Urinary Diversion

Siamak Daneshmand
Editor

Springer

Urinary Diversion

Siamak Daneshmand
Editor

Urinary Diversion

Springer

Editor
Siamak Daneshmand
Institute of Urology
Norris Comprehensive Cancer Center
University of Southern California
Los Angeles
California
USA

ISBN 978-3-319-52185-5 ISBN 978-3-319-52186-2 (eBook)
DOI 10.1007/978-3-319-52186-2

Library of Congress Control Number: 2017933449

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer International Publishing AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Preface

There are few topics in urology today that evoke such strong opinions from surgeons than urinary diversion following radical cystectomy. This is in part due to lack of randomized trials which are virtually impossible to perform and the environment in which the surgeon trained and gained his or her experience. There are more than 30,000 radical cystectomies performed in the United States and Europe annually. It is estimated that up to 80% of men and 65% of women undergoing cystectomy are suitable candidates for continent diversion by means of an orthotopic neobladder. However, today, the vast majority of patients still undergo ileal conduit urinary diversion. Continent diversions have been around for over 30 years, and at select centers around the world including ours, the majority of patients undergo orthotopic diversion. So why the disparity? Many urologists performing cystectomies lack sufficient experience or training to offer continent diversion or believe there are higher complication rates with continent forms of diversion, a perception that is challenged by centers with experience. Most urologists perform no cystectomies or only a few annually. However, all are called on to manage short- and long-term complications related to the urinary diversion

There is no question that each form of diversion is associated with a significant change in quality of life and patients need to adapt to their new norm. Patients with an ileal conduit need to adjust to wearing an external appliance, learn to sleep with a bag, and manage the dermatologic sequela of skin irritation from contact with urine. Those with orthotopic neobladders will need to perform pelvic floor exercises to regain and maintain their continence, learn self-catheterization in case of poor emptying (10–12% in men and up to 30% in women), and manage urinary incontinence particularly at night. Patients with continent cutaneous diversions enjoy excellent continence rates but have to cope with significant stomal stenosis rates and other potential long-term complications. What we as surgeons perceive to be the best form of diversion for the patients may not be what the patient desires. There are many misconceptions in this arena and not enough quality data.

Several investigators have used validated instruments in order to compare quality of life in patients with various types of urinary diversion. It is, however, unclear whether any of these questionnaires accurately capture the complex factors surrounding the patient's experience. The fact that most patients eventually adapt with their form of diversion leads many to think patients are "happy" with an incontinent stoma. Would those same patients "choose" an ileal conduit if they knew they could have a continent form of diversion that would offer excellent functional results? There may not be an ideal form of diversion; however, it seems surgeons should provide a comprehensive and unbiased overview of the various forms of diversion even if not performed personally.

This book will offer a detailed description of various forms of urinary diversions, including the ileal conduit, orthotopic neobladder, and a variety of continent cutaneous diversions with specific focus on the techniques of reconstruction, appropriate patient selection, and management of common complications. Continent cutaneous forms of diversion are becoming a lost art, and it is incumbent on training centers and those who perform this operation routinely to pass on the techniques that have been refined over the last two decades to provide our patients with all possible options. There are a multitude of gratified patients around the world who are living with this form of diversion. The book will also include chapters on management of complications encountered with various forms of diversion including a detailed chapter on pelvic floor rehabilitation following orthotopic diversion for improvement of continence. There is a chapter devoted to quality of life following urinary diversion as well as a review of the current status of tissue engineering in urinary diversion and the prospects that lay ahead. As patients live longer with their diversion, the need may arise for a secondary diversion, and this topic is discussed in a chapter on re-diversion.

This book is suited for the urologist in training or in practice who wishes to not only expand the repertoire of urinary diversions offered to patients but also refine techniques of managing common complications. It will also be suited for nurse practitioners and physician assistants who care for patients undergoing urinary diversion.

Los Angeles
CA, USA

Siamak Daneshmand

Contents

1 **Patient Selection for Urinary Diversion** 1
Eila C. Skinner

2 **Orthotopic Urinary Diversion in Men** 11
Siamak Daneshmand

3 **Orthotopic Urinary Diversion in Women** 25
Georgios Gakis

4 **Continent Cutaneous Urinary Diversion** 39
Jonathan N. Warner and Kevin G. Chan

5 **Robot-Assisted Intracorporeal Urinary Diversion** 55
Ahmed A. Hussein, Youssef E. Ahmed, and Khurshid A. Guru

6 **Complications of Ileal Conduit Diversion** 63
Timothy F. Donahue and Bernard H. Bochner

7 **Use of Regenerative Tissue for Urinary Diversion** 81
Nikolai A. Sopko, Max Kates, Anirudha Singh, Gary D. Steinberg, Norm D. Smith, Mark P. Schoenberg, and Trinity J. Bivalacqua

8 **Long-Term Complications of Urinary Diversion** 101
Erfan Amini and Hooman Djaladat

9 **Stomal Complications** 121
Sumeet Syan-Bhanvadia and Siamak Daneshmand

10 **Pelvic Floor Rehabilitation for Orthotopic Diversion** 143
Eileen V. Johnson and Daniel J. Kirages

11 **Urinary Diversion and Health-Related Quality of Life** 153
Andrew Leone and Scott M. Gilbert

12 **Considerations for Urinary Re-diversion** 171
Richard E. Hautmann and Bjoern G. Volkmer

Index 181

Contributors

Youssef E. Ahmed, MD Department of Urology, Roswell Park Cancer Institute, Buffalo, NY, USA

Erfan Amini Department of Urology, Uro-oncology Research Center, Tehran University of Medical Sciences, Tehran, Iran

Sumeet Syan-Bhanvadia, MD Norris Comprehensive Cancer Center, University of Southern California, Los Angelos, CA, USA

Trinity J. Bivalacqua Department of Urology, The Johns Hopkins Hospital, Baltimore, MD, USA

Bernard H. Bochner Sidney Kimmel Center for Prostate and Urologic Cancers, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Kevin G. Chan City of Hope Cancer Center, Duarte, CA, USA

Siamak Daneshmand, MD Institute of Urology, Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA, USA

Hooman Djaladat The Institute of Urology, Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA, USA

