Podium Session 3: Incontinence, Reconstruction, ED: Postprostatectomy Issues June 29, 2009, 1050–2000

POD-3.01

Promising midterm results of pelvic organ prolapse repair using a transvaginal mesh: a series of 56 cases

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Introduction and Objective: A new surgical technique of pelvic reconstruction using a transvaginal mesh, the Prolift system, attempts to improve the high recurrence and complication rate of conventional surgical treatments for pelvic organ prolapse (POP). The objective of the study was to report our experience on the implantation of the Prolift system.

Materials and Methods: The population of the study included 56 patients operated from July 29, 2005, to August 29, 2008, by one surgeon (LMT). The patients have all undergone the implantation of a transvaginal mesh, the Prolift system, for the treatment of recurrent or high-grade multiple compartment POP (Baden–Walker stage 3 or 4). A concomitant anti-incontinence surgery was performed in 38 patients (68%).

Results: The population had a mean age of 68.1 (46–88), a body mass index (BMI) of 27 (21–40) and a parity average of 3.3 (1–16). Previous POP repair had been performed in 17 patients (30%) and a hysterectomy in 43 (77%). High-grade genital prolapse was present in the anterior vaginal wall in 71% (40/56), apical wall in 45% (25/56) and posterior wall in 48% (27/56). Operating time was on average 98 (70–135) minutes, blood loss 81 (50–300) mL and hospital stay 2.9 (1–10) days. With a median follow-up of 17 months, the cure rate for pelvic organ prolapse was 91% (48/53) and the dry rate was 76% (40/53). Perioperative complications included 1 anterior rectal wall laceration that required primary repair and removal of the entire mesh, as well as 1 prolonged bleeding that required embolisation of the left internal iliac artery. Short-term postoperative complications comprised 10 episodes of transient urinary retention that required immediate tape release in 4 patients, 2 cases of postoperative pain that lasted a maximum of 2 weeks and 1 episode of transient fever. Long-term complications included 5 POP recurrences that required revision in 1 case.

Conclusion: The Prolift system appears to be a safe and effective treatment option for the treatment of recurrent or high-grade multiple compartment POP, because of a low number of complications and a high midterm cure rate. However, long-term follow-up is still needed in order to confirm the safety and effectiveness of the procedure.

POD-3.02

Tolerability of solifenacin in comparison with oxybutynin immediate release in patients with overactive bladder: results of the VECTOR (VEsicare in Comparison To Oxybutynin for oveRactive Bladder Patients) Study

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Introduction and Objective: Various reimbursement plans mandate immediate-release (IR) oxybutynin (oxy) as first-line therapy for overactive bladder (OAB); however, many patients discontinue therapy due to adverse events (AEs) such as dry mouth. The VECTOR study was designed to compare the tolerability of solifenacin (sol) versus oxy IR in patients with OAB.

Materials and Methods: This Canadian, multicentre, prospective, double-blind, double-dummy study randomized 132 subjects with 1 or more urgency episode/24 hour with or without urgency incontinence and 8 or more micturitions/24 hour for 3 or more months to sol 5 mg od or oxy IR 5 mg TID for 8 weeks, as per recommended daily dosages. The primary end point was the incidence and severity of dry mouth. All AEs were determined by direct questioning by the physician at each follow-up visit. If reported, dry mouth severity was graded as mild, moderate or severe. Overactive bladder symptoms were captured using a 3-day diary at baseline and weeks 2, 4 and 8. Two patient-reported outcome (PRO) measures, the Patient Perception of Bladder Condition and Overactive Bladder Questionnaire, were used.

Results: The study was completed by 92 (70%) subjects. Solifenacin was associated with significantly fewer episodes of dry mouth (24/68 v. 53/64, $p < 0.0001$) of which 75% was mild in severity compared with 30% with oxy ($p = 0.001$). Solifenacin was also associated with significantly fewer AEs ($p = 0.003$), lower severity of overall AEs ($p = 0.009$) and fewer treatment-related AEs ($p = 0.0093$) compared with oxy. Significantly fewer subjects in the sol group (2/68) withdrew due to dry mouth compared with the oxy group (12/64, $p = 0.0032$). Both sol and oxy significantly reduced all diary-recorded OAB symptoms and significantly improved PROs from baseline to study end point. No notable differences between the 2 groups were observed in OAB symptoms and PROs at study end point.

Conclusion: At efficacious doses, sol was associated with a significantly better tolerability profile compared with oxy IR and was similarly effective in improving OAB symptoms and PROs. This resulted in fewer withdrawals from therapy. The relatively high incidence of AEs in both groups may be explained as a result of the direct questioning methodology used and patients being informed that dry mouth was the primary study objective.

