Review – Prostate Cancer

Postprostatectomy Incontinence: All About Diagnosis and Management

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1. Introduction

The increasing number of radical prostatectomies entails an increasing number of patients suffering from postoperative stress incontinence. Depending on the study, the incidence of early stress incontinence varies between 0.8% and 87.0% [1–4]. The huge range of reported incontinence rates is most likely determined to a large extent by the unknown influence of the operating physician [5] and the lack of standardized diagnostic and treatment protocols.
of a standardised definition of “incontinence.” Thus, in high-volume centres with small numbers of surgeons, postprostatectomy continence rates are very high, between 91% and 98% [6,7]. Incontinence that persists for >1 yr postoperatively may decrease in these centres to <5% [8] and may even reach 1–2%. The incidence of de novo detrusor overactivity ranges between 2% and 77%, and this may last up to 1 yr [6,9,10]. In addition, men aged <50 yr show a significantly better rate of return to continence than men aged >70 yr [11].

Depending on the value put on urine leakage, the quality of life (QoL) of patients is strongly affected. Therefore, incontinence is one of the most feared complications of radical prostatectomy.

2. Pathogenesis

The risk of incontinence following prostatectomy includes preoperative factors (eg, age and preoperative continence status), intraoperative factors (eg, surgical technique and surgeon’s experience), and postoperative factors [12,13]. A better understanding of the male pelvic anatomy has decreased the postoperative incontinence rate [13,14]; the radical prostatectomy as modified by Walsh revolutionised the surgical technique [15]. Due to the preservation of the neurovascular bundles, postoperative sexual function improved and, in addition, a significant improvement in the postoperative continence rate occurred [16,17].

The precise aetiology of postprostatectomy incontinence has not been completely understood until now; however, dysfunction of the bladder neck as well as intraoperative damage of the nerves and sphincter may play a causative role [18,19]. In this regard, damage of the urethral sphincter can result not only from direct muscle damage but also from damage of the neuronal innervation [20]. According to newly evolving understanding, the reason for incontinence despite good function of the sphincter is a sphincteric laxity due to postoperative intrinsic sphincter deficiency [21,22]. This is caused by a disturbance of the male integral system following surgery (Fig. 1).

Another important factor for sphincter function seems to be the functional urethral length [23]. The minimal length of the functional urethra should be >28 mm [4]. Other authors found no impact of the functional urethral length [9,24]. In addition, the preservation of the bladder neck improves the early continence rate; however, in the long term, the results with and without bladder neck preservation are almost the same [25–28].

The preservation of the puboprostatic ligaments seems to induce no better continence rate [9,29–31]. Potentially, the “tip-sparing prostatectomy” with protection of the seminal vesicles can decrease the rates of incontinence and erectile dysfunction [32]. But further studies are needed to confirm the first results. There are also indications that the restoration of the posterior part of the rhabdosphincter can enhance the results [33,34].

Nevertheless, all studies dealing with potential issues influencing postprostatectomy incontinence have only level III evidence, excluding a few randomised controlled trials. Thus it is not possible to give evidence-based advice concerning the benefit of the different surgical techniques discussed [35].

3. Diagnosis

The diagnosis should be performed in a two-step assessment which includes a urinary diary and a

Fig. 1 – Disturbance of the male integral system following radical prostatectomy: (A) preoperative and (B) postoperative. Sphincteric laxity is due to radical prostatectomy.
questionnaire to assess the complaints (Fig. 2). There are several more or less complicated questionnaires. With the International Consultation on Incontinence Questionnaire—Short Form (ICIQ-SF), recommended by the EAU, a very simple and short questionnaire is readily available [36]. Because of its greater feasibility, the ICIQ-SF is more favourable in daily practice than the well-known King’s Health Questionnaire. Nevertheless, QoL and desire for treatment should be evaluated [37]. In addition, the standardised 1-h pad test has been shown to be useful [38,39].

