PRACTICE PATTERNS FOR IMPROVING OUTCOMES IN WOMEN WITH ILEAL NEOBLADDER: AN EVIDENCE-BASED ANALYSIS

Georgios Gakis

Department of Urology, University Hospital Tübingen, Eberhard-Karls University, Tübingen, Germany

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ABSTRACT

Introduction: The aim of this review is to provide practice pattern on how to obtain best possible oncological and functional outcomes in women with orthotopic neobladder substitutes.

Evidence Synthesis: The treating surgeon has to balance oncological and functional risks as well as patient´s preferences and the final decision must be based on consent between the surgeon and the patient. Long-term survival can be achieved in the majority of neobladder patients even with extravesical, node-negative disease. Therefore, surgeons should not be reluctant to proceed with an ileal neobladder in patients with locally advanded tumour stage excluding T4b stage, any positive soft tissue surgical margin and bulky lymph node disease. During preoperative work-up, women with a positive bladder neck biopsy may be still candidates for an orthotopic neobladder unless a carefully obtained full-thickness biopsy of the urethra reveals evidence of malignancy. The key issue in the follow-up of women with neobladder is to achieve a neobladder capacity of 400-500mL, residual free voiding of sterile urine and the elimination of any outlet or upper tract obstruction. Medical conditions (i.e. arterial hypertension, diabetes mellitus) can also cause renal deterioration in the long-term and therefore demand early and thorough treatment.

Conclusions: The clinical background of the treating urologist is of paramount importance for appropriate patient selection, accurate surgical performance and adequate monitoring of women with ileal neobladders. A high level of patient compliance and willingness to undergo follow-up examinations at regular intervals is mandatory for improved outcomes.

Keywords: bladder cancer, follow-up, neobladder, radical cystectomy.

INTRODUCTION

Over the past two decades, large unicentre data have proven oncological and functional safety of using ileal neobladders in women.[1] While in the first postoperative years after radical surgery the patient's first priority is to survive the potentially recurring disease, functional aspects come to the patient's fore in the long-term.[2] Up to the early 1990s, many surgeons were reluctant to use ileal neobladder reconstruction in females because of the fear that the reduced urethral length might severely impair postoperative continence.[3] Yet, the neobladder procedure in women is challenging as surgical inaccuracy may lead to a broad range of complications with which the patient and referring urologist will have to struggle with in the long-term.[4] As hospital and surgeon volume has been increasingly recognised as critical determinants for reduced postoperative complication rate after neobladder reconstruction, centralisation of this challenging surgical procedure in high-volume centres has been increasingly advocated.[5] The aim of this review is to provide evidence-based practice pattern for obtaining the best possible functional and oncological outcomes in women with neobladder substitutes.

EVIDENCE SYNTHESIS

The Preoperative Decision-Making for Ileal Neobladder in Women

In clinical decision-making the optimal selection and preparation of a patient scheduled for neobladder reconstruction is of paramount importance. The treating surgeon has to balance oncological and functional risks as well as the patient's preferences. The final decision must be based on consent between the surgeon and the patient.[6] The treating surgeon has to pay particular attention to

various factors that may impair outcomes. A good renal function is a prerequisite for neobladder reconstruction as an increased postoperative reabsorption of acid urinary constituents through the ileal mucosa results in an increased acid load in neobladder patients compared to patients with ileal conduits.[7] Therefore, a woman with good renal function will easily compensate metabolic acidosis, provided the neobladder is emptied completely at regular intervals. Most surgeons consider women with creatinine clearance below 50ml/min to be ineligible for a neobladder.[8] Of note, in women with renal insufficiency owing to tumour-related hydronephrosis, upper tract desobstruction via nephrostomy allows for better preoperative evaluation of the exact renal function. In borderline cases, 51 Cr-EDTA clearance is more accurate than the estimated glomerular filtration rate to determine the exact renal function.[9] Furthermore, in younger women with borderline renal function it has to be taken into consideration that a natural age-dependent decline of renal function of approximately 1mL/min each year occurs over the age of 50.[10] Women after renal transplantation can safely undergo a neobladder procedure, provided the transplant and liver function are unrestricted.[11] Impaired liver function is critical in neobladder patients as it may not only lead to severe macrohematuria[12] but also to an aggravation of the renal function.[13] In women with complex or recurrent urethral strictures surgeons should be reserved in offering a neobladder approach as retention is likely to occur postoperatively.[14] Certainly, patients with any mental and physical impairments which preclude the ability to perform clean intermittent catheterisation in case of urinary retention are not candidates for an orthotopic neobladder. In terms of prior pelvic radiotherapy (due to gynecological malignancy) the exact radiotherapeutic field and applied dosage needs to be critically reappraised before excluding a women from an orthotopic approach a priori.[15-17*]

