Long term follow up of bovine dermis pubovaginal slings

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Introduction: *Women at "high risk" for sling failure (advanced age, failed previous anti-incontinence surgery, intrinsic sphincter deficiency, and absence of urethral hypermobility) underwent acellular bovine dermis slings. We evaluate long term outcomes and complications with this material.*

Materials and methods: *We retrospectively identified 41 women who completed 36 month postoperative follow up. Preoperative evaluation included pelvic exam, SEAPI classification, and validated quality of life (QoL) questionnaires. Stress urinary incontinence (SUI) cure equaled SEAPI (S) subset = 0 and negative cough-stress test. Perioperative data was abstracted from the hospital and office chart.*

Results: *The SUI cure rate was 80.5%. Most SUI recurrences occurred within the first 12 months of follow up. Perioperative complications and rates of reoperation for recurrent SUI were low. There was a postoperative improvement in mean SEAPI scores and significant improvement in all QoL indices over preoperative baseline values.*

Conclusions: *At long term follow up, bovine dermis continues to be a durable biologic option for a population at "high risk" for surgical failure after sling surgery. SUI-specific clinical outcomes remain stable, while rates of complications continue to be low. Improvement in QoL indices persists with long term follow up.*

Key Words: female, grafts, outcomes, slings, stress urinary incontinence

Introduction

A suburethral sling constructed from autologous tissue is arguably the "gold standard" for surgical correction of female stress urinary incontinence (SUI).[1] However, in the past decade, there has been a distinct shift toward less-invasive surgical options. Recent U.S. Food and Drug Administration (FDA) publications estimate that approximately 260,000 women underwent surgery to repair SUI in 2010, and more than 80% of these procedures were performed transvaginally with permanent synthetic mesh.[2] While the additional morbidity of graft harvest has been a primary factor leading to the autologous sling being supplanted in popularity by synthetic midurethral slings (MUS), the latter procedures are not without substantial risks. Like all synthetic materials, MUS may be associated with the risk of erosion and extrusion, and inadvertent neurovascular or viscus damage due to trocar passage has also been reported.[3] Furthermore, recent FDA warnings regarding complications incurred after implantation of permanent synthetic mesh for pelvic organ prolapse (POP) and SUI have only served to raise additional questions regarding the long-term implications of using these materials.[4]

Owing to these concerns, there has been a recently renewed interest in biologic materials for SUI and POP. Theoretically, biologic substitutes for SUI have desirable properties of both autologous tissue and synthetic MUS: the biocompatibility of native tissue and less-invasive placement of synthetic grafts. To date, however, medium to long term outcomes with cadaveric allografts and xenografts have been inconsistent.[5-10] Thus, while appealing in theory, an effective and durable biologic substitute for autologous tissue has yet to be introduced.

Acellular, non-cross-linked, fetal bovine dermis is a relatively novel biologic substitute available for sling construction. We have previously reported on medium term follow up of women at "high risk" for surgical failure who underwent bovine dermis slings.[11] At a minimum follow up of 12 months, women undergoing bovine dermis slings had SUI-specific and global cure

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rates similar to women undergoing autologous slings. Improvements in quality of life (QoL) indices were likewise similar. Our objective is to report the long term outcomes of the bovine dermis sling.

Materials and methods

After obtaining Institutional Review Board approval, we conducted a retrospective chart review of all women who underwent a pubovaginal sling with bovine dermis (Xenform Matrix, Boston Scientific, Natick, MA, USA). From 2005 to 2007, women deemed "high-risk" for SUI recurrence and sling failure underwent bovine dermis bladder neck sling. For the purpose of our analysis, "high-risk" factors were defined as: advanced age, failure of previous anti-incontinence surgery, intrinsic sphincter deficiency (ISD; defined by a valsalva leak point pressure (VLPP) ≤ 60 cm H_2O), and absence of urethral hypermobility (hypermobility defined as visually-assessed urethral angle deviation ≤ 30 degrees with straining). All women had either SUI alone or mixed urinary incontinence with a predominant and bothersome stress component. Women with "occult" SUI (detected solely with prolapse reduction) were included in the study. Women with a neurogenic cause for her SUI were excluded from analysis.

