INCONTINENCE

Stress urinary incontinence treatment—surgery first?

Xavier Fritel and Chantale Dumoulin

A randomized trial involving 460 women with stress urinary incontinence compared physiotherapy with midurethral-sling surgery. We question whether the results, showing higher rates of improvement and cure for surgery than for physiotherapy, should change best practice and clinical practice guideline recommendations.

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Labrie *et al.*[1] conducted a randomized controlled trial (RCT) comparing pelvic-floor muscle training (PFMT) with midurethral-sling surgery using suburethral tape for treatment of stress urinary incontinence (SUI) or mixed urinary incontinence (MUI) in which SUI predominates. 230 women were assigned to each treatment group, and outcomes were assessed 12 months after the onset of treatment. As the primary end point, subjective improvement was reported by 90.8% of women who underwent initial surgical treatment, and by 64.4% of the physiotherapy group. Higher rates of subjective cure (85.2% versus 53.4%) and objective cure (76.5% versus 58.8%) were also reported for initial surgery compared with physiotherapy. Labrie *et al.*[1] used a *post hoc* per-protocol analysis to address crossover between treatment groups, finding similar outcomes in women initially assigned to surgery and with crossover to surgery.

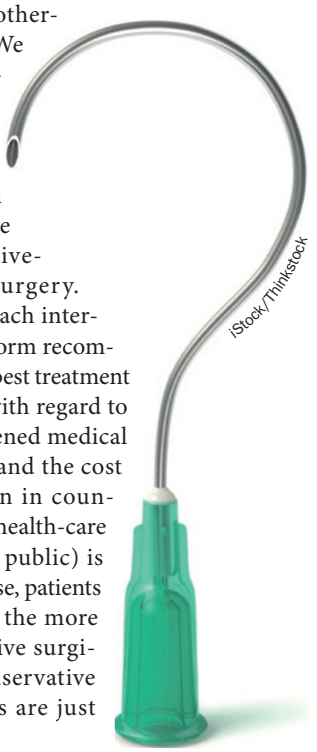
Most guidelines recommend PFMT as the first-line treatment for SUI.[2–4] However, both PFMT and suburethral tape have been shown to be efficient in the treatment of SUI and MUI, although previously these two interventions had not been directly compared. Results from the trial conducted by Labrie *et al.*[1] indicate a higher rate of both subjective and objective improvements in the midurethral-sling surgery group at 1 year. The question therefore arises of whether the results of this study should be used to change best practice and clinical practice guideline recommendations.

Notwithstanding the results, we have some concerns about the application of clinical equipoise in the trial. Before a trial begins, there should exist no decisive evidence that the intervention being tested (in this case, surgery) will be superior to an existing conventional intervention (PFMT) in the identified time period (here, 1 year after the onset of treatment). However, as an RCT progresses, the findings may provide sufficient evidence to convince the investigators of the superiority of one intervention over another. Once this threshold of evidence is passed and there is no longer genuine uncertainty about which treatment is most beneficial, then there is an ethical imperative for the investigator to provide the superior intervention to all participants.

Patients in the study by Labrie *et al.*[1] were allowed to cross over from physiotherapy to surgery before either had been definitively identified as being superior. The crossover rate was particularly high (almost 50%), which makes us wonder if the women included in the physiotherapy group received a real and comprehensive attempt at physiotherapy treatment before being allowed to cross over. According to the results, the women in the physiotherapy group seem to have crossed over at a very early stage, on average after only 7.4 ± 4.4 treatment sessions. This period of time is extremely short and is inadequate in terms of maximizing the effect of PFMT, as it is not considered long enough to address muscle hypertrophy,[5] and it is shorter than the effective PFMT duration as demonstrated in a Cochrane review on PFMT.[6] Moreover, allowing women to cross over too early could ultimately have undermined both the individuals' commitment levels and their internal belief systems. A belief in one's ability to achieve or attain a result, such as a cure, can negatively or positively affect a person's actual ability. Self-efficacy has been identified as a strong predictor of PFMT effectiveness.[7,8] It is also unclear whether the women were taught how PFMT works, were informed of the required commitment it entailed, or were apprised as to what point during the treatment they could expect to see improvement (after how many treatment sessions or weeks of exercise). Thus, it is possible that women crossed over to the surgical intervention because they did not have enough knowledge about how PFMT works, and this might have ultimately biased the results of this study.[1]

The authors recorded short-term adverse events, all of which were associated with surgical treatment. A more detailed description and exploration of the short-term and long-term consequences of surgery would have been useful, including factors such as individual costs to the patient (such as work days lost and losses to physical and social mobility that are crucial to quality of life and continued health) and costs to the health-care system (such as complications and ensuing medical interventions, costs of re-operating or providing corrective surgery, and resource implications).

