Pelvic Organ Prolapse Management in Female Kidney Transplant Recipients

M. Raschid Hoda,* Sigrid Wagner, Francesco Greco, Hans Heynemann and Paolo Fornara

From the Clinic for Urology and Kidney Transplantation Center, University Medical School of Halle/Wittenberg, Halle (Saale), Germany

Abbreviations and Acronyms

POP = pelvic organ prolapse

POP-Q = POP quantitation

Submitted for publication January 17, 2010.

* Correspondence: Clinic for Urology and Kidney Transplantation Center, University Medical School of Halle/Wittenberg, Ernst-Grube-Strasse 40, 06120, Halle (Saale), Germany (telephone: +49-345-5572327; FAX: +49-345-5574692; e-mail: rhoda@ucsd.edu).

Purpose: Pelvic organ prolapse in female postmenopausal kidney transplant recipients may be complicated by adverse events affecting graft function. We describe our experience with pelvic reconstructive surgery in renal transplant recipients.

Materials and Methods: Pelvic reconstructive surgery was done in 16 female renal transplant recipients with pelvic organ prolapse with or without stress urinary incontinence. Intraoperative and postoperative data were recorded prospectively, including medical and surgical history, pelvic organ prolapse quantification measurement, 24-hour pad count, quality of life measurements and graft outcome. Patients were followed up to 12 months.

Results: Mean ± SD age at surgery was 58.3 ± 7.7 years (range 50 to 66). Mean time to renal transplantation was 54.2 ± 15.1 months (range 38 to 123). A total of 12 anterior and 4 combined anterior/posterior colporrhaphies were done. A concomitant suburethral single incision transobturator sling procedure was performed in 8 women. We noted no bladder or rectal injury, bleeding necessitating transfusion or infection. Pelvic floor testing at 12-month followup showed stage I vaginal wall prolapse in only 4 patients (25%). No patient had evidence of de novo incontinence, synthetic sling infection, erosion or rejection. All women reported improved quality of life on the SF-36™ questionnaire. Renal graft function remained stable in all patients.

Conclusions: Pelvic reconstructive surgery is feasible for pelvic organ prolapse in patients with a kidney allograft on immunosuppression. However, concern about impaired graft function, infection and wound healing remains important.

Key Words: kidney, kidney transplantation, prolapse, suburethral slings, female

ADVANCES in immunosuppressive therapy in the last 2 decades have led to substantial improvement in graft and patient survival after renal transplantation. Pelvic floor disorders, including urinary incontinence, fecal incontinence and POP, affect a substantial proportion of women worldwide and increase with age.[1] Recent data from the 2005 to 2006 National Health and Nutrition Examination Survey show that approximately 24% of women have symptoms of at least 1 pelvic floor disorder.[2] This portion increased with age, in that 39% of women 69 to 79 years old and 50% of those 80 years old or older had at least 1 disorder. Since older women are increasingly considered for renal transplantation and women are living longer with a functional allograft, urologists and gynecologists trained in pelvic reconstruction will

0022-5347/10/1843-1064/0
THE JOURNAL OF UROLOGY®

Vol. 184, 1064-1068, September 2010
Printed in U.S.A.
DOI:10.1016/j.juro.2010.05.030

encounter more renal transplant recipients with pelvic organ disorders.

Despite the pressing need for data on surgical management for POP and its outcome in kidney transplant recipients there is a relative paucity of such information in the literature, perhaps because immunosuppressed patients and patients with end stage renal disease are often specifically excluded from such clinical trials. A systematic search of the English and German language MEDLINE® literature from 1966 to January 2010 using the search terms renal transplantation, surgery and incontinence revealed only 3 published case reports of pelvic reconstructive surgery and/or a suburethral sling procedure in renal transplant recipients for a total of 7 cases.[3–5] However, when treating transplant patients with pelvic organ disorders, special caution should be given in regard to the unique medical situation of this patient population, including immunosuppression issues. We present our experience with renal transplant recipients with pelvic organ disorders who underwent transvaginal prolapse and sling surgery.

MATERIALS AND METHODS

A total of 16 women with POP were scheduled for vaginal colporrhaphy. Preoperatively all women were evaluated by general medical and sexual history, physical examination with gynecological examination, 24-hour pad count, videourodynamics and cystoscopy. All patients were examined while in the dorsal lithotomy position. We quantitatively assessed the degree of POP using the POP-Q staging system. These examinations were repeated at each followup visit at 3 and 6 months, and 1 year by an examiner from our department blinded to surgical procedures. Examinations were done with the patient in the dorsal lithotomy position. Before vaginal examination the bladder was emptied and a vaginal specula was routinely used.