After the initial diagnostic work-up a first-line treatment can be started. If the first-line treatment fails, a specialised clinical assessment is indicated (Fig. 2). In a urethrocystoscopy the sphincter and anastomosis region should be evaluated.

According to Stamey, the grade of stress incontinence can be determined to be mild (incontinence only with severe stress, such as coughing or sneezing), moderate (incontinence with minimal stress, including walking), or severe (incontinence during bed rest).

4. Noninvasive therapies

Noninvasive therapy is the first-line treatment for early incontinence that follows prostatectomy within the first 6 mo to 12 mo. In particular, pelvic floor muscle training (PFMT) is the most widely recommended noninvasive treatment.

With regard to the evaluation of conservative management effectiveness for postprostatectomy incontinence, there are, however, some problems. Existing trials are mostly neither randomised nor controlled; a standardisation of treatment is lacking; and the definitions for incontinence and continence vary from study to study. In addition, the normal rate of healing is often not taken into account, and the studied patient groups are very heterogeneous. In numerous studies, PFMT is performed without biofeedback, thus there is no control whether or not the muscle training is performed in a correct way. Therefore, determining whether the training was ineffective due to the inherent ineffectiveness of the treatment or whether it was simply performed in an incorrect way is often elusive. In addition, the
effectiveness of physiotherapy strongly depends on intangible factors like patient motivation and compliance [40,41].

Many urologists already advocate PFMT preoperatively. However, there is no evidence-based data for this recommendation. A recent randomised and controlled study showed an improved postoperative continence rate in patients who had preoperative biofeedback [42]. Another study by Bales et al showed no better outcome for patients starting PFMT with biofeedback preoperatively compared with those who started after radical prostatectomy [43].

Filocamo et al showed a significantly better early continence rate in patients attending a rehabilitation programme with PFMT compared with patients who did not [44]. After 1 yr there was no statistical difference between the incontinence rates of the two groups.

In three different Cochrane analyses, no significant evidence for the use of PFMT without biofeedback or biofeedback alone could be shown (Table 1) [40,45,46]. In the meta-analysis of Hunter et al [40], no significant effectiveness of electrical stimulation could be demonstrated, but this study showed some benefit in patients treated with PFMT and biofeedback. Floratos and van Kampen found some evidence for the use of biofeedback [44,47,48], but only van Kampen took the normal healing rate into account. Other groups found no significance improvement due to the use of biofeedback [43,49,50]. MacDonald et al reviewed eleven trials with a total of 1028 men who performed PFMT for treatment of postprostatectomy incontinence [42]. All of these trials had a control group. The data showed that patients who performed PFMT with or without biofeedback become continent faster than patients who did not perform PFMT.

The only study that showed evidence for the use of electrical stimulation was published in 1976 [51], but there was a number of issues with the study design and statistical analysis. In several subsequent studies no significant effectiveness of electrical stimulation could be shown [40,46]. Transcutaneous electrical nerve stimulation has been recommended by some studies, but again significant data-based evidence has not been provided [20,52].

Behavioural therapies like bladder training, timed voiding, reduction of fluid intake, and reduction of bladder irritants (e.g., coffee and hot spices) have been recommended by the EAU as well as by the International Continence Society for postprostatectomy incontinence even though there is no clinical data-based evidence for this recommendation [37,38,53]. Moreover, there is no standardisation of these behavioural therapies.

5. Pharmacologic treatment

Currently, there is no approved pharmacologic therapy for male stress incontinence. However, for female stress incontinence the use of duloxetine, a serotonin-noradrenalin-reuptake-inhibitor (SNRI), is an established therapy [54]. Specifically, duloxetine blocks the reuptake of noradrenalin and serotonin in the Onuf's nucleus within the sacral spinal cord. Due to the increased concentration of both neurotransmitters, the activity of pudendal motor neurons rises, which in turn increases the striated urethral sphincter tonus and at the same time relaxes the detrusor [55].

In recent years, the efficacy of duloxetine in men has also been evaluated. Despite the efficacy shown, duloxetine has not yet received approval for treatment of male stress incontinence. Nevertheless, duloxetine is commonly used off-label to treat male stress incontinence.