The results of Labrie *et al.*[1] suggest that PFMT might not be as effective as a surgical option in all women with SUI or MUI. However, we need to be able to identify which women are better-served by physiotherapy and which are better-served by surgery as an initial intervention. For example, type of urinary incontinence, circumstances of leakage, severity of urinary incontinence, or pelvic floor morphological defects or dysfunction might be predictors of the likelihood of successful treatment and therefore serve to clarify the respective indications of physiotherapy and surgery.[9,10] We would therefore recommend that future studies include parameters that would enable identification and reporting of the predictors of effectiveness of PFMT or surgery. Further, the cost of each intervention must also inform recommendations as to the best treatment option, specifically with regard to financially overburdened medical health-care systems and the cost to uninsured women in countries where adequate health-care coverage (private or public) is problematic. Otherwise, patients could be directed to the more expensive and invasive surgical option when conservative PFMT interventions are just as effective.



National and international clinical practice guidelines recommend physiotherapy as a first-line treatment for SUI. The results of this study alone should not change current clinical practice. More studies are needed comparing the cost-effectiveness of the two interventions. Women should be given the opportunity to make informed choices supported by evidence for both treatment options.

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Competing interests
The authors declare no competing interests.

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BLADDER CANCER

Always consider extravesical sites when BCG fails

Friedrich-Carl von Rundstedt and Seth P. Lerner

Patients treated with two or more courses of BCG for high-risk non-muscle-invasive bladder cancer are at increased risk of second-site primary tumours of the upper urinary tract and prostatic urethra. A new study highlights the importance of looking for urothelial cancer in extravesical disease sites.

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Intravesical immunotherapy with BCG is the gold-standard treatment for high-risk non-muscle invasive bladder cancer (NMIBC). The rate of complete response to induction therapy is 57% after the first cycle (6 weeks of treatment) and 65–93% after a second induction course or 3-week maintenance course.[1–3] A third induction course for patients with persistent or recurrent disease is generally ineffective and not recommended owing to the high risk of disease progression. Complete transurethral resection of bladder tumour (TURBT) followed by BCG induction and long-term maintenance BCG therapy for up to 3 years is supported by level I evidence from two phase III trials.[2,4]

Giannarini *et al.*[5] now call to our attention a very important requirement for meticulous follow-up assessment of patients with high-risk disease. Extravesical urothelial cancer must be considered in patients with positive urine cytology without visible evidence of disease in the bladder. Prior reports highlight this important issue. For example, in a study of 307 patients, the long-term risk of upper urinary tract (UUT) tumours was 25% (median time to diagnosis of 56 months) compared with 24% for tumours in the prostatic urethra (median time to diagnosis of 11 months).[6] All patients in this study had carcinoma *in situ* (CIS) or high-grade Ta or T1 disease and were treated with TURBT and BCG without maintenance therapy. In a retrospective analysis of 62 patients with high-risk NIMBC who had undergone cystectomy for BCG failure, urothelial carcinoma in the prostatic urethra (detected at endoscopic staging) was shown to be the only independent risk factor for understaging at the time of cystectomy and the 5-year survival probability was significantly lower in these patients compared with those who were not understaged (38% versus 90%).[7] Transurethral resection biopsy of the prostatic urethra at the 5 o'clock and 7 o'clock positions adjacent to the verumontanum is the optimal method for detecting and staging CIS as this area has the highest concentration of prostatic ducts. If there is CIS of the urethra and the patient has had a single course of BCG, then re-induction with BCG with or without interferon-α might be considered after a TURP to open the bladder neck and to restage the urethral tumour to ensure no involvement of the prostatic stroma.

The study by Giannarini *et al.*[5] involved 110 patients who had undergone at least two cycles of BCG and were diagnosed with a second primary urothelial cancer of the prostatic urethra or UUT, or a recurrence in the bladder within a median follow-up period of 9.1 years. Diagnosis was determined by either pathologic biopsy or positive cytology. One of the limitations acknowledged by the authors is that none of the patients received BCG maintenance therapy. Of 110 patients, 52% had a second primary tumour in the UUT or the prostatic urethra (with or without intravesical recurrence); in the remaining 48%, only the bladder was affected. CIS of the bladder was present in 74% and 82% of all patients before the first and second cycle of BCG, respectively. Despite the high incidence of extravesical second-site primary tumours, the presence of these tumours was not independently associated with survival. This finding might result, in part, from the meticulous protocol used to investigate positive bladder cytology in the absence of visible tumour tissue, which is an excellent tool for all urologists treating patients with high-risk disease. The median time to diagnosis of a second primary urothelial cancer was 3.6 years, emphasizing the need for long-term follow-up surveillance.