Tim Donahue Sidney Kimmel Center for Prostate and Urologic Cancers, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Georgios Gakis, MD, FEBU Department of Urology, Eberhard-Karls University Tuebingen, University Hospital of Tübingen, Tuebingen, Germany

Scott M. Gilbert Department of Genitourinary Oncology, H. Lee Moffitt Cancer Center, Tampa, FL, USA

Khurshid A. Guru, MD Department of Urology, Roswell Park Cancer Institute, Buffalo, NY, USA

Richard E. Hautmann University of Ulm, Neu-Ulm, (Donau), Germany

Ahmed A. Hussein, MD Department of Urology, Cairo University, Giza, Egypt

Department of Urology, Roswell Park Cancer Institute, Buffalo, NY, USA

Eileen V. Johnson, PT, DPT, WCS Division of Biokinesiology and Physical Therapy, University of Southern California, Los Angeles, CA, USA

Max Kates The James Buchanan Brady Urological Institute and Department of Urology, The Johns Hopkins School of Medicine, Baltimore, MD, USA

Daniel Kirages, PT, DPT, FAAOMPT Division of Biokinesiology and Physical Therapy, University of Southern California, Los Angeles, CA, USA

Andrew Leone Department of Genitourinary Oncology, H. Lee Moffitt Cancer Center, Tampa, FL, USA

Mark P. Schoenberg, MD Department of Urology, Albert Einstein College of Medicine, New York, NY, USA

Anirudha Singh The James Buchanan Brady Urological Institute and Department of Urology, The Johns Hopkins School of Medicine, Baltimore, MD, USA

Eila C. Skinner Department of Urology, Stanford University, Stanford, CA, USA

Norm D. Smith, MD Department of Urology, University of Chicago, Chicago, IL, USA

Nikolai A. Sopko, MD, PhD The James Buchanan Brady Urological Institute and Department of Urology, The Johns Hopkins School of Medicine, Baltimore, MD, USA

Gary D. Steinberg, MD Department of Urology, University of Chicago, Chicago, IL, USA

Bjoern G. Volkmer Norris Comprehensive Cancer Center, University of Southern California, Los Angelos, CA, USA

Jonathan N. Warner, MD City of Hope Cancer Center, Duarte, CA, USA

1 Patient Selection for Urinary Diversion

Eila C. Skinner

Introduction

The ileal conduit has been the most common form of urinary diversion for over 50 years for patients undergoing radical cystectomy throughout the United States and most of the world. Many patients found the prospect of living with a bag on their side unacceptable so they refused or significantly delayed cystectomy only to succumb to metastatic disease. The development and refinement of continent diversion, and especially the orthotopic neobladder, allowed many patients and their physicians to accept this surgery and to undertake it when the cancer was still curable [1]. Formal studies of quality of life with different forms of diversion have been hampered by the lack of prospective randomized data (admittedly impossible to obtain) [2, 3]. Nevertheless many patients will choose a continent form of urinary diversion if given that option.

For surgeons who are comfortable with the construction of orthotopic and continent cutaneous diversion, almost every patient may be considered at least a potential candidate. There are only a few absolute contraindications that are discussed below. However, the decision about which diversion to choose is a complex one for both patients and their surgeons, and there are multiple factors that need to be taken into consideration. These can be divided into patient-related factors and tumor-related factors. This is a good example of a situation that truly requires shared decision-making between the surgeon, the patient, and his/her family.

E.C. Skinner
Department of Urology, Stanford University,
300 Pasteur Drive, Suite S-287, Stanford, 94305 CA, USA
e-mail: skinnere@stanford.edu

S. Daneshmand (ed.), *Urinary Diversion*, DOI 10.1007/978-3-319-52186-2_1

Patient-Related Factors

Absolute Contraindications

The only absolute contraindications to continent diversion are poor renal function and absence of available bowel to construct the diversion. Generally, a serum creatinine level less than 2 mg/dL or an estimated glomerular filtration rate (eGFR) of at least 40–50 ml/m^2/s is considered the minimum renal function that is acceptable for continent diversion because of the increased acid load that results from absorption from the pouch [4]. Moderate chronic kidney disease above that level may result in a requirement for sodium bicarbonate supplementation but does not appear to otherwise have worse outcomes [5]. A patient with borderline renal function but an obstructed kidney may actually have improved renal function following surgery, and this should be taken into consideration. However, when in doubt a nephrostomy tube should be placed to establish the actual function of the obstructed kidney before surgery.

It is common for patients undergoing radical cystectomy to have some decrease in renal function over the ensuing years. There may be many causes for this including perioperative complications, obstruction, and chemotherapy, but it does not appear to be directly related to the type of urinary diversion. In a prospective study of 484 patients undergoing ileal neobladder reconstruction, approximately 40% had a decrease in eGFR by at least 10 points at 12 months and 58% by 3 years. However, in that study the curves flattened out after 3 years, suggesting that there may not be an ongoing effect of the diversion. Preoperative renal function and obstruction were the strongest predictors of the decline [6]. A similar finding was seen in the Mayo Clinic series. Eisenberg and colleagues retrospectively studied over 1600 patients who had undergone ileal conduit (76%) or continent diversion and noted a similar early decline in renal function. However, the type of diversion was not an independent predictor of the loss in renal function [7].

Patients who have had multiple bowel resections or a history of inflammatory bowel disease (IBD) are poor candidates for continent diversion, though the latter may be considered if the IBD only affected the colon and the patient has been in remission. These are rare problems in the population of patients undergoing cystectomy. It is estimated that fewer than 10% of patients presenting for cystectomy will be excluded by one of these two absolute contraindications [8, 9].

Relative Contraindications

The most common relative contraindications that require considerable surgeon judgment are the patient's comorbidities and general health. Chronological age by itself should not be considered a contraindication. There is tremendous variability in the physical and cognitive function of patients at any given age. Many men and women over age 75 have excellent functional outcomes with both orthotopic and continent cutaneous diversions, though the elderly with orthotopic diversion may require a longer period to regain continence [10–12]. The frail elderly patient who is mostly sedentary may not benefit from these types of reconstructions. Patients with significant cognitive dysfunction or who require assistance with activities of daily living may be best served with an ileal conduit that is easier for a caregiver to manage. A particular challenge is the very elderly patient living independently. It is unclear if one type of diversion is more likely than others to allow such a patient to maintain his/her independence.

