Dr. Lee's rebuttal

Al Shaiji and Brock have provided a thorough review of the animal studies and the limited human studies in penile rehabilitation post–radical prostatectomy (RP).

In their article, the authors define penile rehabilitation as "the application of any drug or device at or after RP, to speed up recovery of erectile function." This, however, is a very broad definition. One of the current problems with penile rehabilitation is that there is no consensus on which penile rehabilitation protocol is effective. In clinical practice, it is most commonly defined as the use of low dose, daily phosphodiesterase 5 (PDE5) inhibitors, supported by limited evidence from very small numbers of subjects.

Although there have been animal studies that support the theory of penile rehabilitation post-prostatectomy, we all realize that results from animal studies will not necessarily be reflected in studies of human populations. Indeed, the limitations of these animal studies were not discussed in the article by Al Shaiji and Brock. The authors of the studies currently published in the literature, including those noted in Al Shaiji and Brock's article, recommend large population-based studies to determine the effectiveness of penile rehabilitation. As well, all of these papers acknowledge that these studies have yet to be performed.

Again, the most profound concern with all previous studies has been the robustness of the results owing to limited sample size and study design (i.e., blinding, randomization, dosing, inclusion of an on-demand comparator and robustness of end point determinations). For example, the recent study by Schwartz and colleagues[1] was cited as evidence that the use of sildenafil provided smooth muscle preservation. However, this study had only 21 patients and did not have a control arm; thus, it is difficult to conclude whether the smooth muscle preservation really was a drug effect. As well, the ranges of smooth muscle content for each of the groups were quite large and the baselines were different, which makes even comparisons between 50 mg and 100 mg difficult. The authors report that "any conclusion suggesting a therapeutic or rehabilitative effect of early sildenafil use after RP is unwarranted due to our small sample size and tissue heterogeneity."[1]

One of the tenets of population studies is that the results and conclusions from the study are only applicable to the population that was studied. An issue with penile rehabilitation studies is that they have looked exclusively at men with reported and/or documented normal erectile function preoperatively. We cannot extrapolate these results to men with pre-existing erectile dysfunction (ED). We all agree that these men are very different and will have varying degrees of penile smooth tissue loss and fibrosis before undergoing surgery. So how can we extrapolate results from men with normal erectile function? How can we recommend penile rehabilitation as the norm for all patients post-RP?

Al Shaiji and Brock suggest in their conclusions that without penile rehabilitation, patients are at risk of permanent structural changes and perhaps loss of opportunity for erectile recovery. The results of the REINVENT (Recovery of Erections: INtervention with Vardenafil Early Nightly Therapy) study refute this suggestion.[2] In the final open label phase of the study, there was no difference in terms of recovery of erections or response to on-demand vardenafil between men who had previously been on placebo for 9 months during the double-blind phase versus those men who were actively treated with either nightly dosing or on-demand dosing. Thus no rehabilitation effect was seen in this population (normal preoperative erectile function). All of the men in the study had sexual activity at least once per week, and so some may argue that the men in the placebo group did receive a form of penile or "sexual" rehabilitation, which might have given them some benefit. For those men randomized to 9 months of placebo, this "sexual rehabilitation" was without the aid of any medication. From this observation, one may deduce that early resumption of sexual activity is a safe and free form of therapy versus costly medication with the potential of side effects, albeit mild in nature. Even with the REINVENT study, which was the largest, best-designed study to date, we cannot make any conclusions for men who had pre-existing ED, as all

men from the study had normal erectile function before surgery.

There is definitely evidence in both animal and human studies that suggests that the application of a drug or device at or after RP may be of possible benefit. The on-demand use of PDE5 inhibitors is cost-effective; easy to use, without the need to adhere to a strict treatment regimen; and has been demonstrated by data to provide clear clinical benefits. Before any other regimen is recommended, it should be supported by robust clinical studies and it behooves us as clinicians to conduct these studies. For men post-RP with ED, what we do know and what many studies have demonstrated is the efficacy of on-demand therapy with PDE5 inhibitors and intracavernosal injection therapy. We can recommend that patients have sexual activity (self or with partner) relatively soon after their RP, and on a regular basis, with the corollary not to expect immediate recovery of their erections. For those men who desire earlier return of sexual function, these treatment options are available.

The positions provided in the Point/Counterpoint series are presented as general information and do not necessarily reflect the personal opinions of the authors.

This article has been peer reviewed.

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References

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2. Montorsi F, Brock G, Lee J, et al. Effect of nightly versus on-demand vardenafil on recovery of erectile function in men following bilateral nerve-sparing radical prostatectomy. *Eur Urol* 2008;54:924-31.