Intraoperative Management of the Urethra

Addressing oncological risk factors for tumour recurrence involving the neobladder in women is of utmost importance as tumour invasion into the neobladder has a detrimental impact on patient´s quality of life and survival.[18] Tumour location at the bladder neck, multiplicity and presence of carcinoma in situ have been reported to be risk factors both for a positive urethral margin and urethral recurrence.[16,18] Therefore, some surgeons advocate that bladder neck biopsy in women is sufficient enough to exclude a malignant urethral margin at cystectomy.[19] Others rely completely on the results of intraoperative frozen section analysis of the urethral margin.[20] However, recurrences involving the neobladder have been reported despite the use of frozen section at the time of surgery.[21-22] These data underlie that the low sensitivity may be not attributable to a low predictive accuracy of frozen section analysis, but rather to undersampling which strengthens the importance of performing a full-thickness biopsy of the urethra. However, as the distal urethral margin may be tumour-free despite the presence of a bladder neck tumour (in the study by Stein et al. in ~60% of the cases[23]), exclusion of women from an orthotopic approach due to primary tumour location at the bladder neck is not justified unless a carefully obtained frozen section of the distal urethral margin evidences malignancy. In conclusion, to reduce the risk of urethral recurrence surgeons need to carefully check the bladder neck at transurethral resection and focus on enlarged pelvic or inguinal lymph nodes at staging investigations. The use of frozen section analysis of the distal urethal margin in case of bladder neck tumour involvement may still allow for the performance of an orthotopic diversion in women, without putting them into an increased risk for urethral recurrence.

Neobladder Reconstruction in Advanced Tumour Stages - To Do or Not To Do?

In terms of tumour stage, the largest neobladder series in women have reported similar 10-year recurrence-free survival rates in organ-confined (≤pT2N0) and extravesical node-negative (≥pT3aN0) disease ranging between 67-71%.[22] These data were confirmed in other series reporting 5-year overall survival rates between node-negative patients with ≤pT2N0 and ≥pT3N0 of 80% and 82%, respectively.[24] Therefore, surgeons should not be reluctant to proceed with an ileal neobladder in patients with locally advanced tumour stage or limited lymph node tumour burden if the affected lymph nodes are completely removable. However, in patients with bulky lymph nodes (>5cm), pelvic or abdominal wall infiltration (staged cT4b) or positive soft tissue surgical margin the treating surgeon should refrain from any orthotopic approach since postoperative adhesions to the pelvic wall will inevitably result in tumour invasion of the neobladder.[18]

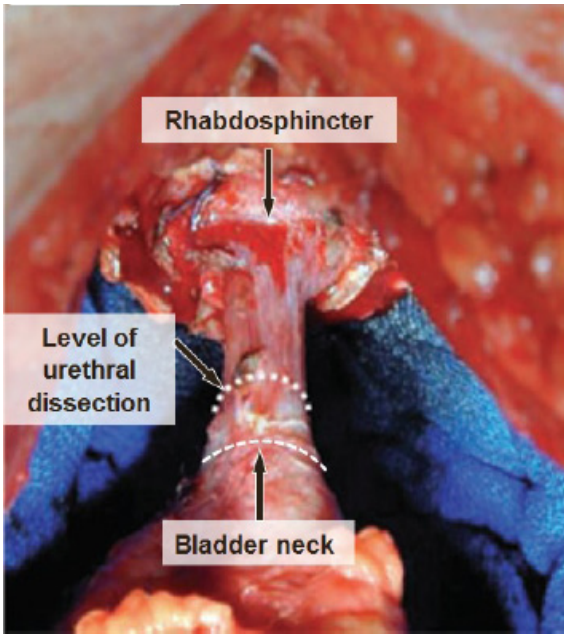
Surgical Aspects for the Reconstruction of the Neobladder Reservoir