Patients undergoing continent cutaneous diversion obviously must be willing and able to self-catheterize through the stoma. Manual dexterity must be reasonable, an issue that arises at times in patients undergoing diversion for a neurourologic problem such as multiple sclerosis or a spinal cord injury. Formal evaluation by an occupational therapist or experienced enterostomal therapist can be helpful in these situations. In addition, inability to catheterize may require urgent medical attention, so patients living in very remote locations may not be best served with a continent cutaneous diversion.

Patients undergoing orthotopic diversion should be willing and able to self-catheterize as well, especially women. In our experience less than 10% of male patients ever need to self-catheterize. Although most men are understandably hesitant about learning that technique, it is rare that a man is unable do it successfully once he has received proper instruction. It is important to differentiate self-catheterization from the indwelling Foley catheter that is placed following transurethral resection of the bladder tumor which is associated with significant discomfort and bladder spasms. Patient should be educated that the neobladder itself is insensate and that spasms are not an issue. Female patients are much more likely to need self-catheterization, with up to 60% having to do it at some point [13]. There are several theories about the cause of this, but so far no technique has dramatically decreased the incidence [14–16]. We currently do uterine-sparing surgery when oncologically safe in an attempt to preserve maximum posterior support to the neobladder and eliminate the risk of vesicovaginal fistula, but with longer follow-up this does not appear to have eliminated the risk of late urinary retention [17].

While most women can learn to self-catheterize, it can be challenging in women with obesity or difficult anatomy. If there is any question about a patient's ability to learn it, we will have them demonstrate that they can do it before making a final decision about the type of diversion to perform.

Several comorbidities deserve special mention. Patients with poor cardiac function, severe COPD, or significant peripheral vascular disease may not tolerate the cystectomy well, and for these patients performing the simplest, quickest diversion often is wise. Cirrhosis is particularly difficult because the excess ammonia absorption from the urine through the bowel wall can tip a patient over into a decompensated liver failure, even with an ileal conduit. In these patients the shortest possible segment should be used, and alternative treatments such as chemoradiation should be strongly considered.

Prior pelvic high-dose radiation is a relative contraindication for orthotopic diversion. The amount of scarring around the urethra and damage to the sphincter area depends on both the dose and the field of radiation applied. High-dose prostate radiation in men and cervical radiation in women appear to be the worst in terms of damage to the external sphincter area and proximal urethra. Prior definitive bladder radiation in typical bladder-sparing protocols and radiation for other malignancies such as colorectal cancer may not cause as much damage to this area. The endoscopic appearance of the sphincter may help determine whether the tissue is healthy, but the final decision has to be made at the time of surgery, assessing the appearance of the urethra when it is divided. Patients who do have a continent orthotopic or cutaneous urinary diversion following pelvic radiation have higher rates of anastomotic stricture, ureteral stricture, and incontinence as well as bowel complications such as anastomotic leak [18, 19].

Men with severe urethral stricture disease and women with stress urinary continence are poor candidates for orthotopic diversion. The latter may be treated with a concomitant sling procedure, but this results in a high risk of requiring self-catheterization. Patients with a documented neurogenic bladder dysfunction should undergo formal urodynamic testing to establish the competence and voluntary control over the urethral sphincter before considering orthotopic diversion.

Finally, men who have had prior radical prostatectomy pose a significant challenge. Dissection of the vesicourethral junction can be challenging in these patients and may be facilitated by intraoperative flexible cystoscopy during the dissection to identify the anastomosis and ensure removal of all of the bladder tissue. If the patient had excellent continence after the prostatectomy, with careful dissection, one can expect good outcomes with orthotopic dissection [20]. Occasionally a patient with known sphincter incompetence will still want to proceed with orthotopic diversion with a plan for an artificial sphincter placement. The cuff can be placed at the time of cystectomy but left inactivated for several weeks. There are few reports of outcomes with AUS placement in patients with continent diversion, but there is a significant revision and infection rate, as might be expected, so it should only be performed by high-volume expert prosthetic surgeons [21].

Cancer-Related Factors

There are several cancer-related factors that are absolute or relative contraindications for orthotopic diversion. Motivated patients who have these are still potentially candidates for continent cutaneous diversion. The primary oncologic contraindication for orthotopic diversion is the presence of urothelial carcinoma at urethral margin on intraoperative frozen section at the time of cystectomy. In men this is most often associated with extensive carcinoma in situ (CIS), especially involving the prostatic urethra. Even if the urethral margin is negative, patients with prostatic urethral involvement are still at increased risk of subsequent urethral recurrence, especially if there is stromal invasion. Stein and colleagues evaluated 768 men who underwent cystectomy without urethrectomy and found an overall risk of urethral recurrence of 7% at 5 years and 9% at 10 years. Median time to recurrence was 2 years. The risk increased from 5% with no prostate involvement on final pathology up to 18% for men with prostatic stromal invasion. CIS alone in the prostate carried an intermediate risk of 12% [22]. Others have found similar results [23]. In general carcinoma in situ in the bladder does not seem to predict subsequent urethral recurrence. Djaladat et al. noted that prostatic stromal invasion was highly associated with positive lymph nodes. In 1553 male patients who underwent cystectomy, prostatic stroma invasion was found on final pathology in 156, and 62% of those also had positive nodes. Of the 33 men with pT4aN0 disease who underwent neobladder reconstruction, surprisingly, urethral recurrence was detected in only 2 (6%) with a median follow-up of almost 5 years [24].

There has been some suggestion that orthotopic diversion could actually protect against urethral recurrence in men. In both the USC (Stein et al.) and Mayo Clinic (Boorjian et al.) series, men who had orthotopic diversion had about a 50% decreased risk of subsequent urethral recurrence even with prostatic stromal invasion [22, 23].

Patients with known prostatic stromal invasion are sometimes encouraged to undergo concomitant urethrectomy at the time of cystectomy. Because of the high probability of nodal involvement, they should be offered neoadjuvant chemotherapy. Those who are very highly motivated to have a continent orthotopic diversion must understand the risk and the need for careful surveillance of the urethra with periodic cytology and urethroscopy. At our institution routine biopsy of the prostatic urethra is not performed as part of a transurethral resection if the mucosa looks normal because the overall benefit is unclear [25]. More commonly, unexpected stromal invasion is discovered on the final pathology after the neobladder has already been constructed. The impact of chemotherapy before or after surgery on the risk of urethral recurrence is unknown.

