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Editorial and Rebuttal from Authors
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Can Penile Size be Preserved after Radical Prostatectomy?

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How often have you as a urologist heard men complain of loss of penile length or girth following radical prostatectomy (RP)? This has received minimal attention compared to other problems after RP, such as erectile dysfunction and incontinence. Yet, for the prostate cancer survivor the loss of penile volume may be associated with a significant negative impact on quality of life. To date, there are only three analyses on this issue in the literature. McCullough et al studied 100 men <6 mo after RP; they took preoperative and postoperative flaccid and erect measurements and demonstrated an overall mean reduction in erect penile length of 9% but a mean reduction in volume of 22% [1]. Munding et al studied 31 men and measured penile length in the stretched flaccid state (accepted as equivalent to erect length) and showed that 71% had a decrease in penile length compared to preoperatively with 48% of men demonstrating a >1-cm loss with a range of loss between 0.5 and 4 cm [2]. Finally, Savoie et al studied 63 patients with preoperative measurements followed by repeat measurement at 3 mo postoperatively and demonstrated that 68% of patients had some degree of length loss [3].

One of the most common explanations given by urologists to patients is that the prostatectomy results in shortening of the urethra, which results in loss of penile length. However, the urethra is a fixed structure at the level of the urogenital diaphragm and cannot be retracted inwards, and, thus, the bladder is brought down to the urethra for the fashioning of the vesicourethral anastomosis. The reasons for penile volume changes can be explained by three main pathologic events: cavernous nerve injury-associated structural alterations in the penis (apoptosis, fibrogenic cytokines production, collagenization), cavernosal hypoxia-induced structural changes in the penis, and sympathetic hyperinnervation (competitive sprouting) [4].

In this issue of *European Urology*, Briganti et al [5] report on their study of a small number of men ($n = 33$) who had excellent preoperative erectile function and underwent bilateral nerve-sparing RP. The authors evaluated patients with pre-RP and post-RP (6 mo postoperatively) assessments including the International Index of Erectile Function (IIEF) questionnaire, duplex Doppler penile ultrasonography, and penile dimension assessment in both the erect and flaccid states. They found no difference between preoperative and postoperative values for IIEF scores, penile Doppler ultrasound parameters, and penile length and girth in the erect and flaccid states.

As the authors state, these data are at odds with (1) the aforementioned penile length assessment data from Fraiman, Munding, and Savoie, (2) other studies demonstrating erectile hemodynamics alterations after RP [6], and (3) animal data with all three phosphodiesterase type 5 inhibitors demonstrating preservation of cavernosal smooth muscle content in a cavernous nerve injury model [7,8].

Most importantly, the study highlights the complex methodologic challenges that we are faced with

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in designing and conducting studies assessing erectile hemodynamics and dimensions in this population. The finding that there was no difference between preoperative and postoperative erectile function (based on IIEF scores) and duplex Doppler ultrasound parameters is unexpected, given the data suggesting that up to 50% of men have arterial insufficiency after RP and at a time point between 4 and 8 mo after RP about 30% of men have venous leak [6]. This is supported by previous work from the authors. It is unclear from the Briganti paper if the postoperative IIEF scores were reflective of the fact that 39% of men were using sildenafil, perhaps elevating the score. The authors state that there was no difference in postoperative IIEF score between sildenafil users and nonusers, but the study was in no way powered to address such a comparison. The other methodologic concern is the technique of duplex Doppler ultrasonography. It appears that only a single dose of 20 μg alprostadil was given at the preoperative and postoperative examinations, yet the literature suggests that 70% of men will need a second dose of vasoactive agent and 30% a third dose [9]. Furthermore, the authors fail to comment on penile pain induced by prostaglandin E_1 with the use of 20 μg alprostadil [10]. It is our clinical experience that 50% of men will experience significant penile pain with this dose and penile pain is an erectolytic factor; thus, it is again unexpected that the postoperative peak systolic velocities (PSVs) were as high as they were (46 cm/s). Indeed, the PSVs preoperatively are higher than expected in a 58-yr-old population, despite their baseline erectile function (EF domain score $\geq$26). Although demographic and comorbidity information was gathered, we are left a little in the dark wondering what, in fact, was the comorbidity profile. Were these men extremely healthy or were they representative of the general RP population? The latter is especially important when we try to extrapolate these data to our individual practices.