It is well-known that postoperative upper tract obstruction due to ureterointestinal stenosis is one leading causes of renal deterioration after neobladder reconstruction. Nonetheless, the majority of studies have shown that neither the use of refluxing nor antirefluxing ureteral implantation techniques provide superior results in terms of improved postoperative renal function.[7,25] Attempting nerve-sparing cystectomy has a positive

impact on postoperative urethral pressure profile[26] and results in improved continence rates.[27] Sparing the lateral vaginal walls allows for improved continence and sexual function via preservation of autonomic nerve supply to the urethra and vaginal lubrication.[27-28]

Another important aspect is the risk of urinary retention which has been shown to be significantly higher in women than in men.[7,24] Large-capacity reservoirs store urine at lower end-filling pressures but the use of less bowel for the creation of a spherical reservoir carries a lower risk for early absorptive complications.[29] Women with large-capacity reservoirs (derived from a 60-70cm ileal segment) will most probably gain earlier satisfactory postoperative continence than women with neobladders of less ileal length. However, long-term continence rates seem not to vary between both groups[24] as the functional capacity of orthotopic reservoir made of shorter ileal segment increases rapidly within the first weeks after surgery from around 150mL to 400-500mL. Conversely, the use of excessive length of ileum may produce a "floppy" low-pressure reservoir that is more prone to retention.[19] In this respect, patient compliance and willingness to actively exercise storing within and emptying the neobladder is of paramount importance in the first months after surgery. To prevent postoperative urinary retention in women, the urethra should be divided approximately 1cm below the bladder neck (Figure 1). Otherwise a mechanical kink at the level of urethro-intestinal anastomosis may occur, especially as orthotopic pouches tend to fall posteriorly during Valsalva maneuver which can be demonstrated on lateral straining cystogram.[30] In this respect, creating posterior support with a omental flap from the posterior vaginal wall to the edges of the endopelvic facia may have some preventive effects.[31]

Figure 1: Level of urethral dissection in relation to the bladder neck and rhabdosphincter in a woman undergoing radical cystectomy with orthotopic neobladder.



Critical Aspects During Follow-Up of Women with Neobladder

The risk of urethral recurrence after neobladder formation in women is quite low (less than 1%).[32] While symptomatic women presenting with urethral bleeding, pain, or palpable mass have to be evaluated promptly, there is no clear evidence supporting a survival benefit with use of a defined follow-up schedule.[32-34] It seems therefore reasonable to tailor surveillance regimens individually according to the patient´s risk factors for urethral recurrence. In the long-term, there are many potential reasons which may cause renal deterioration following orthotopic neobladder reconstruction. Basically, any condition which allows the transmission of high pressure or infected urine into the kidneys can cause renal deterioration (i.e. ureterointestinal stenosis, stone formation and increased post-void residual urine). During follow-up, key issues are to achieve a neobladder capacity of 400-500mL, residual free voiding of sterile urine, and the elimination of any outlet or upper tract obstruction. Recurrent urinary tract infections (even if not symptomatic) should prompt physicians to exclude the presence of residual urine volume and check for electrolyte imbalances. Neobladder patients are at risk of salt loss as sodium excretion is increased through the ileal mucosa,[35] which can cause various symptoms (i.e. apathy, nausea, vomiting, anorexia). These electrolyte imbalances can easily be corrected by sodium bicarbonate supplementation and sodium-rich food intake. Untreated chronic metabolic acidosis also has adverse effects on bone mineral density and may lead to an increased risk for skeletal-related events.[36] Furthermore, vitamin B12 supplementation may become necessary in the long-term, especially in large-capacity reservoirs, and should be checked from the third postoperative year onwards.[7**]

The treating urologists need to be aware of the fact that a postoperative decline in renal function may also be attributable to poorly regulated metabolic diseases (i.e. diabetes, arterial hypertension) or drug-related side effects. Therefore, patients' medication list needs to be checked regularly, and any medical conditions which may cause renal deterioration in the long-term needs to be treated as thoroughly as possible.

CONCLUSION

The clinical background of the treating urologist is of paramount importance for appropriate patient selection, accurate surgical performance and adequate monitoring of neobladder patients. Improved outcomes in women with ileal neobladder mandate a high level of patient compliance and willingness to undergo examinations at regular intervals.

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