Although the number of studies is rather low, the existing two studies show a significant decrease in the number of incontinence episodes with duloxetine [56,57]. Unfortunately, there was no control group in either study.
Filocamo et al evaluated 102 patients with post-prostatectomy stress incontinence randomised into two groups: PFMT + duloxetine versus PFMT alone. Incontinence QoL (I-QoL) significantly improved, and the number of incontinence episodes was significantly reduced in group 1 after 16 wk. However, after 20 wk (4 wk after discontinuation of duloxetine medication), in group 2 the incontinence episode frequency was significantly lower in comparison with group one [58]. The synergistic effect of duloxetine in combination with PFMT can be explained by the fact that PFMT and duloxetine treat two independent therapeutic targets (sphincter activity vs pelvic floor muscle support): the pelvic floor muscle is itself not innervated by fibres originating from Onuf’s nucleus [59].

The most common side-effect of duloxetine and the most common reason for discontinuing therapy is nausea. Yet the risk for nausea can be reduced by a titration dosage which increases the dose over the first weeks up to the final doses of 40 mg twice per day [56].

In early postprostatectomy incontinence, de novo urgency with or without detrusor overactivity may play a certain role [60]. For these patients, additional anticholinergic treatment should be pursued. Currently there are no evidence-based recommendations in the existing guidelines for this treatment.

6. Surgical treatment

Some 2–5% of the patients with incontinence after radical prostatectomy exhibit a persistent incontinence for >1 yr postoperatively despite conservative therapy attempts. For these patients surgical treatment is recommended.

6.1. Injection therapy

Various substances (eg, collagen, teflon, silicone, autologous fat, autologous chondrocytes, dextranomer/hyaluronic acid copolymer) have been used for decades as bulking agents. Overall, the short-term effects are good, but the long-term success rate is poor because collagen, autologous fat, and autologous chondrocytes are subject to quick migration [61,62]. Additionally, with collagen there is a risk of anaphylactic reaction. Westney et al showed a mean duration of response after collagen injection of 6.3 ± 8.14 mo. Complete continence was achieved in 17% of the patients [62]. In several studies treatment with Teflon injection showed a continence rate between 17% and 76% [63,64]. After the detection of Teflon in lymph nodes, spleen, lung, and brain following Teflon injection in the external sphincter in research using animals, the use of Teflon for medical therapies was discontinued [65].

Agents currently used include dextranomer/hyaluronic acid copolymer (deflux), pyrolytic carbon microspheres (duraspHERE), and polydimethylsiloxane (macroplastique). All of these new agents show a slower migration without compromising other organs [66,67]. Short-term data are good, but reaching satisfactory long-term results requires rejections (Table 2) [68–71]. Prior injection of bulking agents does not appear to affect the postoperative result of artificial urinary sphincter implantation [72]. Postinjection inflammations can cause a frozen urethra.

6.2. Stem-cell therapy

The first results for autologous myoblast and fibroblast injections in 63 patients with postprosta-

<table>
<thead>
<tr>
<th>Bulking agent and study</th>
<th>No. of patients</th>
<th>Results after first injection</th>
<th>Side-effects</th>
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<tbody>
<tr>
<td>Macroplastique</td>
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<tr>
<td>Kyllmaa et al [65]</td>
<td>50</td>
<td>After first injection: 12% continent, 56% improved continence</td>
<td>Dysuric complaints</td>
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<td></td>
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<td>After repeated injections (max. 4): Max. 4: 60% continent, 24% improved continence, 16% no change</td>
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<tr>
<td>Imamoglu et al [64]</td>
<td>25</td>
<td>After 1–2 injections: 80% mild incontinence, 23% severe incontinence</td>
<td>Two urinary tract infections</td>
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<td></td>
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<td>One urinary retention</td>
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<tr>
<td>Deflux</td>
<td></td>
<td>After 4–8 wk: 58% continent, 39% improved</td>
<td>Urinary tract infection</td>
</tr>
<tr>
<td>Aloussi [66]</td>
<td>72</td>
<td></td>
<td></td>
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<tr>
<td>Durasphere</td>
<td></td>
<td>No subjective or objective cure</td>
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</table>