POD-3.03

Early return of potency and orgasmic function following aggressive bilateral intrafascial nerve-sparing during trizonal athermal robotic prostatectomy: a prospective cohort study

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Introduction and Objective: We report our experience with early return of sexual function following an aggressive intrafascial nerve-sparing technique during robotic prostatectomy in carefully selected patients with a low risk of extraprostatic extension of cancer.

Materials and Methods: From January to September 2008, 61 men met selection criteria for aggressive nerve sparing: PSA less than 10 ng/dL, clinical stage T2 or less, primary Gleason grade less than 4, cancer volume less than 5% in all cores, and absence of cues suggestive of EPE on endorectal MRI and during surgery. Patients completed baseline IIEF questionnaires before surgery and were prospectively followed up with standardized telephone interviews at regular intervals over a 9-month period. Data collected included the use of erectogenic aids (PDE5i, PGE-1 [alprostadil], etc.). Potency was defined as erections sufficient for penetrative intercourse.

Partial erections were defined as engorgement of the penis not sufficient for penetration (Fig. 1, Fig. 2).

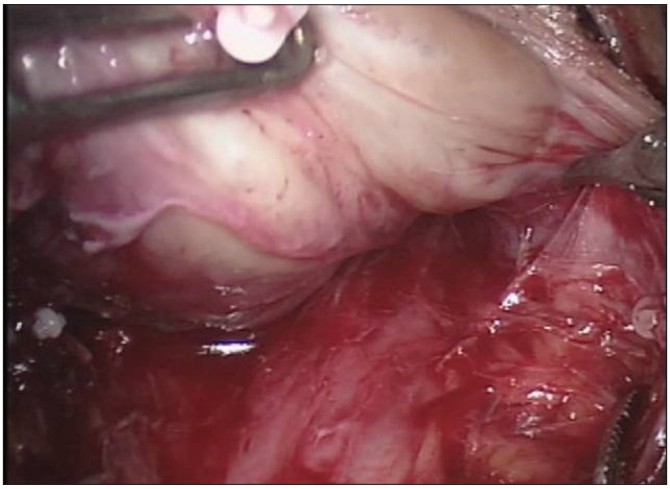

Fig. 1.

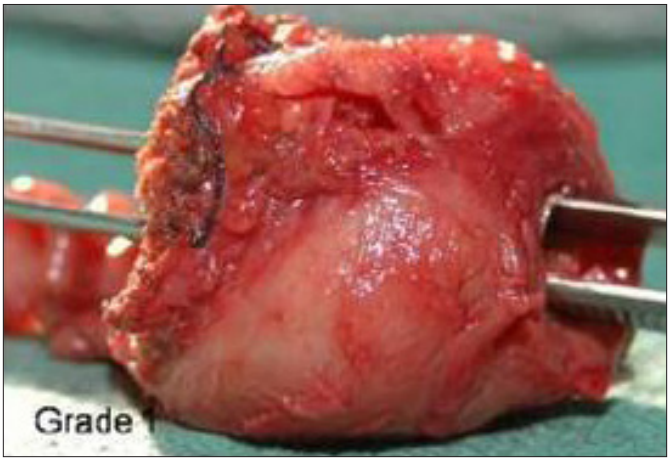

Fig. 2.

Results: Complete follow-up data was available for 59 out of 61 patients receiving aggressive nerve-sparing. Mean age was 55.1 years. Mean PSA 5.51 ng/dL. At a mean follow-up of 26 weeks, 56 men (95%) had partial erections with and without the use of PDE5i, 51 (86%) had erection sufficient for penetrative intercourse and 54 (91.5%) reported return of orgasmic function. Return of potency occurred at 10.2%, 59.3%, 74.6%, 83.1% and 86.4% at 1-, 6-, 12-, 24- and 36-week follow-up. Positive surgical margins occurred in 5 men (8.5%).
Conclusion: Our technique of aggressive bilateral nerve-sparing in carefully selected patients delivers early return of sexual function without compromising cancer control.

POD-3.04

Better short-term outcomes with the U-method compared with the Hammock technique for the implantation of the TVT-SECUR under local anesthesia