For women, there have been a number of careful pathologic studies of patients who underwent cystectomy with concomitant urethrectomy. These have identified the clinical risk factors that are predictive of urethral involvement with urothelial cancer [26, 27]. Tumor location at the bladder neck is the primary predictor. When constructing an orthotopic diversion in women, the urethra is divided just distal to the bladder neck, so it is logical that tumor at that location would be problematic. In the study by Stein and colleagues, approximately 50% of women with bladder neck involvement had extension to the urethra, but there were no skip lesions. This suggested that the intraoperative frozen section of the urethral margin could be reliably used for the final decision regarding preservation of the urethra. In addition, invasion of the cervix or anterior vaginal wall is the predictor of potential urethral involvement. In these two studies of over 400 patients, the presence of carcinoma in situ alone was not predictive of urethral involvement [26, 27].

Prospective studies have confirmed that using these criteria results in a very low risk of urethral recurrence after orthotopic diversion in women [28]. Ali-El-Dein and colleagues prospectively evaluated 180 women undergoing cystectomy and orthotopic diversion with 57 months median follow-up. Two developed urethral recurrence: one had a primary squamous cell cancer of the bladder and the other had urothelial carcinoma with carcinoma in situ of the trigone. In this series they only found uterine or cervical involvement in 1% of patients, which was suspected preoperatively in all patients based on imaging [29].

Locally Advanced Tumor Stage

Many urologists are hesitant to perform continent diversion in patients with locally extensive disease or nodal metastases. This is based on two factors: (1) concern about the possible impact of local recurrence on the diversion itself and (2) a belief that these patients are doomed to suffer distant recurrence and have a shortened life expectancy and will not benefit from the continent diversion.

In fact, local recurrence that affects a neobladder or continent cutaneous diversion is relatively rare, even in patients with locally advanced disease. In the USC study of over 1000 patients, the rate of pelvic recurrence ranged from 6% for patients with organ-confined disease to 13% for those with extravesical extension [30]. In addition, nearly 50% of patients with extravesical tumor extension and 30% of patients with lymph node-positive disease were still alive without evidence of disease 5 years following cystectomy. These results suggest that local recurrence even for patients demonstrating locally advanced or lymph node-positive disease is relatively infrequent, and a significant proportion of these patients will be long-term survivors and may benefit from continent diversion. In a recent update with a total of 1817 patients from the same institution and a median follow-up of 11.7 years, only 81 (4.5%) of patients had pelvic recurrence without distant metastases (Mitra and Colleagues, unpublished data).

If local tumor recurrence does develop in patients with an orthotopic diversion, only a minority will develop problems related to the urinary diversion itself. In a series of 357 male patients who underwent cystectomy and neobladder from Ulm, Germany, local recurrence interfered with the function of an orthotopic neobladder in only ten patients [31].

The presence of a continent diversion does not significantly impact the ability to tolerate systemic chemotherapy when that is required. A catheter is often placed during the hydration portion of the treatments and also decreases absorption of methotrexate from the bowel reservoir if that drug is being used. In addition, local radiation has been applied to patients with a neobladder and appears to be reasonably well tolerated, at least at moderate doses [32].

Shared Decision-Making

So how does a patient facing cystectomy chose among the three options for urinary diversion? For patients with an absolute or significant relative contraindication to continent diversion, an ileal conduit or cutaneous ureterostomy is the only option. That has accounted for a small percentage of the population to date. However, as we are increasingly taking care of older, sicker patients, this percentage has increased somewhat in recent years.

For the rest of the patients, there are several steps to the process of shared decision-making. The first step is education for the patient and the family regarding the pros and cons of each type of diversion. Patients may believe, for example, that the function of an orthotopic neobladder is identical to their native bladder or have been told

Table 1.1 Advantages and disadvantages of the three primary types of urinary diversion

Diversion type	Advantages	Disadvantages
All diversions	Drain kidneys effectively Made out of own bowel tissue	Mucous in urine Most are colonized with bacteria Risk of symptomatic infections Risk of kidney stones Ureteral strictures Metabolic complications
Ileal conduit	Simplest, quickest to perform Familiar to most surgeons Easiest for others to care for Only option if kidney function is poor	Must wear a bag on skin at all times High risk of parastomal hernia Problems with appliance fit, urine leak, skin irritation Stomal stenosis
Orthotopic neobladder	Only slightly longer surgery than conduit Void per urethra, most "natural" No external appliance or stoma	Initial significant incontinence, may not resolve Nighttime incontinence common long-term Most patients wear pads at least some of the time May require self-catheterization (men 10%, women >50%) Neobladder stones (uncommon)
Continent cutaneous diversion "Indiana pouch"	Dry immediately May be able to sleep through night No external appliance	Significantly longer surgery Have to catheterize to empty Risk of stoma problems – difficulty catheterizing or leak, about 20% Many urologists and ER physicians don't know how to manage complications Stones in reservoir

that everyone with a neobladder has to self-catheterize. Table 1.1 highlights the advantages and disadvantages of each type of diversion that we review with patients and their families. Information regarding the actual incidence of specific complications (such as the requirement to self-catheterize for neobladder patients) may be helpful. Each type of diversion requires learning new processes and adaptation in lifestyle in the first few months after surgery. Most studies have shown similar rates of serious early complication for the three types of diversion, but there are more differences in the incidence and specific types of late complications for each one.

Second, patients and their families need help to identify their own priorities and tolerance for the disadvantage of each type of diversion. This is an iterative process as they understand the pros and cons and try to prioritize those for themselves. This may require several discussions over time. Providing written materials, encouraging patients to talk to others who have been through the various procedures, and encouraging open family discussions are all helpful. It is also useful to have a trained physician extender who can help answering specific questions and guide the patient through the process.

