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A novel human cadaver model to investigate a retrourethral transobturator male sling procedure

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Purpose: To develop a cadaver model for the assessment of a male transobturator male sling (retrourethral transobturator sling [RTS], AdVance™; Boston Scientific, USA) to investigate its effect on a simulated abdominal and retrograde leak point pressures (ALPP, RLPP) and the urethral pressure profile (UPP).
Materials and Methods: Three fresh frozen human male cadaver specimens were obtained. A suprapubic tube was inserted into the bladder and connected to a digital manometer to measure bladder pressure. Manual suprapubic pressure was then applied to generate an increase in intraabdominal pressure and measure a simulated ALPP. Subsequent measurements of RLPP and UPP were recorded. All measurements were undertaken prior to and following insertion of a RTS.
Results: The placement of the RTS consistently increased the simulated ALPP for all three cadaver specimens when compared to baseline measures. No leaks occurred at simulated ALPP's of 170 cm H_2O for specimen 1, 160 cm H_2O for specimen 2, and 170 cm H_2O for specimen 3. There was minimal or no change in the RLPP's and UPP's following insertion of the RTS when compared to respective baseline.
Conclusions: A model using fresh unfixed cadavers that incorporates a simulated measurement of ALPP is feasible for male stress urinary incontinence surgical intervention investigations.

Keywords: Cadaver; Male; Suburethral slings; Urinary bladder; Urinary incontinence

INTRODUCTION

Male stress urinary incontinence (SUI) has a significant impact on all domains of quality of life and psychosocial wellbeing [1]. The burden of SUI also includes an economic impact encompassing a range of associated health care management costs and lost work productivity [2]. The overall burden of SUI is expected to increase due to an aging population with an increased life expectancy [3].

SUI is characterized by the involuntary loss of urine following an increase in intraabdominal pressure that exceeds the abdominal or valsalva leak point pressure (ALPP, VLPP). The etiology and pathophysiology of SUI in males is multifactorial and our understanding remains incomplete.

SUI in males following radical prostatectomy (RP) has been attributed in part to the changes in urethral support and urethral sphincter insufficiency [4]. These proposed changes in the position and function of the continence mechanism has led to the development of a range of devices for the surgical management of SUI symptoms [5].

The insertion of retrourethral transobturator sling (RTS, AdVance™; Boston Scientific, Marlborough, MA, USA) devices has been used globally for the management of SUI in males [6,7]. The polypropylene monofilament mesh device is inserted retrourethrally beneath the proximal aspect of the urethral bulb, passing bilaterally through the obturator fossa [8]. Cadaver models have been important for the development of sling devices and to evaluate the effectiveness of these devices for the management of SUI. Increasingly cadaver models are also being accessed for the delivery of open urological surgical training programs to facilitate technical surgical skill set acquisition and for competency assessment [9]. These programs incorporate high fidelity cadaver simulation teaching scenarios, to improve task performance prior to real life surgery [10,11].

Previous cadaver models that have reported the effects of the placement of RTS sling devices have used two standard urodynamic measurements, retrograde leak point pressure (RLPP) and urethral pressure profilometry (UPP). Since RTS devices are designed and used to manage the involuntary loss of urine with increases in intraabdominal pressure, developing a complete cadaver model that incorporates the measurement of a simulated ALPP is warranted. In this investigation we report on the development of a cadaver model used to evaluate the mechanism of action of a RTS device via the study of a simulated ALPP, RLPP and UPP.

MATERIALS AND METHODS

1. Cadaver preparation

Three de-identified, anonymous fresh-frozen unembalmed adult human male cadaveric hemi-pelvis specimens were obtained through an institutional Willed Body Program. Each cadaver had a fully intact lower genitourinary system with no history of lower urinary pathology or surgery. Written informed consent for post-mortem scientific use existed for all three cadavers and all the experimental procedures. Each cadaver was frozen within 4 days of procurement and stored at -20℃ in a freezer. The three cadavers were thawed at ambient temperature prior to the commencement of the experimental procedures. A thorough examination of each cadaver was undertaken by two experienced urological surgeons (W.I.J., J.S.S.) prior to and

during the experimental procedures to confirm that there were no lower urinary tract macroscopic changes or oncologic pelvic disease in all three specimens. The normal tissue handling properties for each cadaver were also checked during the experimental procedures by the two urological surgeons (W.I.J., J.S.S.) to confirm that the completeness of the thawing of each cadaver had been achieved.