Table 2 – Results of recently used bulking agents
tectomy incontinence were published by Strasser et al in 2008. They showed a continence rate of 65% and improvement for an additional 27% of patients [73]. Other groups were not able to confirm these data—most even stopped the treatment; however, none of these results are available in PubMed. In addition, the whole treatment involves a very complicated and time-consuming procedure.

6.3. Slings

6.3.1. Bone-anchored sling systems
The Invance sling uses a silicon-coated polyester sling positioned under the bulbar urethra via a perineal incision. It is attached to both ischiopubic rami by three titanium screws (Fig. 3).

The first data about a bone-anchored sling were reported in 2001, when, in a cohort of 16 patients, a continence rate of 88% with no complications was reported [74]. Onur et al showed a better success rate in a cohort of 46 patients using silicon-coated bone-anchored slings (97% success rate) rather than slings with composite grafts (75%). They recommended the use of bone-anchored slings only for low and intermediate levels of incontinence [75]. Rajpurkar et al reported only a cure rate of 37% in a cohort of 46 patients [76].

In a study with 50 patients, Fassi-Fehri et al reported a 50% cure rate [77]; 26% patients showed an improvement; and 24% patients showed a treatment failure. After radiation, patients had a significantly lower cure rate of 25%. They found significantly more complications, with six cases of acute urinary retention and six cases of persistent perineal pain. Explantation was necessary in four patients.

In a study with 42 patients, Gilberti et al reported a cure rate of 62%; 8% of patients were improved; and 30% of patients had a failed treatment [78]. In 26 patients synthetic material was used; in 4 patients biological material was used; and in 12 patients mixed materials were used. Better results were seen with synthetic slings.

The implantation of an artificial sphincter is still possible after failed bone-anchored sling therapy, with equally results comparing to patients with no surgical pretreatment [79].

6.3.2. Readjustable sling systems
The REMEEX system is a readjustable suburethral sling; it is composed of a monofilament sling connected via two monofilament traction threads to a suprapubic mechanical regulator. The regulator is a permanent subcutaneous implant over the abdominal rectum fascia 2 cm above the pubis. Additionally, implant adjustment is possible via an eternal manipulator (Fig. 4).

The first results for this system were published in 2004 by Sousa-Escandó et al [80]. In this study six patients were treated, and five of them were cured. In a multicentre European study with 51 patients with a mean follow-up period of 32 mo, 33 patients (64.7%) were cured [81]. Twenty-five of these cured patients needed no pads; the other eight patients needed only small pads or sanitary napkins. Almost all patients needed at least one readjustment of the sling under local anaesthesia. The sling had to be removed in three cases: In one case urethral erosion occurred, and in two cases the regulator was infected. In five patients an intraoperative bladder perforation occurred, and three mild perineal haematomas were seen. Perineal discomfort or pain was very common and was treated with oral pain medication. Another group showed similar results in 18 patients [82].

The Argus system was first described by Moreno Sierra et al in 2006 [83]. The system is composed of a radiopaque cushioned system with silicone foam
42 mm × 26 mm × 9 mm thick for soft bulbar urethral compression, two silicone columns formed by multiple conical elements, which are attached to the pad and allow system readjustment, and two radiopaque silicone washers which allow regulation of the desired tension. In a cohort of 48 patients with a mean follow-up of 7.5 mo, Romano et al showed a cure rate of 73%. Three urethral perforations during surgery were reported, and the sling had to be removed in five patients. Seven patients had acute urinary retention, and, except for one patient in which the sling needed to be loosened, it resolved spontaneously. No severe complications were seen.

