

The Value of Preoperative Multichannel Urodynamic Testing for Detecting Occult Stress Urinary Incontinence in Women Undergoing Prolapse Repair Surgery

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ABSTRACT **Background:** Diagnosing occult stress urinary incontinence (OSUI) prior to surgical intervention for pelvic organ prolapse (POP) repair may allow for adding an anti-incontinence procedure and thus prevent postoperative SUI.

Objectives: To compare preoperative detection rates for OSUI by either a multichannel urodynamic investigation or by a plain pelvic examination.

Methods: We retrospectively evaluated the medical charts of all women who underwent urodynamic investigation prior to surgical repair of advanced POP at our institution between 1 January 2006 and 31 December 2012.

Results: In total, 720 women underwent surgical POP repair during the study period, of whom 54 (7.5%) were diagnosed with OSUI preoperatively. Of these patients, 54 (100%) were detected by multichannel urodynamic investigation while only 27 (50%) were detected by a plain pelvic examination ($P = 0.001$). Bladder fullness during the pelvic examination was associated with higher detection rates for OSUI ($P = 0.001$). Women with OSUI who underwent concomitant tension-free vaginal tape and POP repair procedures did not develop de novo SUI or obstructive voiding symptoms (OVS) postoperatively.

Conclusions: Preoperative multichannel urodynamic investigation has significantly higher detection rates for OSUI than a plain pelvic examination. Utilizing this modality resulted in no cases of de novo SUI or OVS postoperatively.

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KEY WORDS: occult stress urinary incontinence (OSUI), pelvic examination, pelvic organ prolapse (POP), urodynamic investigation

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Advanced pelvic organ prolapse (POP) is an increasingly common condition in western countries affecting as much as 16% of all adult women [1]. This condition results from failure of the normal pelvic organ support mechanisms including the pelvic floor, vaginal walls, and suspensory ligaments. While POP usually manifests with a vaginal bulge, it may also be accompanied by urinary and gastrointestinal symptoms as well as sexual dys-

function [2]. Stress urinary incontinence (SUI) is one of the most common conditions associated with POP, as the risk factors for both conditions are very similar [2]. Nonetheless, some women might not present with this problem until surgical repair of their prolapse, a phenomenon known as occult SUI (OSUI) [3]. The assumed mechanism for this entity is that advanced POP may cause urethral kinking and compression, fixing a hypermobile urethra in place and therefore masking SUI. Some researchers have suggested that even a lower degree of POP (i.e., stage II or greater) is also predictive of the development of OSUI following POP surgery [4]. Once normal anatomy is restored and urethral kinking is resolved by POP repair surgery, OSUI might become unmasked and thus symptomatic. This result may occur in 36% to 80% of continent patients with POP and might be severely debilitating and frustrating for both patient and physician [5]. Based on these data, some investigators have advocated performing an anti-incontinence procedure along with POP repair surgery, thereby addressing both OSUI and POP and thus reducing the risk of developing de novo SUI postoperatively. Other clinicians, however, have argued that combining POP repair with an anti-incontinence procedure may be unnecessary and might increase complication rates, including both obstructive voiding and storage symptoms [6,7].

OSUI can be diagnosed by either a pelvic examination with a cough test performed while the prolapsed organs are reduced or via a multichannel urodynamic investigation [5,8]. To date, there are insufficient data regarding the added value of urodynamic testing over a plain pelvic examination in diagnosing OSUI. Moreover, this test is invasive and costly and has high inter- and intra-observer variabilities [9]. The aim of this study was therefore to compare preoperative detection rates for OSUI by either a multichannel urodynamic investigation or by a plain pelvic examination.

PATIENTS AND METHODS

We retrospectively reviewed medical charts of all women who underwent a urodynamic investigation prior to surgical repair of advanced (stage III–IV) POP at our institution between 1 Janu-

ary 2006 and 31 December 2012. Demographic data including age, obstetric and medical history, and previous surgical interventions were obtained from all patient charts. Preoperative pelvic examination findings including the degree of prolapse by the Baden and Walker and the POPQ systems, as well as urodynamic data were recorded from patient medical charts and urodynamic reports [10,11]. Whether OSUI was demonstrated by a pelvic examination or by multichannel urodynamic testing was recorded for all patients, and detection rates were compared between the two modalities.

According to our department's protocol, all preoperative pelvic examinations included a cough test performed on a full bladder with manual reduction of the prolapsed organs. Bladder fullness was determined based on patient's subjective assessment at the beginning of the examination along with a sonographic measurement of the bladder volume via a BladderScan BVI 3000 machine (Verathone, UK). Women were asked to cough vigorously at least three times and the presence or absence of urinary leakage was recorded. For the urodynamic testing the International Continence Society (ICS) standardization protocol was utilized [12]. A urinary tract infection was always excluded by means of a urinary culture and reduction of the prolapsed organs was performed via a vaginal pessary. The reconstructive pelvic surgery was performed, and the postoperative follow-up data were recorded.