To evaluate clinical symptoms we used a customized questionnaire designed at our clinic. Also, preoperatively and at 12-month followup patients completed the validated, translated SF-36 quality of life questionnaire. SF-36 is a multipurpose, short form health survey with 36 questions that yields an 8-scale profile of functional health and well-being scores as well as psychometrically based physical and mental health summary measures, and a preference based health utility index. The usefulness of SF-36 to estimate the disease burden and compare disease specific benchmarks with general population norms has been shown in articles describing more than 200 diseases and conditions, including transplantation and incontinence.[6] The questionnaire was completed independently.

Traditional anterior or posterior colporrhaphy without mesh graft were done depending on prolapse type in each patient. All procedures described were part of our routine clinical care but patients were informed about the procedures and written consent was obtained from all. For anterior colporrhaphy after dissecting out the mucosal flaps we used plication interrupted sutures. Approximating vertical mattress sutures were used to bring the lateral aspects of the mobilized connective tissue attachments at the arcus tendineus fasciae pelvis. For posterior colporrhaphy we excised a triangular mucosal flap. A running locked suture was placed starting from the apex. Three interrupted sutures were made to approximate the levator muscles.

Eight patients underwent a concomitant suburethral single incision transobturator sling procedure for stress urinary incontinence. The tape was 8 cm long with self-fixating tips for anchorage in the obturator internus muscle and membrane. This procedure was started with an approximately 1.5 to 2 cm mid urethral vaginal incision. The paraurethral tissue was dissected with scissors, creating a tunnel up to the pubic bone inferior ramus. The sling was advanced into the obturator internus muscle and obturator membrane below the inferior pubic ramus with a needle. Tension-free sling positioning was ensured by inserting a forceps handle between tape and urethra. The insertion angle was 45 degrees in the direction of the adductor longus muscle tendon. The vaginal incision was closed with polyglactin sutures.

Our routine perioperative antibiotic prophylaxis includes 1 dose of a first-generation cephalosporin or equivalent in penicillin sensitive individuals within 1 hour before surgery. Postoperative assessment was done at 2 weeks, and at 3, 6 and 12 months. Any intraoperative and postoperative complications and interventions were noted.

Statistical analysis of POP-Q measurements and quality of life data were done using SigmaPlot®, version 11. We performed between group comparison of nonparametric skewed dependent variables using the Wilcoxon matched pairs test with significance considered at 0.05%.

RESULTS

At our institution 16 renal transplant patients with a mean ± SD body mass index of 25.2 ± 3.8 kg/m^2 (range 20.9 to 29.6) underwent pelvic reconstructive surgery at a mean age of 58.3 ± 7.7 years (range 50 to 66). All patients underwent cadaveric renal transplantation a mean of 54.2 ± 15.1 months (range 38 to 123) preoperatively. The table lists preoperative

Demographics in 16 patients

Variables	No. Pts (%)
Parity:	
1	2 (12.5)
2	6 (37.5)
3	8 (50)
Vaginal wall prolapse:	12 (75)
Anterior	
Anterior + posterior	4 (25)
Preop prolapse stage:	
II	10 (62.5)
III	6 (37.5)
Postop prolapse stage:	12 (75)
0	4 (25)
I	