Preoperatively, all women underwent physical examination with cough-stress testing (CST), post-void residual (PVR), voiding diary, multichannel urodynamics, validated QoL questionnaires {Incontinence Impact Questionnaire (SF-IIQ-7) and Urogenital Distress Inventory (UDI-6)}. Additionally, the QoL due to urinary problems was determined using a Visual Analog Score (VAS) of 1 to 10. Women were asked to respond to the following question "If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?" and rate their answer from 1 (miserable) to 10 (very happy). Standardized postoperative follow-up at 6 weeks, 6 months, and annually thereafter included physical exam with CST, PVR, and QoL questionnaires. CST was performed in the comfortable lithotomy position at ≥ ½ functional bladder capacity (obtained from voiding diary). Urodynamics were not routinely performed postoperatively. Demographic data was obtained from the office chart and perioperative data was abstracted from the hospital chart.

Informed consent was obtained prior to each procedure. Concomitant prolapse or additional surgery was performed prior to sling placement. Our technique for bovine dermis slings has been previously described.[11]

We employed the subjective subset of the SEAPI score in our definition of success.[12] Cure of SUI was considered when the woman had no subjective complaints of SUI (SEAPI (S) = 0) and a negative CST. The remaining SEAPI subscores were evaluated before and after surgery to assess the impact of the sling on emptying, pad use, and urgency urinary incontinence (UUI). All statistical analyses were

TABLE 1. **Preoperative demographic and urodynamic data (means ± standard deviation)**

N	41
Age (years)	67.6 ± 9.4
Race (% Caucasian)	95.1%
BMI	28.0 ± 5.1
Gravity	3.3 ± 2.3
Parity	2.9 ± 1.6
Initial presentation	
SUI only	9.8%
MUI	63.4%
Occult SUI	
Without UUI	9.8%
With UUI	14.6%
Pads/day	1.8 ± 2.0
Baden-Walker grade	
Anterior	2.2 ± 1.3
Posterior	1.2 ± 0.9
Apical	1.9 ± 1.4
Urodynamic indices	
VLPP (cm H2O)	66.8 ± 21.2
% with DO	4.9%
Preoperative SEAPI (total)	7.9 ± 3.4
Preoperative QoL Indices	
IIQ	12.5 ± 6.5
UDI-6	9.7 ± 4.8
VAS	2.0 ± 1.5
Study inclusion criterion	
Age > 70	48.8%
Failed previous anti-incontinence surgery	48.8%
ISD (VLPP ≤ 60 cm H_2O)	43.9%
% women with > 1 criterion	39%

N = number of women; BMI = body-mass index; SUI = stress urinary incontinence; MUI = mixed urinary incontinence; VLPP = valsalva leak point pressure; DO = detrusor overactivity; QoL = quality of life; IIQ = Incontinence Impact Questionnaire (SF-7); UDI-6 = Urogenital Distress Inventory; VAS = Visual Analog Score; ISD = intrinsic sphincter deficiency.

TABLE 2. **History of previous pelvic surgery**

None	12.2%
Hysterectomy	85.4%
Colporrhaphy	
Anterior (includes colporrhaphy with interposition graft)	29.3%
Posterior	22%
Apical prolapse	
Sacrospinous ligament suspension	2.4%
Abdominal sacral colpopexy	4.9%
Incontinence procedure	
Suspension (transvaginal, transabdominal)	41.5%
Bladder neck sling (autologous, allograft, xenograft)	19.5%
Midurethral sling (retropubic and transobturator polypropylene)	4.9%
Bulking agent	4.9%
% > 1 incontinence procedure	12.2%

conducted using MedCalc 9.3.2 software (Belgium), $p < 0.05$. To determine if a given ratio or interval variable was normally distributed, its skewness and kurtosis confidence intervals were examined. Variables that passed this test of normality were analyzed using the paired t-test (equal variance assumption, two-tailed, alpha = 0.05). If a variable failed the test, the Wilcoxon sign rank test (two-tailed, alpha = 0.05) was used.