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Introduction and Objective: The new midurethral sling TVT-SECUR, used for the treatment of stress urinary incontinence (SUI), shows a potential for implantation under local anesthesia, because of a less invasive technique using minimal vaginal dissection as well as avoidance of retropubic space and obturator fossa. This is a prospective, clinical study with objective to report our experience with the implantation of the TVT-SECUR under local anesthesia, with the use of questionnaires.
Materials and Methods: The population consisted of 48 women operated on from Jan. 23, 2007, to Oct. 14, 2008. The implantation of the TVT-SECUR under local anesthesia was done by one surgeon (LMT). The Hammock technique, similar to the transobturator tape dissection, was used in the first 23 cases and the U-Method, similar to the retropubic tape dissection, in the last 25 cases.
Results: The population included 48 patients with a median follow-up of 12 months. Mean age of the population was 61 (38–85) years old, 40% (19/48) had genuine SUI and 8% (4/48) had undergone a previous anti-incontinence surgery. Mean OR time was 31 (15–45) minutes. Regarding local anesthesia satisfaction, 98% (47/48) required 1 mg IV of midazolam or less and 77% (37/48) required only 50 ug of fentanyl. Visual Analog Scale for pain immediately and 1 week after surgery showed a mean score of 19/100 and 29/100, respectively. At 1 week, 2 months and 6 months after surgery, the improvement in SUI symptoms rate was 82% (18/22), 76% (16/21) and 69% (11/16) for the Hammock technique, compared with 73% (16/22), 100% (15/15) and 100% (13/13) for the U-Method. Postoperative complications included 6 partial tape exposures, all with the Hammock technique, that needed surgical revision in all cases. With the U-Method, there were 2 cases of transient urinary retention, lasting 2 and 14 days.
Conclusion: Local anesthesia and light sedation provided satisfactory analgesia during implantation of the TVT-SECUR. However, this new midurethral sling has shown concern regarding improvement in SUI symptoms and complication rate early in the study, with the use of the Hammock technique. Change of the technique in the last 25 cases, using the U-Method instead, helped improve the cure rate and lower the number of complications.

POD-3.05

Botulinum toxin A in neurogenic detrusor overactivity: results of patient reported outcomes from a Canadian multicentre randomized trial

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Introduction and Objective: We evaluated the effect of intradetrusor Botulinum toxin A (BoNT-A) for neurogenic detrusor overactivity (NDO) in a prospective randomized, placebo-controlled trial, and report the analysis of data from patient questionnaires.
Materials and Methods: Fifty-seven subjects (34 men and 23 women, mean age 57 yr) with urodynamically demonstrated NDO secondary to either spinal cord injury (SCI) ($n = 38$) or multiple sclerosis (MS) ($n = 19$) and urinary incontinence (UI) (≥ 1 occurrence/d) received BoNT-A 300U or placebo (saline), injected into 30 sites in the detrusor, sparing the trigone. Anticholinergics were discontinued at 3 weeks posttreatment and could be resumed at 50% of the previous dosage at 4 weeks. At week 36, all subjects were offered open-label BoNT-A. The International Consultation on Incontinence Questionnaire (ICIQ) and Urinary Incontinence-Specific Quality of Life Instrument (I-QOL) were completed at baseline and weeks 6, 24 and 36, and at weeks 48 and 60 (12 and 24 wk following open-label BoNT-A). This analysis includes all randomized subjects (28 BoNT-A, 29 placebo); with 26 and 23 subjects, respectively, who received open-label BoNT-A when offered at week 36.
Results: Treatment with BoNT-A, compared with placebo, significantly reduced mean scores for the frequency of urine leakage at weeks 6 and 24, and interference of urine leakage with life at weeks 6, 24 and 36 (based on ICIQ), and significantly improved mean total QOL scores at weeks 6, 24 and 36 (based on I-QOL), versus baseline. Upon receiving open-label BoNT-A injections, comparable improvements in these 3 parame-

ters were observed in both the group initially assigned to BoNT-A and those initially assigned to placebo.
Conclusion: BoNT-A had a beneficial effect on frequency of UI, and resulting interference with life and QOL impact, in people with NDO secondary to SCI or MS. These improvements were maintained for 24–36 weeks posttreatment. Following open-label treatment with BoNT-A, similar improvements were also seen in patients who had been initially randomized to placebo. To our knowledge, this is the first North American placebo-controlled randomized study investigating the efficacy of BoNT-A in this patient population (Table 1).

Table 1. POD-3.05. Mean change from baseline in selected patient questionnaire parameters

Parameter	6 wk	24 wk	36 wk	48 wk	60 wk
Frequency of urine leakage score*					
BoNT-A	–1.64†	–7.71†	–0.74	–1.73	–1.52
Placebo	–0.14	–0.04	–0.12	–1.83	–1.39
Interference of urine leakage with life scale‡					
BoNT-A	–3.36†	–2.39§	–2.15§	–3.00	–2.56
Placebo	0.34	–0.69	–0.48	–4.22	–3.05
I-QOL score (total)¶					
BoNT-A	19.52†	16.27§	7.91§	21.5	15.36
Placebo	–2.23	0.44	–1.91	21.64	16.55

*5-point scale: 0 = never, 5 = all the time.
†$p < 0.0001$.
‡10-point scale: 0 = not at all, 10 = a great deal.
§$p < 0.05$.
¶Higher scores indicate better QOL.