Women whose medical charts and urodynamic reports were incomplete or absent were excluded from the study. Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 24 (SPSS, IBM Corp, Armonk, NY, USA). Continuous variables were compared using paired student *t*-test or Wilcoxon signed rank test while categorical variables were compared using chi-square or McNemars' test. $P < 0.05$ was considered statistically significant for all comparisons. The study was approved by the Carmel Medical Center Institutional Review Board Committee for Human Subjects (No. 0080-16-CMC).

RESULTS

At our institution, 720 patients underwent surgical POP repair during the study period. All underwent both preoperative pelvic examination and a multichannel urodynamic investigation. Of these patients, 54 (7.5%) were detected for OSUI by a multichannel urodynamic investigation but only 27 (3.75%) were detected by a plain pelvic examination ($P = 0.001$) [Table 1]. The patients who were diagnosed with OSUI by a plain pelvic examination were also detected by the urodynamic investigation. Bladder fullness during the pelvic examinations was associated with higher detection rates for OSUI (62.1% vs. 17.4% for a full vs. an empty bladder, respectively, $P = 0.001$). All 54 women who were diagnosed with OSUI eventually underwent concomitant tension free vaginal tape (TVT) and POP repair

procedures. Of these patients, 40 had a comprehensive postoperative evaluation with a mean follow up time of 20 ± 17.9 months. None of these patients complained of de novo SUI and none had long-standing urinary retention or de novo obstructive voiding symptoms postoperatively [Table 2]. While all patients had overactive bladder (OAB) symptoms preoperatively, only 22 patients (55%) complained of these symptoms postoperatively. Prolapse severity at all compartments was significantly reduced postoperatively [Table 2].

DISCUSSION

These results indicate that in women with advanced POP, preoperative plain pelvic examination was able to detect only 50% of OSUI cases diagnosed by a multichannel urodynamic investigation. Bladder fullness was the strongest predictor for the detection of OSUI by a plain pelvic examination. Surgical repair of POP with concomitant TVT was found to be safe and effective in patients with OSUI.

Table 1. Demographic and clinical characteristics of patients with occult stress urinary incontinence (n=54)

Characteristics	Values
Age, years	64.6 ± 9.6
Parity	3 (1–10)
Diabetes	11 (20.4)
Menopause	50 (92.6)
Overactive bladder symptoms	54 (100)
Urinary urgency	47 (87.0)
Urinary frequency	53 (98.1)
Nocturia	47 (87.0)
Urge urinary incontinence	21 (39.6)
Overt stress urinary incontinence	0 (0)
Obstructive voiding symptoms	37 (68.5)
Cystocele (grade) ¹	3 (1–4)
Ba point (cm) ²	3.94 ± 2.4
Apical prolapse (grade) ¹	3 (1–4)
C point (cm) ²	0.63 ± 3.7
Rectocele (grade) ¹	2 (0–4)
Bp point (cm) ²	-0.22 ± 2.5
Occult stress urinary incontinence method of diagnosis	
Urodynamic investigation	54 (100)
Pelvic examination	27 (50)

Values are presented as mean ± standard deviation, median (range), or number (percent)

¹By the Baden and Walker halfway system [10]

²By the POPQ system [11]

Table 2. Preoperative and postoperative clinical characteristics of patients with occult stress urinary incontinence (n = 40)

	Preoperative	Postoperative	P value
Stress urinary incontinence	0 (0)	0 (0)	
Overactive bladder symptoms	40 (100)	22 (55.0)	< 0.0001
Urinary urgency	36.0 (90.0)	10 (25.0)	< 0.0001
Urinary frequency	39 (98.0)	7 (17.5)	< 0.0001
Nocturia	35 (87.5)	19 (47.5)	< 0.0001
Urge urinary incontinence	16 (41.0)	7 (17.5)	0.012
Obstructive voiding symptoms	28 (70.0)	1 (2.5)	< 0.0001
Cystocele (grade) ¹	3 (2–4)	0 (0–1)	0.005
Ba point (cm) ²	5.1 ± 1.66	-2.55 ± 1.9	0.005
Apical prolapse (grade) ¹	3 (2–4)	0 (0–3)	0.003
C point (cm) ²	1.9 ± 3.7	-3 ± 3.65	0.003
Rectocele (grade) ¹	3 (1–4)	1 (0–3)	0.004
Bp point (cm) ²	-0.22 ± 2.1	-1.44 ± 2.7	0.212