Finally, it is important that we physicians recognize how much our own bias can influence the decision. Physicians are trained to be persuasive, and it is relatively easy to influence patients' decisions just based on how the options are presented to them and the inflections of the advice delivered. There are marked differences in the rate of continent diversion at various institutions, even at those with specialists who have extensive experience in continent diversion [33]. Nationally less than 20% of patients undergo continent diversion, compared to 60–75% at some high-volume centers [34]. One center reported a marked decrease in continent diversion over a 5-year timespan, almost certainly reflecting physician bias rather than any radical difference in their patient population [35]. Many urologists today have had little exposure to continent diversion in training or after and may not want to refer the patient out to a center where that option may be offered [36]. There is also a significant financial disincentive for surgeons to perform a procedure that takes extra time when there is not a concomitant increase in reimbursement [37].

Conclusions

Continent urinary diversion is not new or experimental and should be considered as a potential option for each patient undergoing cystectomy and urinary diversion. There are few absolute contraindications which only exclude a minority of patients undergoing cystectomy today. The ultimate decision about the best diversion for a specific patient requires consideration of both cancer-related and patient-related factors and requires truly shared decision-making between patients, their physicians, and their families.

References

1. Hautmann RE, Paiss T. Does the option of the ileal neobladder stimulate patient and physician decision toward earlier cystectomy? J Urol. 1998;159:1845.
2. Gerharz EW, Mansson A, Hunt S, Skinner EC. Quality of life after cystectomy and urinary diversion: an evidence based analysis. J Urol. 2005;174:1729–36.
3. Ahmadi H, Lee CT. Health-related quality of life with urinary diversion. Curr Opin Urol. 2015;25(6):562–9.
4. Hautmann RE, Abol-Enein H, Davidsson T, et al. International Consultation on Urologic Disease - European Association of Urology Consultation on Bladder Cancer 2012. Eur Urol. 2013;63(1):67–80.
5. Winters B, Cai J, Daneshmand S. Short-term change in renal function in patients undergoing continent versus non-continent urinary diversions. UroToday Int J. 2013;6(2):art 20.
6. Skinner EC, Fairey AS, Groshen S, Daneshmand S, Cai J, Miranda G, Skinner DG. Randomized trial of Studer Pouch versus T-pouch orthotopic ileal neobladder in bladder cancer patients. J Urol. 2015;194(3):433–40.
7. Eisenberg MS, Thompson RH, Frank I, et al. Long-term renal function outcomes after radical cystectomy. J Urol. 2014;191(3):619–25.
8. Ashley MS, Daneshmand S. Factors influencing the choice of urinary diversion in patients undergoing radical cystectomy. BJU Int. 2010;106(5):654–7.
9. Hautmann RE, de Petriconi RC, Volkmer BG. Lessons learned from 1000 neobladders: the 90 day complication rate. J Urol. 2019;184:990–4.
10. Navon JD, Wong AK, Weinberg AC, et al. A comparative study of posteropative complications associated with the modified Indiana pouch in elderly versus younger patients. J Urol. 1995;154:1325–8.

11. Sogni F, Brausi M, Frea B, et al. Morbidity and quality of life in elderly patients receiving ileal conduit or orthotopic neobladder after radical cystectomy for invasive bladder cancer. Urology. 2008;71:919–23.
12. Ahmadi H, Skinner EC, Simma-Chiang V, Miranda G, Cai J, Penson DF, Daneshmand S. Urinary functional outcome following radical cystoprostatectomy and ileal neobladder reconstruction in male patients. J Urol. 2013;189(5):1782–8.
13. Bartsch G, Daneshmand S, Skinenr EC, Syan S, Skinner DG, Penson DF. Urinary functional outcomes in female neobladder patients. World J Urol. 2014;32(1):221–8.
14. Ali-El-Dein B, Gomha M, Ghoneim MA. Critical evaluation of the problem of chronic urinary retention after orthotopic bladder substitution in women. J Urol. 2002;168:587.
15. Gross T, Mejerhans Ruf SD, Meissner C, et al. Orthotopic ileal neobladder substitution in women: factors influencing urinary continence and hypercontinence. Eur Urol. 2015;68(4):664–71.
16. Skinner EC, Comiter CV. Can we improve the functional outcomes of orthotopic diversion in women? Eur Urol. 2015;68(4):672–3.
17. Ali-El-Dein B, Mosbah A, Osman Y, El-Tabey N, Abdel-Latif M, Eraky I, Shaaban AA. Preservation of the internal genital organs during radical cystectomy in selected women with bladder cancer: a report on 15 cases with long-term follow-up. Eur J Surg Oncol. 2013;39(4):358–64.
18. Eisenberg MS, Dorin RP, Bartsch G, Cai J, Miranda G, Skinner EC. Early complications of cystectomy after high dose pelvic radiation. J Urol. 2010;184(6):2264–9.
19. Abbas F, Biyabani SR, Talati J. Orthotopic bladder replacement to the urethra following salvage radical cystoprostatectomy in men with failed radiation therapy. Tech Urol. 2001;7:20–6.
20. Huang EY, Skinner EC, Boyd SD, Cai J, Miranda G, Daneshmand S. Radical cystectomy with orthotopic neobladder reconstruction following prior radical prostatectomy. World J Urol. 2012;30(6):741–5.
21. Simma-Chiang V, Ginsberg DA, Teruya KK, Boyd SD. Outcomes of artificial urinary sphincter placement in men after radical cystectomy and orthotopic urinary diversions for the treatment of stress urinary incontinence: the University of Southern California experience. Urology. 2012;69(6):1397–401.
22. Stein JP, Clark P, Miranda G, et al. Urethral tumor recurrence following cystectomy and urinary diversion: clinical and pathological characteristics in 768 male patients. J Urol. 2005;173:1163.
23. Boorjian SA, Kim SP, Weight CJ, Cheville JC, Thapa P, Frank I. Risk factors and outcomes of urethral recurrence following radical cystectomy. Eur Urol. 2011;60(6):1266–72.
24. Djaladat H, Mitra AP, Miranda G, Skinner EC, Daneshmand S. Radical cystectomy and orthotopic urinary diversion in male patients with pT4a urothelial bladder carcinoma: oncological outcomes. In J Urol. 2013;20(12):1229–33.
25. Donat SM, Wei DC, McGuire MS, Herr HW. The efficacy of transurethral biopsy for predicting the long-term clinical impact of prostatic invasive bladder cancer. J Urol. 2001;165:1580.
26. Stein JP, Cote RJ, Freeman JA, et al. Indications for lower urinary tract reconstruction in women after cystectomy for bladder cancer: a pathological review of female cystectomy specimens. J Urol. 1995;154:1329.
27. Stenzl A, Draxl H, Posch B, et al. The risk of urethral tumors in female bladder cancer: can the urethra be used for orthotopic reconstruction of the lower urinary tract? J Urol. 1995;153:950.
28. Stein JP, Penson DF, Lee C, Cai J, Miranda G, Skinner DG. Long-term oncological outcomes in women undergoing radical cystectomy and orthotopic diversion for bladder cancer. J Urol. 2009;181(5):2052–8.
29. Ali-El-Dein B, Abdel-Latif M, Ashamallah A, et al. Local urethral recurrence after radical cystectomy and orthotopic bladder substitution in women: a prospective study. J Urol. 2004;171:275.
30. Stein JP, Lieskovsky G, Cote R, et al. Radical cystectomy in the treatment of invasive bladder cancer: long-term results in 1,054 patients. J Clin Oncol. 2001;19:666.

