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Platinum Priority – Editorial and Reply from Authors

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Tension-free Vaginal Tape and Beyond: Our Challenges and the Future of Anti-incontinence Therapy

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All the available data resources, including population-based studies, government census data, and targeted epidemiologic studies, indicate that the number of women with or at risk for urinary incontinence (UI) is rapidly rising. According to a recent US National Institutes of Health (NIH)-sponsored study, there was a 5% rise in the prevalence of UI between 2001 and 2007, escalating the prevalence to 53% of women [1]. Extrapolation of prevalence based on US census data estimated as much as a 300% increase in the proportion of women in need of care within the next two decades [2]. Moreover, with women all across the globe living longer and healthier lives, we should predict that we will have to deliver more effective UI treatments.

Against this background and regarding the report by Serati and colleagues in this issue of *European Urology* [3], it is timely to reflect on our progress in treating the largest segment of UI, namely, stress urinary incontinence (SUI), and its mainstay of treatment, tension-free vaginal tape (TVT). The report by Serati et al. could be considered a landmark article because it represents a case series of TVT from a single institution (and a single surgeon) that in both efficacy [4] and adverse events [5] mimics the results reported by multicenter randomized clinical trials (RCTs).

This similarity in results is both good and not so good! It is promising that outcomes after TVT or midurethral slings could be duplicated in the hands of the most active surgeons. However, the bothersome observation remains that in either a single-institution case series or multi-institution RCT, we impose an adverse event on at least one-third of our patients. In the Serati et al. report, up to 30% of patients developed de novo urgency. Similarly, results of two of the largest RCTs involving midurethral slings

revealed a nearly 42% rate of side effects [5]. One can attempt to tease out the differences in types of adverse events, but the big picture remains the same.

The other important finding reported by Serati's group is that obese women have a much higher likelihood of recurrent incontinence after undergoing the TVT procedure. Again, similar findings have been reported from analysis of large RCTs with midurethral slings [6]. These observations become concerning, especially as the previously mentioned NIH study attributes the increase in incontinence to obesity and diabetes [1]. Combining these two findings would suggest that in the coming years, we should expect a higher rate of failures for our increasing number of obese patients when treated with our mainstay anti-incontinence procedure!

It is intriguing to note that over the past two decades or so, we have witnessed a series of quiet changes in the mainstay of anti-incontinence procedures. Starting with what was named *tension-free vaginal mesh*, or TVT [7], we now increasingly use the term *midurethral sling* [4], and one could wonder why. Having the theorist of Integral theory and co-inventor of TVT, Peter Petros of the Royal Perth Hospital in Australia, as my visiting faculty member, I have come to learn that the change in the name has both semantic and pathophysiologic roots that may have gone unnoticed. In the *original* TVT, the intention of mesh placement in the midurethra was not to provide a hammock band underneath the urethra but to create a tunnel through which the deficient pubourethral ligaments (PUL) would be restored by fibrous tissue reaction. However, replacement of the original Merseline mesh (Ethicon Inc., Sommerville, NJ, USA) with polypropylene mesh resulted in two changes: (1) replacement of a

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nonelastic and irritative mesh (Merseline) with an elastic and nonreactive one (polypropylene) and (2) the role of the mesh becoming more of a hammock support than facilitator of PUL reformation. As such, the change in name and content went hand in hand in the next generations of midurethral slings (eg, transobturator, minislings). The question is how have these changes, if any, contributed to our current state of affairs in treatment of SUI?

I would propose that almost two decades after the introduction of TVT and midurethral slings into clinical practice, and by any modern industrial standards of quality, a 30–40% rate of adverse events is simply unacceptable. Whether or not this is due to changes in names or mechanisms of action is not relevant. Can any of us imagine what would happen if one-third of all cars, computers, food packages, or any other commodity we purchase would fail or result in recalls? Moreover, it is unlikely that the manufacturer would remain in business after such recalls and failures. In addition, I would propose that what is reported here and from the large RCTs may only represent the tip of the iceberg in terms of longer term complications of slings. As we have learned from experimental studies on models of slings [8,9], the presence of de novo urgency and urge incontinence may herald the beginning of long-term bladder remodeling, higher rates of urinary tract infection, and other problems that are not captured in shorter-term clinical studies [10,11]. It is with this understanding that I propose that now, after two decades of experience and data with TVT or midurethral slings, we should start reflecting on the challenges we face in treatment of SUI. This is imperative, given the expected rapid increase in the number of patients we will see in the next 20 yr who will have comorbidities associated with increased UI-treatment failure rates [2]. On the one hand, we have procedures that are easily done by many physicians who can replicate the results of RCTs. On the other hand, it appears that we have reached a ceiling in efficacy and complication rates. As a group, we have not been able to eliminate a rather high rate of unwanted and expected complications of those procedures.

It is only within the context of this reflection that we would look at long-term results of TVT, as reported by Serati et al, not as the peak of our achievement but only as a step in the process of achieving further goals of curing SUI and not exchanging it for other bothersome adverse events.

It is imperative for us to continue our quest toward a better understanding of the pathophysiology of SUI, including the cause and root analysis of failures, and

recurrent or persistent SUI. Otherwise, and as reported by Serati and others, the odds are against us because the numbers of women and those with higher body mass indices are increasing rapidly. The quest that may lead us to nonsling treatments of incontinence not too far in our future! Additional evidence on the effectiveness of cell-based therapies in our medical disciplines may provide an opportunity for us to regain the original concept of regeneration of the failed PUL for treatment of SUI or perhaps to develop other pathophysiologic treatment approaches.

Conflicts of interest: The author has nothing to disclose.

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