Results

From January 2005 to January 2007, 63 women underwent pubovaginal sling surgery with bovine dermis, with 41 (65%) completing at least 36 months of follow up and making up the current study population. The 37 women from the original report were part of the current analysis. Preoperative demographics, urodynamic findings, and QoL indices are summarized in Table 1. Women who did not attain 36 month follow up or were lost to follow up did not differ significantly in demographic characteristics. The history of previous pelvic surgery is summarized in Table 2. The majority of women underwent concomitant surgery at the time of sling, with only 7.3% undergoing sling alone. The incidence of concomitant surgical procedures was: hysterectomy (9.8%), anterior colporrhaphy (51.2%), posterior colporrhaphy (24.4%), vaginal vault suspension (24.4%), abdominal sacral colpopexy (22%), and colpocleisis (14.6%). Two women underwent exploratory laparotomy and ventral herniorrhaphy.

At a mean follow up period of 47.6 ± 7.4 months, 33 women (80.5%) achieved a cure of their SUI. Six of eight SUI recurrences were observed by the 12 month follow up visit. Thirty-eight women (92.7%) said they would undergo surgery again, while 40 (97.6%) would recommend the surgery to a friend. There was a postoperative improvement in all QoL indices, Table 3, with the difference in the QoL indices reaching statistical significance ($p < 0.05$). Sling surgery with bovine dermis was not associated with a negative impact on postoperative emptying and UUI, Table 4. There was also an improvement in the percentage of women who reported no postoperative emptying symptoms, no pad use, and no UUI compared with preoperative baseline status.

Postoperative surgical complications, hospital readmissions, and reoperations were infrequent, with 73.2% of patients having an uneventful perioperative and postoperative course. There was one intraoperative cystotomy that was recognized and primarily repaired, with the patient having an uneventful recovery after indwelling urethral catheter drainage. No woman underwent sling incision or revision for urinary retention, extrusion, or infection. One woman underwent an autologous rectus fascia (ARF) sling after developing recurrent SUI and three women underwent

TABLE 3. **Change between mean preoperative and postoperative quality of life indices**

Measure	Preoperative	Postoperative	p
IIQ	12.5 ± 6.5	2.2 ± 4.4	< 0.01
UDI-6	9.7 ± 4.8	2.4 ± 3.2	< 0.05
VAS	2.0 ± 1.5	8.7 ± 1.9	< 0.05

IIQ = Incontinence Impact Questionnaire (SF-6); UDI-6 = Urogenital Distress Inventory; VAS = Visual Analog Score.

TABLE 4. **Changes in pad use, urinary storage, and emptying symptoms after sling surgery (via SEAPI subjective subset)**

Symptom	% reporting no preop problems	Change in symptom after sling surgery					% reporting no postop problems
		Resolution	Improvement	Unchanged	Worsened	De novo	
Emptying	34.1%	51.2%	4.9%	39.0%	2.4%	2.4%	82.9%
Pad use	39.0%	34.1%	12.2%	48.8%	2.4%	2.4%	70.7%
Urge incontinence	19.5%	39.0%	19.5%	34.1%	4.9%	2.4%	56.1%

periurethral bulking. One woman developed partial vaginal mesh extrusion from a concomitant POP repair and required operative debridement. Using the modified Clavien criteria,[13] we observed two Grade I complications (iron supplements for anemia, diuretic treatment for congestive heart failure exacerbation) and three Grade II complications (lower urinary tract infection requiring antibiotic treatment). No patient required transfusion of blood products.

Discussion

A biologic graft incorporates into the host via a process called remodeling. After implantation, the human body generates an initial immune response that consists of local vasodilation, followed by an influx of neutrophils to the site of graft implantation and activation of the complement cascade.[3] Type III collagen is secreted by immature fibroblasts and there is an influx of proteins and fibrinogen to the implant site. Within several days, the neutrophil response begins to subside and macrophages enter the wound to begin phagocytosing dead cells. Neovascularization begins and replacement of Type III collagen with a stronger, less elastic Type I collagen allows the wound to regain some of its tensile strength. Once host tissue infiltrates the graft, a transformation of function should occur and the graft begins to function like host tissue. Ultimately, it is the inability to remodel and retain strength that has deterred the routine use of biologics in pelvic reconstruction.