All the experimental procedures were completed in a fully equipped surgical environment and complied with the principles outlined in the Declaration of Helsinki. Each cadaver was placed in the lithotomy position and a low level midline incision was made to identify the bladder. An 18 French (F) catheter was introduced into the bladder via a cystotomy. Two purse-string sutures were used to secure the suprapubic tube and to ensure that no leakage of fluid occurred around the cystotomy. The open suprapubic tube was connected via a three-way stopcock to a digital manometer (Omega Engineering, Norwalk, CT, USA) and an infusion pump (Fig. 1). The bladder was then filled with 200 mL of saline, which allowed for palpation directly above the pubic symphysis.

1) ALPP

Manual pressure was applied directly to the exposed bladder by a member of the investigating team for the determination of a simulated ALPP (Fig. 2). The simulated ALPP, measured by a second investigator, was equal to the bladder pressure at which the first sign that urine was observed at the urethral meatus. At the completion of the simulated ALPP measurements the bladder was then emptied.
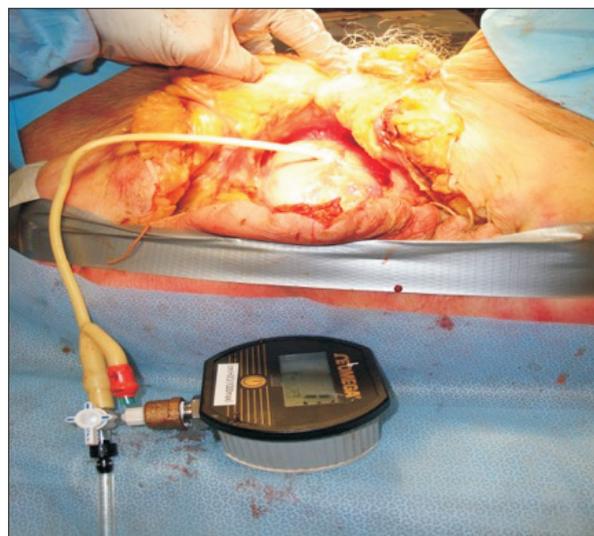

Fig. 1. Cadaveric model with an open suprapubic tube connected to a digital manometer (Omega Engineering).

Fig. 2. Gradual increase in manual compression directly over the exposed bladder that resulted in an increase in intravesical pressure was used to measure the abdominal leak point pressure (ALPP).

2) RLPP

RLPP was measured at the completion of the simulated ALPP measurement procedures. A 16 F catheter was placed inside the fossa navicularis and connected to a calibrated digital manometer and a fluid column. Sphincterotomy with retrograde perfusion was used to measure urethral resistance via the RLPP procedures previously described [12].

3) UPP

An air-charged catheter and automatic puller device was connected to a commercially available urodynamic machine for the measurement of UPP [13].

4) RTS placement procedures

Each cadaver underwent insertion and placement of the RTS (AdVance™) by an experienced urologist as described by Rehder and Gozzi [8]. The urethra was fully mobile prior to RTS insertion. Simulated ALPP, RLPP and UPP measurements were repeated after RTS placement. At least two separate recordings of the simulated ALPP, RLPP and UPP were made for each cadaver before and after placement of the RTS.

2. Statistical analysis

Data were described as the mean for each cadaver specimen and summarized as mean±standard deviation using Excel (Microsoft).