31. Hautmann RE, Simon J. Ileal neobladder and local recurrence of bladder cancer: patterns of failure and impact on function in men. J Urol. 1999;162:1963.
32. Formenti SC, Keren-Rosenberg S, Crocitto L, Skinner D, Petrovic Z. Radiosensitivity of Kock ileal reservoir. Int J Radiat Oncol Biol Phys. 1997;39(5):1053–7.
33. Hautmann RE, Abol-Enein H, Lee CT, Mansson W, Mills RD, Penson DF, Skinner EC, Studer UE, Thueroff JW, Volkmer BG. Urinary diversion: how experts divert. Urology. 2015;85(1):233–8.
34. Kim SP, Shah ND, Weight CJ, Thompson RH, Wang JK, Karnes J, Han LC, Ziegenfuss IF, Tollefson MK, Boorjian SA. Population-based trends in urinary diversion among patients undergoing radical cystectomy for bladder cancer. BJU Int. 2013;112(4):478–84.
35. Lowrance WT, Rumohr JA, Clark PE, Chang SS, Smith Jr JA, Cookson MS. Urinary diversion trends at a high volume, single American tertiary care center. J Urol. 2009;182(5):2369–74.
36. Chang SS, Smith Jr JA, Herrell SD, Cookson MS. Assessing urinary diversion experience in urologic residency programs-are we adequately training the next generation? J Urol. 2006;176(2):691–3.
37. Skinner EC. Choosing the right urinary diversion: patient's choice or surgeon's inclination? Urol Oncol. 2011;29:473–5.

Orthotopic Urinary Diversion in Men

2

Siamak Daneshmand

Introduction

Although the ileal conduit remains the most commonly performed urinary diversion around the world, it is estimated that more than 80% of men undergoing urinary diversion are candidates for an orthotopic diversion [1]. Indications for orthotopic diversion have been covered in a previous chapter and will not be discussed again here. Even at bladder cancer centers of excellence, there is significant disparity in rates of continent diversion. Reasons for this variation include surgeon experience, philosophy, and commitment to management of subsequent complications. Misconceptions regarding the functional outcomes and complications can also heavily influence the discussion with patients regarding choice of diversion [2]. In a study examining the choice of urinary diversion within the framework of a standardized preoperative counseling, only 6% of patients who were eligible for a continent urinary diversion chose to undergo an ileal conduit for personal reasons [3]. Many patients are reluctant to undergo radical cystectomy when they believe they need a urostomy. Offering orthotopic diversion may indeed encourage patients to undergo more timely cystectomy. One study documented significant higher 5-year survival rates in patients undergoing orthotopic neobladders compared to an ileal conduit. At several pioneering institutions including ours, the orthotopic neobladder remains the gold standard form of urinary diversion following radical cystectomy. Orthotopic diversions rely heavily on a functional external urethral sphincter to prevent incontinence; however, other factors such as pouch size and compliance also play a role in maintaining continence. An ideally functioning orthotopic urinary diversion will allow the patient to void volitionally several times a day and store urine at low pressures at night. In general, some form of Valsalva maneuver is required to empty the reservoir. In this chapter we will mainly review the techniques of orthotopic urinary

S. Daneshmand, MD
Institute of Urology, Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA, USA
e-mail: daneshma@med.usc.edu

S. Daneshmand (ed.), *Urinary Diversion*, DOI 10.1007/978-3-319-52186-2_2

diversion and discuss modern postoperative management focusing on enhanced recovery protocols. Complications related to orthotopic diversion are covered in another chapter.

Preoperative Preparation

Preparation of the Urethra During Radical Cystectomy

Apical dissection of the prostate and urethral complex is of critical importance in order to ensure optimal functional outcomes. Once the bladder has been completely freed and mobilized posteriorly, attention is then directed anteriorly to the pelvic floor and urethra. All fibroareolar tissue between the anterior bladder wall and prostate is dissected away from the pubic symphysis. The endopelvic fascia is incised adjacent to the prostate and the levator muscles are carefully swept off the lateral and apical portions of the prostate. If nerve sparing is to be performed then the lateral prostatic fascia is incised and the neurovascular bundles are gently peeled off the prostate. The superficial dorsal vein is identified, ligated, and divided. With tension placed posteriorly on the prostate, the puboprostatic ligaments are identified and incised. The dorsal venous complex is ligated and divided. The apex of the prostate and membranous urethra should then become visible. The urethra is then incised anteriorly and laterally right at the apex of the prostate. Six 2-0 polyglycolic acid sutures are placed in the anterior urethra, carefully incorporating only the mucosa and submucosa of the striated urethral sphincter muscle anteriorly. Following this, two posterior urethral sutures are placed, incorporating the rectourethralis muscle or the caudal extent of Denonvilliers' fascia. The posterior urethra can then be divided and the bladder is removed. It is critical to perform a frozen section of the distal urethral margin to exclude tumor involvement.