6.3.3. Functional retrourethral sling

The functional retrourethral sling (AdVance sling) is a new and innovative sling suspension which offers, for the first time, a nonobstructive, functional therapeutic approach (Fig. 5). Other slings, including the Pro-ACT system and the artificial urinary sphincter, achieve continence mainly by compression of the urethra [85,86]. In urodynamic studies no obstruction of the urethra due to the retrourethral sling was seen [87]. The sling adjusts the changed anatomy after radical prostatectomy by repositioning the lax and descended supporting structures of the sphincter to the former preoperative position. Thus continence can again be achieved.

This sling was first described by Rheder and Gozzi. In the first report, 20 patients and 4 cadavers were treated. The cure rate, defined as no pad use, was 40%, and the improvement rate, defined as 1–2 pads per day, was 30% [87]. In a recent study with 67 patients these data were confirmed: The cure rate was 52%, and the improvement rate 38% [88].

6.3.4. Pro-ACT system

The Pro-ACT system is an adjustable therapy option; it uses the principle of augmenting titration for optimal urethral coaptation. Two balloons are placed bilaterally at the bladder neck. Titanium ports are placed in the scrotum for volume adjustment (Fig. 6). Postoperative readjustment is very simple, and only local anaesthesia is necessary. This system was first introduced in 2000.

A study of the ProACT system was first published by Huebner and Schlarp in 2005. In 117 patients with a mean follow-up period of 13 mo, an improvement in 92% of the patients could be shown. Sixty-seven percent of the patients were dry, and in 8% there was no improvement. After 2 yr, QoL improved from 34.7 to 66.3. The balloons were readjusted a mean of three times. Pad use decreased from a mean of six pads per day to a mean of one pad per day. In 32 patients reimplantation was necessary, with a success rate of 75% [89]. In 2007 Huebner and Schlarp published another study comparing their first 50 patients with their last 50 patients. In group one 52% of patients were dry; in group two 60% of patients were dry. In group two a better overall response was seen as well as better improvement of QoL and shorter operative time. The pad reduction was significant and similar in both groups [90].

Trigo-Rocha et al reported comparable data [91]. Gregori et al reported on the use of ultrasound-guided placement of the balloons to reduce complications and to advance the perfect placement of the balloons [92]. The data show that the complication rate declines and the success rate improves with the surgeon’s experience.

The ProACT system is not recommended after radiation therapy due to a higher complication rate and an unsatisfactory success rate.

6.3.5. Artificial urinary sphincter

The artificial urinary sphincter (AUS) is, despite the new surgical treatment options, still the gold
standard for the surgical treatment of male incontinence. The technique is well-engineered. Since the first introduction of the AS-721 in 1972 the artificial sphincter has been modified several times to the current AS-800 (Fig. 7). Nevertheless, the intervention is expensive and requires invasive surgery and experienced surgeons. It has a high rate of infection and a high rate of urethral atrophy due to the sustained high occlusion pressures on the urethra. In addition, the patient must have the mental and physiologic ability to handle the sphincter.

The success rate of the AUS is still the best compared with all the other available surgical treatment options for postprostatectomy incontinence. Even the long-term results are very good [93,94].

Age should not be considered as an exclusion factor for AUS implantation. The procedure has a high rate of success even in men aged >75 yr [95].

In 2003 Wilson et al published a new implantation technique with only a single scrotal incision. The regulation balloon was placed in the cavum retzii. In a cohort of 37 patients, a cure rate of 66% was achieved. Operative time can be reduced with this new technique. Follow-up after 1 yr showed no difference in complication rate between the single-incision technique and the traditional method [96]. Sotelo et al also showed no increased risk for the single-incision technique compared with the double-incision technique in high-risk patients with a history of radiation therapy and cryotherapy [97]. Nevertheless most urologists still use the two-incision technique.

Double-cuff systems are used to reduce urethral atrophy and increase continent rates. A recently published study of 56 patients showed no difference between single- and double-cuff systems except for a higher risk of complications and additional surgeries for the single-cuff patients [98].

