

Re: Penile Sonographic and Clinical Characteristics in Men with Peyronie's Disease

Smith JF, Brant WO, Fradet V, Shindel AW, Vittinghoff E, Chi T, Huang YC, Davis CB, Conti S, and Lue TF.

J Sex Med 2009;6:2858–2867.

Expert's summary:

The aim of this study is to describe the sonographic characteristics (tunica thickening, septal and intracavernosal fibrosis, and calcification) of the penis in Peyronie's disease (PD) and correlate them with the clinical course.

Tunica thickening was the most prominent sonographic finding (50% of patients) associated with a decreased ability to have intercourse. Calcifications was the second most prominent finding (31% of patients), especially in diabetic men or men with severe curvature. Men with septal fibrosis (20%) were less likely to have penile shortening, diabetes, hypertension or coronary artery disease but more likely to be able to have intercourse. Finally, men with intracavernosal fibrosis (15% of patients) were more likely to have penetration difficulty during intercourse, an additional penile deformity or rapid onset of disease but less likely to have penile pain.

This comprehensive analysis of sonographic findings highlight the fact that PD is a heterogeneous disease. Penile ultrasound may allow for a better understanding of PD and targeted approaches

Expert's comments:

The etiology of Peyronie's plaque formation and development of calcification is not fully understood. Furthermore, the natural course of PD is variable and the efficacy of several conservative treatments remains questionable [1–3]. Major problems are the polymorphism of the lesions and the lack of a classification system for the disease.

Each of the four ultrasound characteristics presented in this study appeared to be associated with a different spectrum of clinical and PD-specific characteristics. It is important to focus our research on the relationship between sonographic findings and functional outcomes.

Men with intracavernosal fibrosis were more likely to have clinical features associated with a more severe form of PD while a history of previous penile injury was associated with lower odds of having tunica thickening. Furthermore, discrete penile trauma was found in only a minority of men with PD.

These data seem to complement previously reported patterns of calcifications that reflect different stages of the disease from the acute phase to the stabilized one [4]. While patients in the acute phase may benefit from conservative therapy, the only treatment option in patients with stabilized disease may be surgical intervention.

Therefore, the 'classic' role of ultrasound in localizing/measuring plaques and identification of stabilized disease can be expanded. We still need to elucidate why certain findings on ultrasound are correlated with patient characteristics. This may allow not only for a better understanding of the disordered anatomy in PD but also to guide targeted treatment approaches.

Conflicts of interest: The author has nothing to disclose.

References

- [1] Mulhall JP, Schiff J, Guhring P. An analysis of the natural history of Peyronie's disease. J Urol 2006;175:2115–8.
- [2] Hauck EW, Diemer T, Schmelz HU, Weidner W. A critical analysis of nonsurgical treatment of Peyronie's disease. Eur Urol 2006;49:987–97.
- [3] Russell S, Steers W, McVary KT. Systematic evidence-based analysis of plaque injection therapy for Peyronie's disease. Eur Urol 2007;51:640–7.
- [4] Bekos A, Arvaniti M, Hatzimouratidis K, Moysidis K, Tzortzis V, Hatzichristou D. The natural history of Peyronie's disease: an ultrasonography-based study. Eur Urol 2008;53:644–51.

Konstantinos Hatzimouratidis

2nd Department of Urology and Center for Sexual and Reproductive Health,
Aristotle University of Thessaloniki, Greece

E-mail address: kchatzim@med.auth.gr

DOI: 10.1016/j.eururo.2010.02.014

Re: Early Sacral Neuromodulation Prevents Urinary Incontinence After Complete Spinal Cord Injury

Sievert KD, Amend B, Gakis G, et al.

Ann Neurol. In press. doi:10.1002/ana.21814

Expert's summary:

In this prospective observational study, the authors investigated the effect of bilateral sacral neuromodulation (SNM) in 10 patients with complete spinal cord injury (SCI). Six additional patients declining SNM served as controls. Early bilateral SNM in patients with complete SCI during spinal shock prevented detrusor overactivity and urinary incontinence, provided normal bladder capacity, reduced urinary tract infection rates, and improved bowel and erectile function without nerve damage. The mean follow-up was 30.5 mo.

Expert's comments:

SNM has become a well-established and widely accepted treatment modality in recent years for refractory non-neurogenic lower urinary tract dysfunction (LUTD). Originally, SNM was not considered an option for neurogenic LUTD, and SNM has been attempted without success in complete chronic SCI patients [1]. Prevention of LUTD before irreversible effects occur is a convincing concept and the findings reported by Sievert and colleagues are exciting. Although the mechanism of action of SNM is not well understood, it seems to involve modulation of spinal cord reflexes and brain networks by peripheral afferents. Acute SCI leads to detrusor acontractility and complete urinary retention, which is followed by the development of detrusor overactivity incontinence caused by C-fiber-mediated spinal reflex pathways [2], probably related to the interrupted regulatory mechanism between the lower urinary tract and midbrain [3].