Table 1. The ALPP and RLPP for the three cadaver specimens prior to and following RTS insertion

Cadaver	Native ALPP (cm H$_2$O)	Post RTS ALPP (cm H$_2$O)	Native RLPP (cm H$_2$O)	Post RTS RLPP (cm H$_2$O)
1	30.5	>170	25.2	21.0
2	22.5	>160	14.5	10.5
3	21.0	>170	11.0	12.5
Mean±SD	24.7±5.1		16.9±7.4	14.7±5.6

ALPP, abdominal leak point pressure; RLPP, retrograde leak point pressure; RTS, retrourethral transobturator sling; SD, standard deviation.

RESULTS

The three fresh-frozen human cadavers were Caucasian males with an age at time of death of 63, 76, and 79 years, weighing 68 kg, 61 kg, and 82 kg, respectively. The results for each cadaver for the simulated ALPP and RLPP prior to and following RTS insertion are presented in Table 1. The baseline simulated ALPP ranged between 21.0 cm H$_2$O and 30.5 cm H$_2$O. The corresponding baseline RLPP's were more variable ranging between 11.0 cm H$_2$O and 25.2 cm H$_2$O. The placement of the RTS consistently resulted in substantial increases in the simulated ALPP for all three cadaver specimens when compared to the baseline measurements. There were no leaks observed at pressures of 170 cm H$_2$O for specimen 1 and 3 and 160 cm H$_2$O for specimen 2, which were the highest pressures the investigators were able to generate. The placement of the RTS resulted in a small mean decrease in the RLPP (2.2±3.2 cm H$_2$O) compared to the native RLPP baseline measures in all three cadavers with a decrease in RLPP in specimen 1 and 2 and an increase in RLPP in specimen 3. In specimens 1 and 2 there was no change in the UPP from baseline after the RTS placement. There was a short area of compression to 30 cm of H$_2$O above baseline found in specimen 3.

DISCUSSION

Human cadaver studies provide an important model for the development and evaluation of surgical procedures that are designed for the management of SUI in males [8,14,15]. Increasingly cadaver models are also incorporated into urological surgical training programs for open surgical skill set acquisition and assessment [9], to improve task performance in preparation for real life clinical situations [11]. To our knowledge there are a limited number of cadaver studies that have evaluated the RTS mechanism of action [8,14]. In our investigation we were able to access fresh-

frozen, unembalmed human cadaver specimens that were completely thawed prior to the experimental procedures which allowed for the flexibility of soft tissue and vascular structures to be maintained. The two experienced urologists did not experience any changes to the normal tissue handling properties for each cadaver, in particular around bulbar urethra for the placement of the RTS. We also did not identify any obvious change in the resistance to the suprapubic manual pressure that was applied during the simulated ALPP measurement procedures or during the insertion of the 16F catheter for the RLPP measurement procedures.

Fresh-frozen unembalmed cadavers offer a useful training model with precise anatomical structures and more 'lifelike' tissue handling properties with visual and tactile feedback. In our cadaver model, all three specimens had undergone a complete thawing protocol and demonstrated a native baseline simulated ALPP. The baseline simulated ALPP for all three cadaver specimens was comparable to previously reported VLPP measurements in males following RP prior to placement of the RTS [16]. VLPP and ALPP are both defined as the lowest pressure that is measured by bladder or abdominal pressure at which the urethral resistance is overcome and leakage is observed in the absence of a detrusor contraction [17,18]. Clinically, a sudden or sustained increase in pressure is achieved via a voluntary cough, laughing, sneezing or valsalva manoeuvre for example when lifting heavy weighted objects. Clinically, intraabdominal pressure is usually estimated indirectly via rectal manometry [19]. In the present investigation, our cadaver model allows for the direct measurement of intravesical pressure via a novel method, allowing for the determination of a simulated ALPP.