Values are presented as mean ± standard deviation, median (range), or number (percent)

¹By the Baden and Walker halfway system [10]

²By the POPQ system [11]

OSUI is a well-established phenomenon where SUI is masked by advanced POP and becomes asymptomatic [13]. While some women describe alleviation or disappearance of SUI along with the progression of POP symptoms, others may not experience SUI at all [14]. The proposed mechanism for OSUI involves urethral kinking and a cushioning effect by a large cystocele, which interferes with the transmission of the intra-abdominal pressure to the bladder [15]. Surgical repair of advanced POP might unmask the urethral support weakness and thus render previously continent women overtly incontinent. This phenomenon is not uncommon, and approximately 25% of continent women with POP will develop SUI once the prolapsed organs are reduced, either by a vaginal pessary or following surgical intervention [5]. De novo SUI following POP repair surgery might be frustrating and can severely affect a patient’s satisfaction from her surgery. Therefore, every effort should be made to identify susceptible women preoperatively. There is an ongoing debate regarding the benefit of adding an anti-incontinence procedure in women who undergo surgery for POP. While some investigators advocate a one-step approach, including concurrent prolapse repair and an anti-incontinence surgery for all women, others recommend a two-step approach, where only the prolapse is repaired initially followed by an anti-incontinence procedure at a later stage

if needed [5]. Advocates of the one-step approach claim that it may avoid the need for a second surgery and that genital prolapse repair by itself does not address the problem of OSUI [16,17]. Bergman and colleagues [18] have shown that while Burch colposuspension and TVT are effective anti-incontinence surgeries, anterior colporrhaphy even when combined with a Kelly plication has a 5-year success rate for SUI of only 37% [18]. In the Colpopexy and Urinary Reduction Efforts (CARE) trial, Brubaker and co-authors [17] found that continent women who underwent abdominal sacrocolpopexy with Burch colposuspension had significantly lower rates of postoperative de novo SUI than those who underwent abdominal sacrocolpopexy alone. Likewise, in the Outcomes following Vaginal Prolapse Repair and Midurethral Sling (OPUS) trial, Wei et al. [19] found that a prophylactic midurethral sling inserted during prolapse surgery in continent women resulted in lower postoperative urinary incontinence rates. In a recently published meta-analysis, Baessler et al. [20] confirmed that a midurethral sling appears to be of benefit in women with POP and OSUI.

In contrast to these data, advocates of the two-step approach claim that combining POP repair with an anti-incontinence procedure might increase complication rates, including both obstructive voiding and storage symptoms [6,7,21]. These complications might be more pronounced with the Burch colposuspension rather than with the TVT procedure [22]. Nonetheless, in the CARE study, the addition of a Burch colposuspension did not increase the incidence of other lower urinary tract symptoms [17]. Likewise, in our current study, de novo voiding and storage symptoms were uncommon among patients who underwent concomitant prolapse repair and a TVT procedure. It should be stressed however, that long-term follow-up was restricted to only 74% of the study population. Advocates of the two-step approach also argue that while preoperative diagnosis of OSUI is quite common, actual postoperative de-novo SUI requiring an additional anti-incontinence surgery occurs in only 5.3–7.7% of patients [23,24]. These data underscore the importance of meticulous patient selection for concomitant POP repair and anti-incontinence procedures. Ideally, we would like to accurately identify patients who may benefit from a combined approach without significantly increasing the rates of de novo postoperative voiding or storage symptoms.

The correlation between the clinical and urodynamic assessment of SUI in patients with and without POP has been investigated with conflicting results. While patients with no prolapse exhibit a relatively good correlation between the clinical and urodynamic diagnosis of SUI [25], those with combined POP and SUI demonstrate a more complex picture, with only 25–30% of patients with clinical SUI showing urodynamic stress incontinence [5]. OSUI can be diagnosed preoperatively by either a pelvic examination with manual reduction of the prolapsed organs or via a multichannel urodynamic investi-

gation [5,8]. To date, data are inconclusive regarding the sensitivity and specificity of each of these diagnostic modalities regarding OSUI. Nonetheless, our results indicate that multi-channel urodynamic testing may indeed have superior detection rates for OSUI compared to a plain pelvic examination. This finding may be attributed to either the higher bladder filling volumes or to the utilization of vaginal pessaries during the urodynamic investigation. The former assumption is supported by the higher probability of detecting OSUI when the pelvic examination was performed with a full rather than with an empty bladder. Still, urodynamic investigation is costly and invasive and has been associated with high inter- and intra-observer variabilities [9]. Hence, the role of this modality in the preoperative diagnosis and management of OSUI in women with advanced POP has yet to be determined. Meanwhile, we suggest that if a urodynamic investigation is not performed preoperatively, a plain pelvic examination with a full bladder may still diagnose a large proportion of patients with OSUI, especially if performed while the prolapsed organs are reduced to alleviate urethral kinking.