Another approach to problems associated with the AS-800 was the development of a new artificial urinary sphincter with a conditional occlusion that reduces the pressure on the urethra and allows the possibility of a self-adjustment of the pressure while increasing abdominal pressure. The first results are promising. In this small group of nine patients, the continence rate was similar to the continence rate after the placement of the AS-800. No serious adverse events occurred [99], but further studies are needed to evaluate the long-term benefit for the urethra.

7. Conclusions

Incontinence following radical prostatectomy is still the most feared complication for men. Due to modified surgical techniques, incontinence rates have been decreasing in recent years. However, even in high-volume departments the incontinence rate remained around 1% after 1 yr postoperatively. The diagnosis of postprostatectomy incontinence according to the two-stage assessment recommended by the EAU guidelines has proven to be successful.

However, the recommendations for treatment options are still only given generally without a clear association with stage and severity of incontinence. This limitation can only be overcome in the future if sufficient evidence is provided by future clinical studies. Moreover, there exists no single precise definition for incontinence, therefore a fair comparison of study results is often not possible.

For early postprostatectomy incontinence, non-invasive therapies like PFMT, biofeedback, and electrical stimulation are, in general, strongly recommended, although there is no strong data to support these recommendations. In addition, there is no conclusive data concerning the optimal timing to begin treatment—specifically for preoperative versus postoperative—noninvasive therapy. Further prospective placebo-controlled studies with sufficient power are required to provide stronger evidence for these recommendations. The combination of physiotherapy and medical treatment with duloxetine shows better results in the short-term compared with either of the two therapies alone (Table 3).

Based on the evidence gathered for all patients shortly after removal of the catheter, supervised PFMT with biofeedback can be recommended. Additional treatment with duloxetine is useful to support the early success. But due to the lack of approval of duloxetine for male incontinence,
patients might have a reimbursement problem with their health insurance.

If noninvasive therapy fails, surgical therapy options are recommended, but the natural healing rate should be taken into account. Only in severe incontinence should surgical therapy be considered before 6 mo to 12 mo after radical prostatectomy.

For severe or persistent incontinence the artificial urinary sphincter is still the gold standard of treatment. The AS-800 is associated with high continence and high patient satisfaction rates. It is currently the reference treatment for refractory sphincter incompetence in men (Table 3).

In recent years, numerous minimally invasive treatment options with different success rates have been investigated. But new surgical techniques must at least match the results of the artificial sphincter. Nevertheless, the patient demand for minimally invasive treatment options is high, and often, poorer results are accepted by the patients in order to avoid an artificial sphincter. Slings can be recommended for patients with persistent mild or moderate incontinence. For patients with severe incontinence the artificial sphincter is recommended, but slings can also be used for patients who prefer a less invasive treatment.

Stem-cell therapy should not be recommended currently.

For the development of new, more successful, and potentially patient-specific treatment options, it is necessary to improve and deepen our understanding of the different pathophysiologic mechanisms of male postprostatectomy incontinence.

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**Study concept and design:** Bauer, Stief.

**Acquisition of data:** Bauer.

**Analysis and interpretation of data:** Bauer, Gozzi, Bastian.

**Drafting of the manuscript:** Bauer.

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**Table 3 – Quality of evidence for male incontinence treatment options**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Level of evidence</th>
<th>Grade of recommendation</th>
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<tr>
<td>PFMT</td>
<td>2</td>
<td>B</td>
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<tr>
<td>Duloxetine</td>
<td>3–4</td>
<td>C</td>
</tr>
<tr>
<td>PFMT + Duloxetine</td>
<td>1</td>
<td>A</td>
</tr>
<tr>
<td>Bulking agents</td>
<td>3</td>
<td>B</td>
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<tr>
<td>Slings</td>
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<tr>
<td>ProAct</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td>AUS</td>
<td>1</td>
<td>A</td>
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PFMT = pelvic floor muscle training; AUS = artificial urinary sphincter.

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[47] Floratos DL, Sonke GS, Rapidou CA, et al. Biofeedback versus verbal feedback as learning tools for pelvic muscle...


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