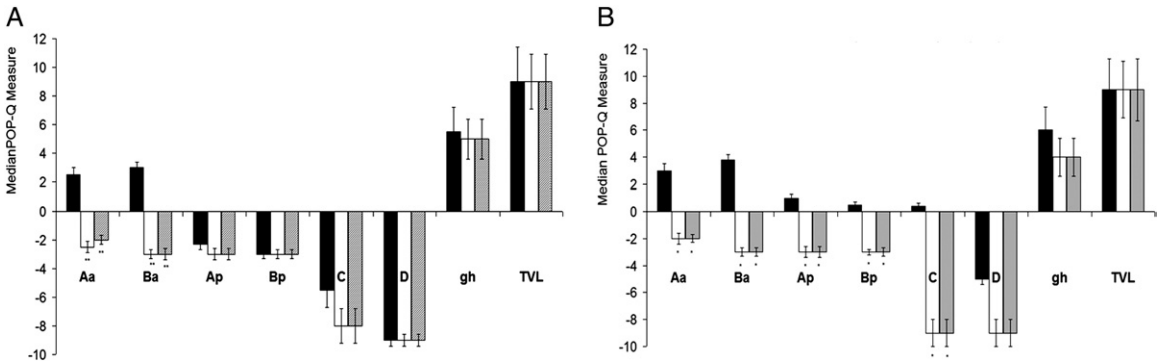

Figure 1. Median POP-Q in cm at baseline (black bars), and 6 (open bars) and 12 (gray bars) months of followup. *A*, anterior colporrhaphy in 12 patients. *B*, combined anterior and posterior colporrhaphy in 4 patients. *Aa*, anterior vaginal wall midline. *Ba*, most distal position of upper anterior vaginal wall from vaginal cuff or anterior vaginal fornix to point Aa. *Ap*, posterior vaginal wall midline proximal to hymen. *Bp*, most distal position upper posterior vaginal wall from vaginal cuff or posterior vaginal fornix to point Ap. *C*, most distal cervical edge or vaginal cuff leading edge after hysterectomy. *D*, posterior fornix site in woman with cervix. *gh*, genital hiatus. *TVL*, total vaginal length. Single asterisk indicates Wilcoxon matched pairs test $p < 0.05$ vs preoperatively. Double asterisks indicate Wilcoxon matched pairs test $p < 0.01$ vs preoperatively.

patient characteristics. The maintenance immunosuppression protocol was standardized in all recipients, consisting of a triple combination of tacrolimus, methylprednisolone and mycophenolate mofetil.

Preoperatively symptoms of vaginal bulging, stress urinary incontinence, frequency and urgency, and bowel symptoms such as anal incontinence or constipation were reported by 91.3%, 42%, 26% and 28.7% of patients, respectively. Sexual symptoms such as dyspareunia, decreased desire and decreased intercourse frequency were present preoperatively in 83% of patients.

Pelvic reconstructive surgery was successfully done and tolerated in all transplant patients. Transvaginal anterior wall colporrhaphy was performed in 12 patients (75), and 4 (25%) underwent combined anterior and posterior wall colporrhaphy. A concomitant suburethral single incision transobturator sling procedure was done in 8 patients (50%). No women underwent concomitant hysterectomy. Mean ± SD operative time was 42.3 ± 17.1 minutes (range 25 to 69) and mean hospitalization was 5.9 ± 1.8 days (range 4 to 9). There was no bladder or rectal injury, bleeding necessitating transfusion, voiding dysfunction, groin or pelvic pain, sling erosion, vaginal infection, de novo stress urinary incontinence or repeat intervention.

Pelvic floor testing 12 months postoperatively revealed good surgical results with stage I vaginal wall prolapse in 4 patients (25%). Figure 1 shows the results of POP-Q measurement. At followup visits no patient had evidence of recurrent POP. We noted no voiding dysfunction, de novo stress urinary incontinence or sling implant erosion during the entire followup.

Quality of life was measured in all patients using SF-36. Compared to preoperative values all women reported improved quality of life in all SF-36 domains (fig. 2). No patient had impaired graft function 3 months postoperatively, as shown by stable serum creatinine as a measure of graft function (preoperative vs postoperative mean 1.32 ± 0.12 vs 1.11 ± 0.39 mg/dl). The glomerular filtration rate, urinary protein and 24-hour diuresis were used to monitor transplant kidney graft function. Each remained stable during the perioperative period and at subsequent followups.

DISCUSSION

Advances in renal transplantation have improved patient survival considerably, in that untreated voiding dysfunction and POP could contribute to

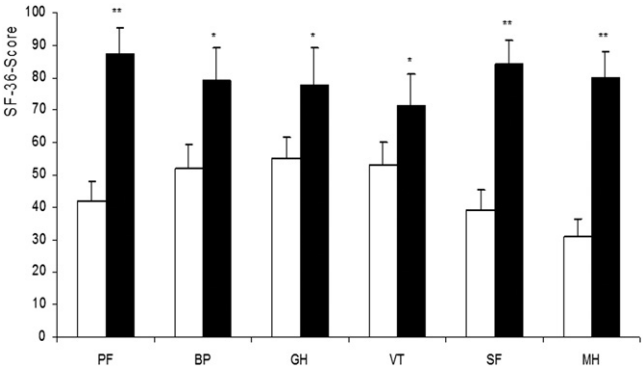

Figure 2. Mean ± SD quality of life changes on SF-36 at 12 months (black bars) in 16 patients. *PF*, physical function. *BP*, bodily pain. *GH*, general health. *VT*, vitality. *SF*, social function. *MH*, mental health. Open bars represent preoperative. Single asterisk indicates Wilcoxon matched pairs test $p < 0.05$ vs preoperatively. Double asterisks indicate Wilcoxon matched pairs test $p < 0.01$ vs preoperatively.