LIMITATIONS

The main study limitations include its retrospective design and the lack of data regarding the outcomes of patients who were not diagnosed with OSUI preoperatively. Hence, the negative predictive value of both a plain pelvic examination and a multi-channel urodynamic investigation could not be calculated.

STRENGTHS

The study's main strengths are the comprehensive data available regarding both preoperative pelvic examination and multi-channel urodynamic testing for all study participants as well as preoperative and postoperative urinary and prolapse symptoms.

CONCLUSIONS

Multichannel urodynamic testing may be more sensitive than a plain pelvic examination in detecting OSUI. If the former is not performed, it is preferable that the pelvic examination is conducted with a full, rather than an empty, bladder to increase OSUI detection rates. Performing a midurethral sling surgery in patients diagnosed with OSUI was found to be associated with favorable outcome and low complication rates. Further research, preferably using a prospective design should focus on finding the optimal modality for the preoperative detection of OSUI. This attention may allow for tailoring an anti-incontinence procedure to selected patients who are prone to develop de novo SUI postoperatively rather than to all patients undergoing POP surgery. This personalized approach, which is also supported by a recent review by Cohn and co-authors [13], has the potential benefit of reducing both perioperative morbidity and the risk for developing de novo lower urinary tract symptoms postoperatively.

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Capsule

Adaptive immune responses to SARS-CoV-2 persist in the pharyngeal lymphoid tissue of children

Most studies of adaptive immunity to SARS-CoV-2 infection focus on peripheral blood, which may not fully reflect immune responses at the site of infection. Using samples from 110 children undergoing tonsillectomy and adenoidectomy during the COVID-19 pandemic, **Xu et al.** identified 24 samples with evidence of previous SARS-CoV-2 infection, including neutralizing antibodies in serum and SARS-CoV-2-specific germinal center and memory B cells in the tonsils and adenoids. Single-cell B cell receptor (BCR) sequencing indicated virus-specific BCRs were class-switched and somatically hypermutated, with overlapping clones in the two tissues. Expanded T

cell clonotypes were found in tonsils, adenoids, and blood post-COVID-19, some with CDR3 sequences identical to previously reported SARS-CoV-2-reactive T cell receptors (TCRs). Pharyngeal tissues from COVID-19-convalescent children showed persistent expansion of germinal center and antiviral lymphocyte populations associated with interferon (IFN)- γ -type responses, particularly in the adenoids, and viral RNA in both tissues. The results provide evidence for persistent tissue-specific immunity to SARS-CoV-2 in the upper respiratory tract of children after infection.

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Capsule

Lentiviral gene therapy for Artemis-deficient SCID

The DNA-repair enzyme Artemis is essential for rearrangement of T- and B-cell receptors. Mutations in *DCLRE1C*, which encodes Artemis, cause Artemis-deficient severe combined immunodeficiency (ART-SCID), which is poorly responsive to allogeneic hematopoietic-cell transplantation. **Cowen** and co-authors conducted a phase 1–2 clinical study of the transfusion of autologous CD34+ cells, transfected with a lentiviral vector containing *DCLRE1C*, in 10 infants with newly diagnosed ART-SCID. The authors followed them for a median of 31.2 months. Marrow harvest, busulfan conditioning, and lentiviral-transduced CD34+ cell infusion produced the expected grade 3 or 4 adverse events. All the procedures met prespecified criteria for feasibility at 42 days after infusion. Gene-marked T cells were detected at 6 to 16 weeks after infusion in all the patients. Five of 6 patients who were followed for at least 24 months had T-cell immune

reconstitution at a median of 12 months. The diversity of T-cell receptor β chains normalized by 6 to 12 months. Four patients who were followed for at least 24 months had sufficient B-cell numbers, IgM concentration, or IgM isohemagglutinin titers to permit discontinuation of IgG infusions. Three of these four patients had normal immunization responses, and the fourth has started immunizations. Vector insertion sites showed no evidence of clonal expansion. One patient who presented with cytomegalovirus infection received a second infusion of gene-corrected cells to achieve T-cell immunity sufficient for viral clearance. Autoimmune hemolytic anemia developed in four patients 4 to 11 months after infusion. This condition resolved after reconstitution of T-cell immunity. All 10 patients were healthy at the time of this report.

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