The insertion of the RTS sling acted preferentially during the simulated ALPP testing procedures, resulting in a substantial increase in the simulated ALPP with minimal or no changes in RLPP and UPP when compared to respective baseline measures. This preferential action of the RTS is consistent with previous investigations where a significant increase in VLPP has been reported in males following RTS insertion [16,20,21]. Furthermore, clinical studies involving male suburethral slings have demonstrated no increase in voiding pressure or the presence of bladder outlet obstruction, suggesting that slings do no function via compressive mechanism [16,22]. Our investigation suggests that in a cadaver model the RTS does not augment continence by sustained urethral compression, demonstrated by little change in UPP, but rather by increasing ALPP's when there is an increase in intra-abdominal pressure.

The RTS is a non-circumferential device that when correctly inserted allows males to maintain the ability void spontaneously. As a suspension sling device, the RTS is positioned 8 to 10 mm suburethrally with no direct pressure on the urethral wall or lumen [7,23]. When the RTS is positioned correctly and continence management is achieved, indentation at the inferior margin of the urethral bulb occurs >10 mm distal to the penile bulb, causing proximal indentation of the corpus spongiosum [24]. In our cadaver specimens the minimal or absent changes in baseline RLPP and UPP measurements following RTS insertion, indicates that over-tensioning of the sling did not occur. Since RLPP has been reported as an accurate method to measure urethral resistance [12,25,26], a sustained increase in static outflow obstruction due to excessive urethral lumen compression following RTS insertion did not occur in our cadaver model.

Physical repositioning and dorsal support of the distal portion of the membranous urethra and the urethral sphincter complex has also been reported following RTS insertion [7,8,27]. Retraction of the mesh arms causes elevation of the bulbar urethra ventrally and cranially, 2 to 4 cm into the pelvic outlet [8,21,24,28]. Since the device is a fixed non-elastic structure, opposition to, or cushioning of the caudal descent of the membranous urethra and the distal sphincteric urethral complex occurs via the corpus spongiosum tissue, temporarily during periods where there is an increase in intraabdominal pressure [23]. It has been proposed that this dynamic bulbar compression temporarily increases the longitudinal length of the zone of urethral luminal co-aptation within the membranous urethra [27]. This dynamic and transient increase in urethral pressure ultimately facilitates a temporary period of outflow obstruction. The cadaver model presented in this investigation provides provisional support for the dynamic urethral compression mechanism of action of the RTS.

We have considered a number of limitations in this investigation. Only three cadavers positioned in the lithotomy position were accessed which limits the generalizability of the results. However, despite the small sample size it is encouraging that we have consistent findings for the three cadaver specimens. The cadaver specimens that were used in our investigation also had no history of RP. The majority of RTS placements occur in males following RP with a minority of cases following holmium laser enucleation, transurethral resection or irradiation of the prostate [29,30]. An alteration in the course of the sling could potentially occur in our non-RP cadaver model and may be a potential source of bias. Despite the thorough examination of each

cadaver that was undertaken by the two experienced urological surgeons (W.I.J., J.S.S.) prior to and during the experimental procedures, the compliance and suppleness of tissue may be different to living humans. The simulated ALPP that was used may also be different to an ALPP measured in living humans. Future cadaver models could also include the use of a rectal pressure measurement device to further validate the increase in intravesical pressure during the simulated ALPP procedures. Future studies could also develop the cadaver model reported in this investigation to include the use of specimens following RP.

CONCLUSIONS

A fresh-frozen unembalmed human cadaver model incorporating the measurement of a simulated ALPP is feasible for future studies investigating surgical interventions of SUI. Our preliminary findings in a small sample of human fresh-frozen male cadavers confirms our understanding of the mechanism of action of the AdVance™ RTS sling which functions to increase the ALPP when there is an increase in intra-abdominal pressure with no change in RLPP.

CONFLICTS OF INTEREST

All authors declare that no remuneration or agreement limited in any way their ability to acquire, interpret or publish this data. Control of the primary dataset has at all times been held by the members of this investigating team. Dr William I. Jaffe declares current and Dr Jaspreet S. Sandhu declare previous lectures, consultancy work and participation in research trials for American Medical Systems, Inc. The cadaver specimens for this investigation were supplied by American Medical Systems, Inc. Minnesota, USA.

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