patient morbidity and possibly to mortality. POP and urinary incontinence are common conditions that negatively affect quality of life in millions of women.[7] However, population based epidemiological studies of POP are rare, although it is a common indication for pelvic surgery in older women. Up to 75% of women presenting for routine gynecological care show some prolapse and 3% to 6% have descent beyond the hymen.[8,9] Currently no conclusive data are available on the incidence and overall clinical impact of these conditions in renal transplant patients on immunosuppression.

Heit et al estimated the prevalence and severity of urinary incontinence and its impact on daily living activity in kidney transplant recipients.[10] After interviewing 123 patients they identified urinary incontinence in 28% of female renal transplant patients. Using the incontinence severity index and the incontinence impact questionnaire they further noted that urinary incontinence alone seems to have less impact on daily living activity in renal transplant recipients than in nontransplanted incontinent women with similarly severe incontinence.[11] However, they did not evaluate POP presence or absence. Nevertheless, although to our knowledge it has not been evaluated to date, POP may complicate the midterm and long-term course of renal transplantation since it may be associated with post-void residual urine, urgency, recurrent urinary tract infections and pad use. In our series symptoms of vaginal bulging, stress urinary incontinence, frequency and urgency, and bowel symptoms such as anal incontinence and constipation were reported by most patients. Thus, even in this group of chronically ill patients urinary incontinence and POP are bothersome conditions and many patients seek treatment for pelvic floor disorders. As recently noted by Barber et al,[12] improvements in clinical symptoms and quality of life are more important measures of treatment success in this patient group than anatomical results alone.

An important issue when treating renal transplant patients for POP is the risk of graft injury, which is a serious complication and associated with a high mortality rate. This is particularly important for pelvic surgeons who perform extensive pelvic dissection, retractor placement or retropubic trocar passage for tension-free vaginal tape implantation and who may use synthetic mesh implants. Thus, it is mandatory to consider the pelvic location of the transplanted kidney, ureter and ureteral orifice. In our series all transplanted kidneys were located in the pelvis with the ureteral orifices located in the bladder dome. As in traditional colorrhaphy techniques, in this series we performed 8 suburethral single incision transobturator sling procedures. All procedures were successful and uncomplicated. The transobturator suburethral tape is a novel technique that is applied as surgical treatment for stress urinary incontinence. This approach prevents the risk of bladder, bowel or vascular injury because it avoids the retropubic space.[13]

Synthetic mesh graft implants as pelvic tissue reinforcement or an anti-incontinence sling is widely used by pelvic reconstructive surgeons.[14] These implants regularly induce a local inflammatory reaction to initiate adherence to pelvic connective tissue.[15] However, since multiple immunosuppressive agents are used in transplant patients to avoid transplant graft rejection, there may be concern about an increased risk of infection and impaired wound healing in these patients. Also, immunosuppression may lead to alterations in the initiation of local inflammatory response to a synthetic mesh implant, which may jeopardize the ability of these patients to incorporate synthetic mesh. To our knowledge no data exist to date to support the safety and efficacy of vaginal mesh in renal transplant patients.

Three reports have been published to date on suburethral sling procedures in renal transplant patients.[3–5] Shveiky et al reported 3 transobturator sling procedure cases done concomitantly with traditional pelvic reconstructive surgery.[5] At a mean 12.6-month followup all patients were cured of prolapse and incontinence with no evidence of synthetic mesh infection, rejection or erosion. The 2 other case reports included suburethral sling procedures for stress incontinence (mid urethral synthetic retropubic and transobturator slings) done 6 and 2 years after transplantation.[3,4] Each procedure was successful and without complications at 1 and 8-month followup.

A few case reports have been published of the safety of synthetic or prosthetic materials in transplant patients on immunosuppression. Mazzucchi et al reported the safety and efficacy of abdominal polypropylene mesh implants for incisional hernia repair in renal transplant patients.[16] O'Malley et al reported 1 successful implantation of an AMS 800™ artificial urinary sphincter prosthesis in a male renal transplant patient with stress urinary incontinence.[17] Kocjancic et al reported implantation of a sacral neuromodulator for functional voiding dysfunction in a renal transplant recipient.[18] In all cases no local or systemic infection was noted that resulted in impaired transplant graft function.

