYMPTOMS ON LAPAROSCOPIC RADICAL PROSTATECTOMY SPECIMEN.

Hypothesis / aims of study
Prostatic inflammation induces fibrotic changes in peri-urethral prostatic tissues, and it is related with pelvic pain and lower urinary tract symptoms (LUTS). We investigated the morphologic and pathologic findings of peri-urethral tissue on laparoscopic radical prostatectomy specimen.

Study design, materials and methods
From Jan 2015 to Feb 2016, we underwent laparoscopic retropubic radical prostatectomy, we checked appearance of prostate apex and collected peri-urethral tissue from 22 patients.
Patients who had prostate cancer were divided in two groups according to patients with or without inflammation. A 4-peri-urethral core bench biopsy was carried out on each radical prostatectomy specimen to evaluate the extent of peri-urethral inflammatory infiltrate and collagen and elastin amount. Verhoeff-van Gieson staining was used to assess the elastin and collagen core amount, which was graded through a visual scale of 0 to 3. Score 0 patients were without inflammation group (N=4), score 3 patients were inflammation group (N=5). The clinical findings such as international Prostatic Symptoms Score (IPSS) and National Institutes of Health/Chronic Prostatitis Symptom Index (NIH/CPSI) compared using the Mann-Whitney U test. Spearman correlation analysis tested the association between variables.

Results
A significant difference was found between the two groups in terms of International Prostatic Symptoms Score ($p<0.05$) and NIH/CPSI ($p<0.05$). Patients with peri-urethral inflammation have more severe LUTS and chronic pelvic pain. A positive correlation was observed between inflammation, International Prostatic Symptoms Score, Bladder Outlet Obstruction Index and collagen amount, whereas inflammation was inversely correlated with elastin amount.

Interpretation of results
Fibrotic changes within the peri-urethral prostate tissue secondary to prostate chronic inflammation might promote urethral stiffness, as a consequence. This negative impact on urethral function could eventually cause urinary obstructive symptoms. LUTS are not always associated with an inflammation dependent prostate enlargement.
Current studies report a lower elastic content and a higher collagen peri-urethral amount in prostate specimens from patients with LUTS symptom. Peri-urethral tissues obtained from men treated with retropubic radical prostatectomy and complaining of LUTS have higher inflammatory infiltrate, were significantly stiffer, with significantly higher collagen content and lower glandularity, than those obtained from men without LUTS.
Patients could experience LUTS secondary to chronic prostate inflammation and inflammation-dependent peri-urethral fibrotic changes, also regardless to the prostate volume.
Peri-urethral prostate biopsy is an operator-dependent procedure that could be responsible for a certain grade of variability among findings. In order to overcome this problem, radical prostatectomy specimens can be sectioned with a special microtome to obtain complete prostate macro-sections where prostate areas could eventually be comprehensively studied. We obtained peri-urethral tissues only from radical prostatectomy specimens; therefore, we cannot exclude that peri-urethral fibrosis could eventually be a consequence of an unusual histological alteration as a result of the co-presence of prostate cancer. However, in partial support of the goodness of our histological sections, although prostate cancer could arise from a whole prostate, we never observed prostate cancer on peri-urethral specimens. Prostate inflammation and for inflammation-dependent peri-urethral fibrotic tissue modifications is related with LUTS and chronic pelvic pain. Translationally, these results would suggest that an appropriate management of fibrosis might ultimately also benefit patients presenting with coexisting LUTS.

Concluding message
This experimental study suggests that prostate inflammation may induce fibrotic changes within the peri-urethral prostate tissues, which may eventually promote LUTS and pelvic pain. Further studies are needed to more comprehensively understand the complex biology of the prostate inflammatory network in promoting different facets of LUTS severity and potential therapeutic solutions.

References
1. Metabolic syndrome correlates with peri-urethral fibrosis secondary to chronic prostate inflammation
2. Chronic inflammation in the pathogenesis of benign prostatic hyperplasia.
3. Prostatic fibrosis is associated with lower urinary tract symptoms.

Disclosures
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