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THE ROLE OF SMOOTH MUSCLE IN THE PATHOGENESIS OF PELVIC ORGAN PROLAPSE – AN IMMUNOHISTOCHEMICAL AND MORPHOMETRIC ANALYSIS OF THE UTEROSACRAL LIGAMENT

Hypothesis / aims of study
The uterosacral ligaments (USL) are an important part of the pelvic support system. One of the most frequently investigated hypothesis regarding the pathophysiology of pelvic organ prolapse (POP) focuses on the connective tissue composing the USL, based on clinical correlation of POP with connective tissue damage. However, in addition to collagenous fibres the USLs contain a considerable amount of smooth muscle. Functionally, the USL therefore comprises static (collagenous fibres) and dynamic (smooth muscle) properties required for pelvic floor suspension. The purpose of the present study was to characterize the smooth muscle component in the USL, to identify possible morphologic changes contributing to the pathogenesis of pelvic organ prolapse and to find clues for the role of smooth muscle in the POP.

Study design, materials and methods
To minimize the influence of risk factors as age, parity or hormone replacement, we formed paired data from a given collective of patients. 18 premenopausal POP patients were matched to non-POP patients of similar age and parity. The POP group contained patients with POP stages II-IV. Patients with POP stage 0 were included in the control group. In paraffin sections of samples obtained from hysterectomy the smooth muscle component of the USL was studied by smooth muscle actin (SMA) immunohistochemistry as indicator for structural abnormalities and by morphometric determination of nuclear size as measure for the functional state of the muscle cells. The ethics committee approved the investigation protocol and every patient signed a consent form prior to surgery, allowing the excision of tissue samples and their use for research purposes.

Results
In premenopausal patients with pelvic organ prolapse the size of smooth muscle cell nuclei was significantly reduced (25.45 μm², SD 1.92) in comparison to patients without POP (28.87 μm², SD 2.92) of similar age and parity. Between right and left USL no significant differences in nuclear size were present. Quantitative morphometric analysis of the sections the USL showed no significant difference in the content of smooth muscle between the POP and non-POP group. SMA immunostaining revealed a smooth regular distribution of reaction product in the muscle cells of the non-POP group. In patients with POP the intracellular reaction product showed disruption and uneven granular distribution. This phenomenon was distinctly visible in 8 out of 9 POP patients and in none of the paired controls without POP. Immunohistochemistry of SMA showed a granular patchy distribution of the reaction product in the POP group.

Interpretation of results
Our findings indicate structural defects in USL smooth muscle cells by SMA immunohistochemistry and reduced functional state of USL smooth muscle cells expressed by a reduced nuclear size.

Concluding message
We conclude that the functional state and the structural integrity of smooth muscle component of the pelvic floor are impaired in POP patients, indicating a possible role of smooth muscle in the pathogenesis of POP.

FUNDING: None