Orthotropic Neobladder Reconstruction

Most ileal reservoirs use 60 to 75 cm of the terminal ileum, which is detubularized and folded in a variety of ways to recreate the native bladder's spherical shape. There are numerous types of neobladders described in various textbooks which include variations in the folding technique, location of the ureteroileal anastomosis and presence or absence of an antireflux mechanism. The pouch should be closed with absorbable sutures and metal staples should be avoided to prevent stone formation [4]. The two most common forms of urinary diversion around the world are the Hautmann "W" and the Studer neobladders with the various modifications. Both afford a low pressure reservoir with a refluxing ureteroileal anastomosis and have been associated with excellent functional outcomes. The T pouch and extraserosal tunnel techniques may be advantageous when an antireflux mechanism is desired or necessary.

Hautmann Neobladder

This ileal neobladder was developed by Hautmann and colleagues and is a large-capacity, spherical (W configuration) reservoir that attempts to optimize initial volume and potentially reduce nighttime incontinence [5]. An approximately 70 cm of the distal ileum is isolated, the bowel continuity is restored and the mesenteric trap is closed. The ileal section that reaches the urethra most easily is identified and marked with a traction suture along the antimesenteric border. The isolated bowel segment is then arranged in a "W" shape and is opened along the antimesenteric border except for a 5-cm section along the traction suture where the incision is curved to make a U-shaped flap. The four limbs W are then sutured to one another with a running absorbable suture. A small full-thickness segment of bowel is excised in the site for the urethral anastomosis, which is then performed with the sutures tied from inside the neobladder. After the neobladder is brought down to the pelvis and the urethral sutures are secured, the ureters are implanted from inside the neobladder through a small incision in the ileum. The remaining portion of the anterior wall is then closed with a running absorbable suture.

Initially Hautmann used an antireflux ureteral anastomosis; however, due to the incidence of ureteroileal strictures, the author modified this technique to a freely refluxing, open end-to-side anastomosis implanted into short tubularized segments at each end of the W. This resulted in a decrease in ureteroileal stenosis from 9.5% to 1% [6].

The Hautmann pouch has a larger initial capacity than the Studer pouch, which has been attributed to earlier and improved nighttime continence. Nocturnal incontinence rates are subject to variation in reporting, patients' sleep patterns, and desire to stay dry overnight vis-a-vis getting uninterrupted sleep. The physiology of incontinence at night includes increased nocturnal urine production, absent sensation of fullness, and lack of physiological storage and feedback reflexes. Continence does indeed depend on the functional characteristics of the reservoir; however, most smaller ileal reservoirs provide a low pressure system and reservoir capacity of over 500 cc after a few months. Despite the fact that most patient ultimately end up with a large, low pressure reservoir, nocturnal continence rates vary widely and are typically not related to pouch size. A comparison of the two different neobladders in one study showed similar continence with over 50% nocturnal incontinence [7].

Modified Studer Pouch

The technique of the neobladder construction in this chapter will focus on a slight modification of the Studer pouch. This ileal reservoir was initially described by Studer and colleagues and included a long, afferent, isoperistaltic, tubular ileal segment. The afferent limb functions to decrease significant vesicoureteral reflux when the patient voids by Valsalva maneuver. Its ease of construction has led this to become one of the most popular form of orthotopic diversion in the United States.

The reservoir portion uses the optimal double-folded U configuration as originally described by Kock. Studer and his group reported on 480 procedures performed over a 20-year period with excellent long-term results in terms of continence, preservation of renal function, and less than 3% ureteroileal stricture rate [8].

The terminal portion of the ileum (54–56 cm long is isolated approximately 15–20 cm proximal to the ileocecal valve). The distal mesenteric division is made along the avascular plane between the ileocolic artery and terminal branches of the superior mesenteric artery. The proximal mesenteric division, however, is short and provides a broad vascular blood supply to the reservoir. In addition, a small window of mesentery and 5 cm of small bowel proximal to the overall ileal segment are discarded, ensuring mobility to the pouch and small bowel anastomosis (Fig. 2.1). A standard side-to-side, functional end-to-end bowel anastomosis is performed using staplers.

The reservoir is constructed from 40 to 44 cm of distal ileum with each limb of the "U" measuring 20–22 cm, and a proximal 15 cm segment of ileum used as the afferent limb. If ureteral length is short or compromised, a longer afferent ileal segment (proximal ileum) may be used. The proximal end of the isolated afferent ileal segment is closed with absorbable suture. The isolated ileal segment is opened about 2 cm away from the mesentery (Fig. 2.2). The previously incised ileal mucosa is then oversewn with two layers of a running 3-0 polyglycolic acid suture starting at the apex and running upward to the afferent limb. The reservoir is then closed by folding it in half in the opposite direction to which it was opened (Fig. 2.3).