Sievert and colleagues hypothesize that early SNM may preserve nerve plasticity, such that C fibers remain silent, detrusor overactivity is avoided, and sympathetic preganglionic neuron activation in the thoracolumbar cord is suppressed. Further studies, however, are required to elucidate the exact mechanism of action. In addition, it would be of great interest to investigate whether noninvasive neuromodulation provides similar results as the invasive and quite costly SNM.

Nevertheless, if the benefits of early SNM in patients with complete SCI are reproduced in randomized trials and if these findings are conveyed to patients with other neurologic diseases or injuries, the management of neurogenic LUTD will be completely revolutionized. We are breaking new ground in neuro-urology. What a promising future!

Conflicts of interest: The author has acted as a consultant for Medtronic and Allergan.

Re: MicroRNA Regulation of Oncolytic Herpes Simplex Virus-1 for Selective Killing of Prostate Cancer Cells

Lee CYF, Rennie PS, Jia WWG

Clin Cancer Res 2009;15:5126–35

Experts' summary:

The authors developed a novel strategy for the treatment of prostate cancer combining three aspects: the oncolytic destruction of cells infected with a herpesvirus, the regulatory role of microRNAs (miRNAs) in protein synthesis, and the downregulation of certain miRNAs in cancer cells. MiRNAs are endogenous RNAs of about 22 nucleotides that decisively control the translation from messenger RNA to protein. To date, some 700 human miRNAs have been identified and about 1000 are predicted.

By genetic manipulation, the authors created a special type of virus, the replication of which was inhibited by miRNAs found to be downregulated in prostate cancer. Injections of the modified viruses into subcutaneous tumors with human prostate cancer cells in mice reduced the tumor volume dramatically without substantial toxicity to other normal tissues. Since prostate cancer cells do not contain these inhibitory miRNAs, viral replication could occur without restraint, inducing strong oncolytic effects. In contrast, animals treated with unmodified viruses died of herpetic viral complications. The authors concluded that this principle of miRNA-based regulation of viral replication could be a useful tool to target cancer cells selectively and prevent normal tissues from viral damage.

Experts' comments:

This study shows for the first time how data from the exciting miRNA research could be applied to develop novel treatments for prostate cancer. MiRNAs are key molecules with either oncogenic or tumor suppressive activities in the regulation of all hallmarks of cancer [1]. The identification of their regulatory role may not only help better understanding of prostate cancer carcinogenesis but also, in addition to their use as diagnostic

References

- [1] Schurch B, Reilly I, Reitz A, Curt A. Electrophysiological recordings during the peripheral nerve evaluation (PNE) test in complete spinal cord injury patients. *World J Urol* 2003;20:319–22.
- [2] De Groat WC, Yoshimura N. Mechanisms underlying the recovery of lower urinary tract function following spinal cord injury. *Prog Brain Res* 2006;152:59–84.
- [3] Blok BF, Holstege G. The pontine micturition center in rat receives direct lumbosacral input. An ultrastructural study. *Neurosci Lett* 2000;282:29–32.

Thomas M. Kessler

Department of Urology, University of Bern, 3010 Bern, Switzerland

E-mail address: tkessler@gmx.ch

DOI: 10.1016/j.eururo.2010.02.015

and prognostic biomarkers, may lead to novel therapeutic strategies [2].

Current miRNA-based strategies in cancer treatment focus mainly on approaches to inhibit oncogenic miRNAs, to replace tumor-suppressive miRNAs, or to modulate the expression of regulatory miRNAs. In contrast to these direct interactions with miRNA regulatory networks, the present study is based on an intelligent combination of different biologic aspects with the regulatory role of miRNAs as a key element. Furthermore, this therapy concept offers the opportunity to optimize the oncolytic effect regarding the selectivity and efficiency against cancer cells by using further specifications of viral replication [3].

The principle of intratumoral/intraprostatic injection of the miRNA-regulated virus as used in the present study can be assumed to be a feasible approach to focal therapy of image-guided ablation of prostate cancer [4].

In conclusion, this study presents a promising novel treatment strategy for prostate cancer and generally exemplifies the manifold potential of miRNAs for clinical practice in future.

Conflicts of interest: The authors have nothing to disclose.

References

- [1] Schaefer A, et al. *Urol Oncol* 2010;28:4–13.
- [2] Wang V, et al. *BioDrugs* 2009;23:15–23.
- [3] DeFatta RJ, et al. *Cancer Gene Ther* 2002;9:505–12.
- [4] Polascik TJ, Mouraviev V. *Urology* 2009;74:726–30.

Annika Schaefer, Klaus Jung*

Department of Urology, University Hospital Charité and Berlin Institute for Urological Research, Berlin, Germany

*Corresponding author. Department of Urology, University Hospital Charité, Berlin Institute for Urological Research, Schumannstr. 20/21, D-10117 Berlin, Germany.

E-mail address: klaus.jung@charite.de

DOI: 10.1016/j.eururo.2010.02.016