Surgical outcomes with the two most common biologic grafts, cadaveric fascia lata and porcine dermis, have been unpredictable at best. Fitzgerald et al cited a 20% failure rate within 3 months of surgery after cadaveric allograft sling, and graft material was frequently absent or difficult to identify during reoperations.[7] Outcomes after porcine dermis sling have also been conflicting. Abdel-Fattah et al reported that outcomes after porcine dermis placed at the midurethra approximated those after synthetic MUS at 3 years of follow up,[6] whereas Giri et al found that porcine dermis had a higher failure rate compared to ARF in sling construction.[14] Much of the unpredictability has been attributed to the steps during processing of biologic material, whether it is freezing for cadaveric allografts or cross-linking for xenografts. In previous studies of porcine dermis cross-linked with diisocyanate cell ingrowth has been limited to the graft surface.[9,10,15] It is the cross-linking that appears to be associated with vaginal sling extrusion.

At a minimum of 36 months of follow up in our study, bovine dermis has been associated with durable SUI-specific cure rates and high rates of satisfaction. The majority of the women who develop recurrent SUI do so within the first year of follow up, and it is unclear to us whether this is due to the material, patient factor, or a technical aspect of the procedure. Surgery for these complex patients is safe and the complication rates, including those by Clavien classification, were low. Likewise, sling surgery with bovine dermis did not negatively impact postoperative emptying or UUI.

As this tissue is not frozen or cross-linked during processing, bovine dermis may integrate better into host tissue than other biologic grafts such as cadaveric allografts and porcine dermis. We did not observe any vaginal extrusion or infection; however, we have little additional information regarding its long term integration and biocompatibility profile. In our initial assessment, we noted myxoid degeneration of the bovine graft in one patient undergoing repeat sling.[11] While this finding suggested the possibility of early graft failure, no definitive conclusions can be drawn as no other women have, to date, undergone additional anti-incontinence surgery.

Despite its use in plastic surgery for several years, there is little in the literature regarding bovine dermis for any pelvic floor reconstruction indications. Goldstein et al prospectively evaluated this material in 45 women at four centers for reconstruction of an anterior or posterior compartment defect in women with high-grade POP.[16] The authors found that 74% of their patients maintained stage 0 or 1 in the repaired compartments at 12 months of follow up. Likewise, scores on validated QoL questionnaires continued to demonstrate a sustained

improvement at 12 months. No graft-related erosions were reported. Grimes et al used bovine dermis in four of 69 women who underwent posterior compartment repair augmented with a biologic graft and found that, overall, biologic graft augmentation did not appear to improve anatomic or functional outcomes.[17] The authors did not subcategorize their outcomes by biologic material. An additional study cited good long term outcomes after bovine dermis was used for reconstruction of a ureteral stricture.[18]

Along with the novel report of long term durability for a biologic sling substitute the current study has several additional strengths. Our definition of cure is rigorous and employs both subjective and objective criteria, with all women undergoing standardized, long term follow up. Validated QoL indices are used and the reporting of complications is comprehensive. There are also several limitations to interpreting results of this study. First, as with our initial medium term outcomes, this study is a retrospective review of cases at a single institution. Hence, surgical outcomes may not necessarily be extrapolated to other institutions. Second, this most recent study also does not compare outcomes after bovine dermis to ARF, considered by many to be the graft of choice for complex SUI patients. While we continued to use ARF at sister institutions that do not have access to bovine dermis, our analysis revealed that the populations in the two institutions were quite disparate and did not allow for proper comparison. Third, it can certainly be argued that our criteria for a "high risk" patient were arbitrarily chosen. Finally, the failure to follow up rate (34.9%) may have an impact on interpretation of results. We acknowledge that the loss of a significant percentage of our original population may skew the SUI-specific cure rates significantly, especially if an "intent-to-treat" analysis is considered. However, there is currently no consensus regarding whether patients fail to follow up because they are pleased or disappointed with their outcomes, and several authors have shown that success rates for patients lost to follow up were similar to those who maintained routine follow up.[19,20]

Conclusions

At long term follow up, bovine dermis continues to be a durable sling material in a population of women at "high risk" for surgical failure. SUI-specific clinical outcomes remain stable at a minimum of 36 months and rates of complications continue to be low. Poor vaginal healing and extrusion have not been observed. Acellular bovine dermis should be considered as a viable material in the complex population. □