The measurement of the impact of RP on penile morphology has numerous challenges. (1) Patient number is important, and the study under review is unlikely to be powered adequately to define the impact of RP on penile dimensions, with only 33 patients included. (2) What two points should be used to define penile length; the classic points are tip of glans and the pubic bone. The authors here use the pubopenile skin junction, which fails to account for the size of the prepubic fat pad. Might this fat pad have shrunk after surgery and thus overestimated the penile length? (3) The technique of the penile length measurement is also important. How hard is the penis stretched? How rigid is the penis on erect length measurement? Is the penis pulled directly anterior or is the patient lying supine and the penis pulled toward the ceiling. Variations in this technique between preoperative and postoperative measurement may have an impact on the results. (4) The person recording the penile dimension measurements is of critical importance; having a single person do both preoperative and postoperative measurements is important to limit the interobserver variability, but so is having that person blinded on the postoperative visit as to the penile dimensions at baseline. It is not clear if this was the case in this study. Furthermore, it is not apparent that any assessment of the intraobserver variability in length/girth measurement was conducted, by looking at this in the first 10 patients. (5) The ambient environment for penile dimension measurement is also critical and should be declared, specifically, the gender of assessor and the ambient room temperature, both of which may have an impact on corporal smooth muscle tone and thus length, at least in the flaccid state. (6) The timing of the penile dimension measurement postoperatively will likely affect the results because penile shortening in the first 3 mo after surgery is likely related to cavernosal smooth muscle hypertonia and definitive penile length loss generally takes >6 mo. Thus, might this study have chosen a time point too early to define penile length/girth loss?

These issues notwithstanding, any rigorous assessment of sexual function in the RP population must be welcomed because there is an onus on us as scientists and clinicians to clarify the pathophysiology and optimal treatment of sexual dysfunctions (including morphologic changes) in this population.

Conflicts of interest

Grants: Pfizer, Astellas, Vivus.
Consultant: Pfizer, Lilly, Auxilium, J&J, Vivus.

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Rebuttal from Authors re: John Mulhall. Can Penile Size be Preserved after Radical Prostatectomy? Eur Urol 2007;52:626–8

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Since the combined effect of prostate cancer stage migration and refinements in surgical techniques has significantly improved oncologic outcomes of patients with prostate cancer, increasing attention is currently being paid to quality-of-life issues after radical prostatectomy (RP). In this context, it is very common for practicing urologists to deal with patients' complaints on postoperative penile size. However, little attention has been previously paid to this topic. Only four studies addressed this issue and reported significant decreases in penile length after RP at different points in time [1–4]. Conversely, our study represents the first trial suggesting that in selected patients who maintain normal erectile function after RP, penile size does not change [5]. Several aspects of our study need to be stressed. First, we strongly believe that patient selection represents the key to the explanation of our results. Our patient population represents a unique cohort of subjects. We included preoperatively fully potent (Erectile Function domain score of the International Index of Erectile Function [IIEF-EF] $\geq$26), young (<65 yr), and sexually active patients affected by clinically localised prostate cancer. No patient had diabetes mellitus or previous cardiovascular morbidity. All patients were treated by a single high-volume surgeon performing a standardised bilateral nerve-sparing procedure, which has been associated with high recovery rates of sexual function after surgery [6]. This was confirmed by the fact that only 3 of 33 (9%) patients developed postoperative erectile dysfunction (ED) based on the IIEF-EF score. This clinical scenario is substantially different compared to previous trials assessing penile length change after RP [1–4]. First, only a few patients enrolled in the mentioned trials were treated with a nerve-sparing approach. Second, the vast majority of the patients enrolled were affected by postoperative ED when penile length was measured. Because the lack of neurovascular bundles preservation and subsequent penile oxygenation may provoke structural penile fibrotic changes [7], it is not surprising that patients with postoperative ED also complained of reduction in penile size after RP. This was true regardless of the time of penile length evaluation after surgery. Conversely, preservation of full potency as well as of active sexual life might break this vicious cycle and maintain a vital penile structure. This, in substance, differentiates our study from previous published trials [1–4]. Nevertheless, we agree with Mulhall that our study is not devoid of limitations [8]. Thirty-nine percent of our patients used sildenafil on demand after surgery and this may represent a confounding factor. However, the use of phosphodiesterase type 5 inhibitors (PDE5-Is) is frequent in everyday practice and we believe that one of the values of our study is that it is representative of what is seen in a population of patients enjoying satisfactory postoperative results. We would like to consider our study as a proof of principle that fully potent patients treated with bilateral nerve-sparing radical prostatectomy (BNSRP) maintaining a full potency after surgery (either with or without pharmacologic aids) do not

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