POD-3.06

Prospective randomized clinical trial of trans-obturator tape versus tension-free vaginal tape for the treatment of stress urinary incontinence in women: outcome at 12 months

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Introduction and Objective: The tension-free vaginal tape (TFVT) and trans-obturator tape (TOT) have become the most commonly performed surgical treatments for stress urinary incontinence (SUI) in North America. Alternative routes to placement of the tape may impact on safety and efficacy. We conducted a randomized clinical trial to compare the effectiveness of TOT to TFVT in providing objective cure of SUI in women at 12 months postoperatively.
Materials and Methods: Women with SUI were randomly allocated to receive either TOT or TFVT procedures. Patients were reviewed at 12 months after surgery. The primary outcome was objective evidence of "cure" evaluated by standardized pad test (cure defined as < 1 g urine leaked). Other outcomes included subjective cure, incontinence-related quality of life (QOL), satisfaction with outcome, return to usual activities, voiding dysfunction and surgical complications. A sample of 100 patients per group (total 200) was required to find 15% absolute difference in cure rate. Primary analysis compared the proportion of patients in each group who were cured at 12-month follow-up, using Fisher exact test.
Results: One hundred ninety-nine women were randomized in the study (94 in the TOT and 105 in the TFVT Group). Sixty-eight (81%) women in the TOT group were "cured," versus 67 (77%) in the TFVT group (not statistically different). On vaginal exam, the tape was palpable or visible for 68 (80%) women in the TOT and 24 (27%) in the TFVT group ($p < 0.001$). Quality of life improved significantly from baseline in both groups (improvement in IIQ-7 score from 38 to 8, both groups).
Conclusion: At 12 months, the majority of women had minimal leakage, and their QOL had improved significantly, but differences were not observed between groups. The presence of palpable tape is concerning: longer follow-up is needed to determine if this outcome predisposes to extrusion or resolves over time.

POD-3.07

Comparison of 2 overactive bladder antimuscarinic treatments on heart rate in subjects 50 years of age or older

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Introduction and Objective: Faster heart rate (HR) and/or reduced HR variability (HRV) can affect cardiovascular (CV) morbidity and mortality particularly for older patients (pts) with CV disease. Since overactive bladder (OAB) prevalence increases with age and 45% or more of OAB patients also have CV disease, the potential impact of antimuscarinic OAB treatments on HR and HRV is of clinical interest. In this study we attempt to confirm previously observed differential effects of darifenacin (DAR) and tolterodine (TOL) on HR/HRV in healthy volunteers, similar in age to OAB patients.
Materials and Methods: In this crossover study, healthy subjects (≥ 50 yr), were randomized to 1 of 6 treatment sequences, each comprising three 7-day dosing periods (DAR 15 mg, TOL 4 mg, placebo [PBO]) separated by 14-day washouts. Mean HR and HRV over 24 hours were assessed at baseline and steady state exposure (day 7 of each dosing period) using 24-hour Holter monitoring.
Results: Of 117 randomized subjects (mean age 58.4 yr, 63.2% women), 108 completed all 3 dosing periods. The use of tolterodine resulted in a statistically significant increase in mean HR per 24 hours versus DAR and versus PBO (Fig. 1). The use of tolterodine also resulted in a statistically

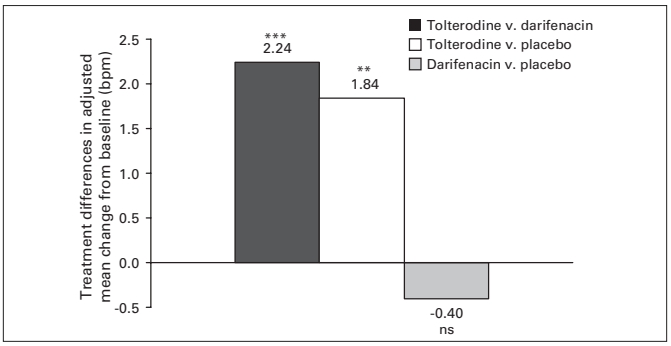

Fig. 1. Change from baseline in mean heart rate over 24 hours: treatment differences in adjusted mean change from baseline, at the end if each study period. **$p = 0.0037$; ***$p = 0.0004$ (analysis if covariance model, which included effects of treatment, sequence, study period and baseline mean HR over 24 h as fixed effects, and subjects within sequences as random effects).

significant reduction in 2 of 3 HRV parameters per 24 hours versus DAR (both $p < 0.01$) and 1 of 3 HRV parameters versus PBO ($p = 0.0219$). In contrast, DAR did not affect any HR or HRV parameters versus PBO. Most common adverse event (AE) was dry mouth (13.3% DAR, 5.4% TOL, 0.9% PBO). There was 1 serious AE (hypersensitivity with DAR).
Conclusion: This study confirms TOL increases HR and decreases HRV compared with darifenacin, which had similar effect to placebo in healthy subjects, similar in age to typical OAB patients. Since increased HR and reduced HRV are associated with increased CV risk, careful selection of antimuscarinics for OAB patients could minimize an unnecessary drug induced CV risk.