References

1. Appell RA, Dmochowski RR, Blaivas JM et al. Guideline for the Surgical Management of Female Stress Urinary Incontinence: 2009 Update; Female Stress Urinary Incontinence Guideline Update Panel: 2009 American Urological Association, Inc. 2012 Revised. American Urological Association Education & Research, Inc.
2. Wein AJ. Voiding function and dysfunction, bladder physiology and pharmacology, and female urology. *J Urol* 2011;186(6): 2328-2330.
3. Gomelsky A, Dmochowski RR. Biocompatibility assessment of synthetic sling materials for female stress urinary incontinence. *J Urol* 2007;178(4 Pt 1):1171-1181.
4. http://www.fda.gov/MedicalDevices/Safety/ Alertsand Notices/ucm262435.htm.
5. Nicholson SC, Brown AD. The long-term success of abdominovaginal sling operations for genuine stress incontinence and a cystocele: A questionnaire-based study. *J Obstet Gynaecol* 2001; 21(2):162-165.
6. Abdel-Fattah M, Barrington JW, Arunkalaivanan AS. Pelvicol™ pubovaginal sling versus tension-free vaginal tape for treatment of urodynamic stress incontinence: a prospective randomized three-year follow-up study. *Eur Urol* 2004;46(5):629-635.
7. Fitzgerald MP, Mollenhauer J, Brubaker L. Failure of allograft suburethral slings. *BJU Int* 1999;84(7):785-788.
8. O'Reilly KJ, Govier FE. Intermediate term failure of pubovaginal slings using cadaveric fascia lata: a case series. *J Urol* 2002;167(3): 1356-1358.
9. Cole E, Gomelsky A, Dmochowski RR. Encapsulation of a porcine dermis pubovaginal sling. *J Urol* 2003;170(5):1950.
10. Gomelsky A, Haverkorn RM, Simoneaux WJ, Bilello S, Kubricht WS 3rd. Incidence and management of vaginal extrusion of acellular porcine dermis after incontinence and prolapse surgery. *Int Urogynecol J Pelvic Floor Dysfunct* 2007;18(11):1337-1341.
11. Wilson CM, Williams BJ, Bilello S, Gomelsky A. Bovine dermis: a novel biologic substitute for autologous tissue in sling surgery. *Int Urogynecol J Pelvic Floor Dysfunct* 2008;19(12):1671-1676.
12. Raz S, Erickson DR. SEAPI QMM Incontinence Classification System. *Neurourol Urodyn* 1992;11(3):187-199.
13. Clavien PA, Sanabria JR, Strasberg SM. Proposed classification of complications of surgery with examples of utility in cholecystectomy. *Surgery* 1992;111(5):518-526.
14. Giri SK, Hickey JP, Sil D et al. The long-term results of pubovaginal sling surgery using acellular cross-linked porcine dermis in the treatment of urodynamic stress incontinence. *J Urol* 2006;175(5):1788-1792.
15. Gandhi S, Kubba LM, Abramov Y et al. Histopathologic changes of porcine dermis xenografts for transvaginal suburethral slings. *Am J Obstet Gynecol* 2005;192(5):1643-1648.
16. Goldstein HB, Maccarone J, Naughton MJ, Aguirre OA, Patel RC. A multicenter prospective trial evaluating fetal bovine dermal graft (Xenform® Matrix) for pelvic reconstructive surgery. *BMC Urol* 2010;10:21.
17. Grimes CL, Tan-Kim J, Whitcomb EL, Lukacz ES, Menefee SA. Long-term outcomes after native tissue vs. biological graft-augmented repair in the posterior compartment. *Int Urogynecol J* 2012;23(5):597-604.
18. Koziak A, Kania P, Marcheluk A, Dmowski T, Szcześniewski R, Dorobek A. Reconstruction of long ureteral obstructions using acellular collagen membranes. *Ann Transplant* 2004;9(4):18-20.
19. Ballert KN, Rose AE, Biggs GY, Rosenblum N, Nitti VW. Outcomes of patients lost to follow up after mid urethral synthetic slings – successes or failures? *J Urol* 2010;183(4):1455-1458.
20. Stav K, Dwyer PL, Rosamilia A, Lee J. Long-term outcomes of patients who failed to attend following midurethral sling surgery – A comparative study and analysis of risk factors for non-attendance. *Aust N Z J Obstet Gynaecol* 2010;50(2):173-178.