Other issues to be considered when treating transplant patients for pelvic organ disorders are actual graft function, interval to transplantation and comorbidities, such as cardiovascular and pulmonary diseases, metabolic and hormonal disorders, and im-

paired connective tissue. These factors may increase anesthesia and surgery risks, and result in impaired transplant graft function or even an acute episode of graft rejection. Thus, these patients should be carefully prepared for the operation, including monitoring for stable graft function and the optimal therapeutic range of baseline immunosuppression with consultation with nephrologists and anesthesiologists before the procedure.

CONCLUSIONS

Transvaginal reconstructive surgery for POP with or without slings for incontinence can be done safely in well selected renal transplant recipients. However, urologists involved in pelvic reconstructive surgery should be aware of the potential complications when operating in these immunosuppressed patients and weigh these risks against potential benefits.

REFERENCES

1. Wu JM, Hundley AF, Fulton RG et al: Forecasting the prevalence of pelvic floor disorders in U.S. women: 2010 to 2050. Obstet Gynecol 2009; **114:** 1278.
2. Nygaard I, Barber MD, Burgio KL et al: Prevalence of symptomatic pelvic floor disorders in US women. JAMA 2008; **300:** 1311.
3. Danilovic A, Baracat F, Montellato NID et al: Use of transobturator suburethral tape for surgical treatment of stress urinary incontinence in a renal transplant patient. Clinics 2005; **60:** 433.
4. Hamzeh R and Oligbo N: Tension-free tape procedure for a woman with transplanted kidney. Br J Obstet Gynecol 2005; **112:** 508.
5. Shveiky D, Blatt A, Sokol AI et al: Pelvic reconstructive surgery in renal transplant recipients. Int Urogynecol J Pelvic Floor Dysfunct 2009; **20:** 551.
6. Gómez-Besteiro MI, Santiago-Pérez MI, Alonso-Hernández A et al: Validity and reliability of the SF-36 questionnaire in patients on the waiting list for a kidney transplant and transplant patients. Am J Nephrol 2004; **24:** 346.
7. Olsen AL, Smith VJ, Bergstrom JO et al: Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol 1997; **89:** 501.
8. Swift S, Woodman P, O'Boyle A et al: Pelvic Organ Support Study (POSST): the distribution, clinical definition, and epidemiologic condition of pelvic organ support defects. Am J Obstet Gynecol 2005; **192:** 795.
9. Samuelsson EC, Victor FT, Tibblin G et al: Signs of genital prolapse in a Swedish population of women 20 to 59 years of age and possible related factors. Am J Obstet Gynecol 1999; **180:** 299.
10. Heit M, Blackwell L, Thomas S et al: Prevalence and severity of urinary incontinence in kidney transplant recipients. Obstet Gynecol 2004; **103:** 352.
11. Heit M, Blackwell L and Ouseph R: Comorbidities affect the impact of urinary incontinence as measured by disease-specific quality of life instruments. Int Urogynecol J Pelvic Floor Dysfunct 2005; **16:** 6.
12. Barber MD, Brubaker L, Nygaard I et al: Defining success after surgery for pelvic organ prolapse. Obstet Gynecol 2009; **114:** 600.
13. Gauruder-Burmester A and Popken G: The Mini-Arc sling system in the treatment of female stress urinary incontinence. Int Braz J Urol 2009; **35:** 334.
14. Sung VW, Rogers RG, Schaffer JI et al: Graft use in transvaginal pelvic organ prolapse repair: a systematic review. Obstet Gynecol 2008; **112:** 1131.
15. Pierce LM, Rao A, Baumann SS et al: Long-term histologic response to synthetic and biologic graft materials implanted in the vagina and abdomen of a rabbit model. Am J Obstet Gynecol 2009; **200:** 546.e1.
16. Mazzucchi E, Nahas WC, Antonopoulus I et al: Incisional hernia and its repair with polypropylene mesh in renal transplant recipients. J Urol 2001; **166:** 816.
17. O'Malley KJ, Hickey DP, Kapoor A et al: Artificial urinary sphincter insertion in renal transplant recipients. Urology 1999; **54:** 923.
18. Kocjancic E, Crivellaro S, Favro M et al: Sacral neuromodulation for urinary retention in a kidney-transplant patient. Urol Int 2005; **75:** 187.