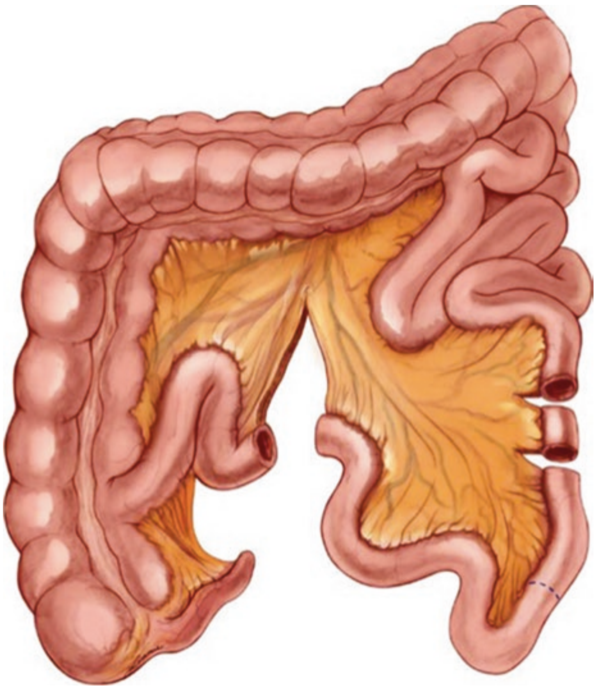


Fig. 2.1 Isolation of bowel segment

Fig. 2.2 Opening the isolated bowel segment

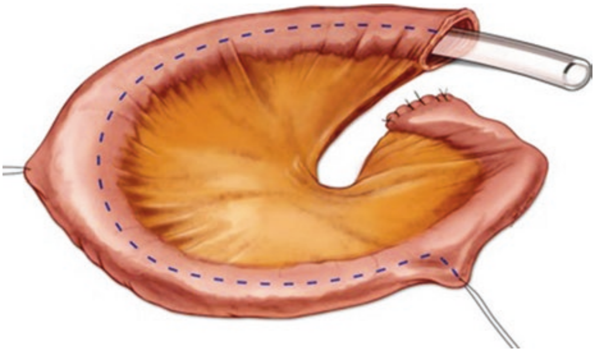
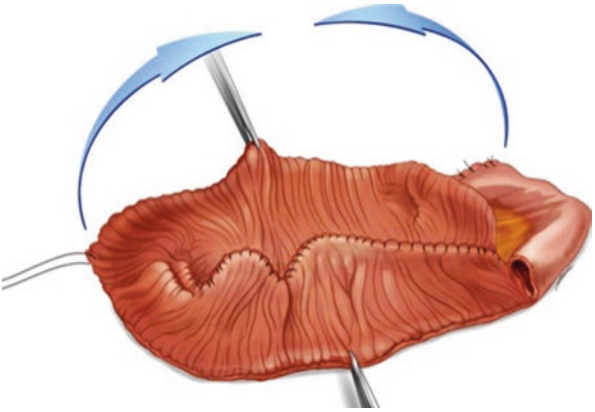


Fig. 2.3 Folding of the reservoir



T Pouch Modification

In an effort to preserve an antireflux mechanism but avoid the potential long-term complications seen with the Kock nipple valve, the T pouch was developed via a modification of Ghoneim and Abol-Enein's serous-lined ureteral tunnel [9]. Similar to the Studer neobladder, the T pouch contains a 15 cm antirefluxing afferent limb. The ileum is divided between the proximal afferent ileal segment and the 44-cm segment, and the antireflux mechanism is created by anchoring the distal 3–4 cm of the 15 cm afferent ileal segment into the serosal-lined ileal trough formed by the base of the two adjacent 22-cm ileal segments. Mesenteric windows are opened between the vascular arcades on the T-limb (Fig. 2.4a). A series of 3-0 silk sutures are then used to approximate the serosa of the two adjacent 22-cm ileal segments at the base of the "U" with the sutures being passed through the previously opened windows of Deaver to anchor the afferent limb. Initial descriptions of the T pouch included tapering the distal portion of the afferent segment after it had been fixed into the tunnel to decrease its diameter and decrease the risk of reflux. However, these efforts appeared to be associated with occasional late stenosis of the end of the afferent valve. In 2004 we stopped tapering the distal afferent limb with improved results. When the incision in the "U" limb of reservoir reaches the level of the afferent ostium, it is extended directly lateral to the antimesenteric border of the ileum

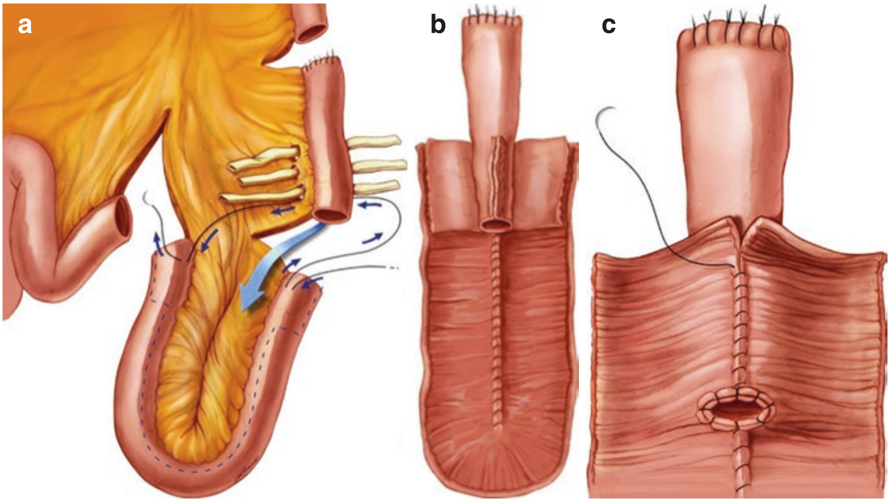


Fig. 2.4 (**a**) Mesenteric windows are opened between the vascular arcades on the T-limb. (**b**) Construction of the antirelux mechanism using a flap-valve technique. (**c**) Anastomosis of the ileal flaps to the afferent ileal limbtion

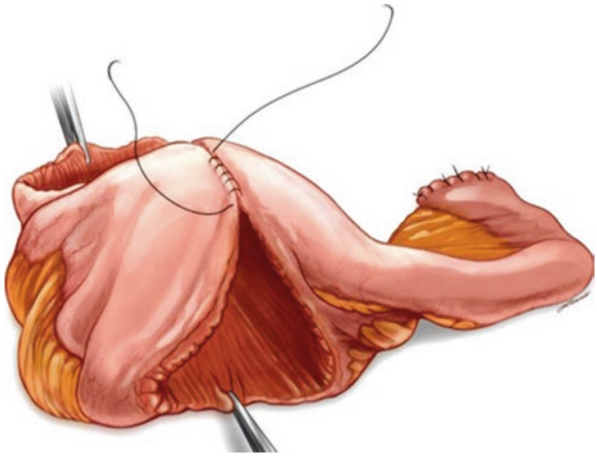


Fig. 2.5 Closure of the anterior wall of the neobladder. Note the neobladder neck at the end of the suture line is left open for the urethral anastomosis

and carried upward (cephalad) to the base of the ileal segment. This incision provides wide flaps of ileum that are brought over the afferent ileal segment and sutured in two layers to create the antireflux mechanism in a flap-valve technique (Fig. 2.4b). An interrupted mucosa-to-mucosa anastomosis is then performed between the ostium of the afferent ileal limb and the incised intestinal ileal flaps with 3-0 polyglycolic acid sutures (Fig. 2.4c). The rest of the neobladder is constructed in the same fashion as the Studer pouch.

Once the reservoir is folded in half, the anterior wall is closed with a two-layer 3-0 polyglycolic acid suture that is watertight. Note that the anterior suture line is stopped just short of the (patient) right side to allow insertion of an index finger, which will become the neobladder neck (Fig. 2.5). Conversely, a new hole can be

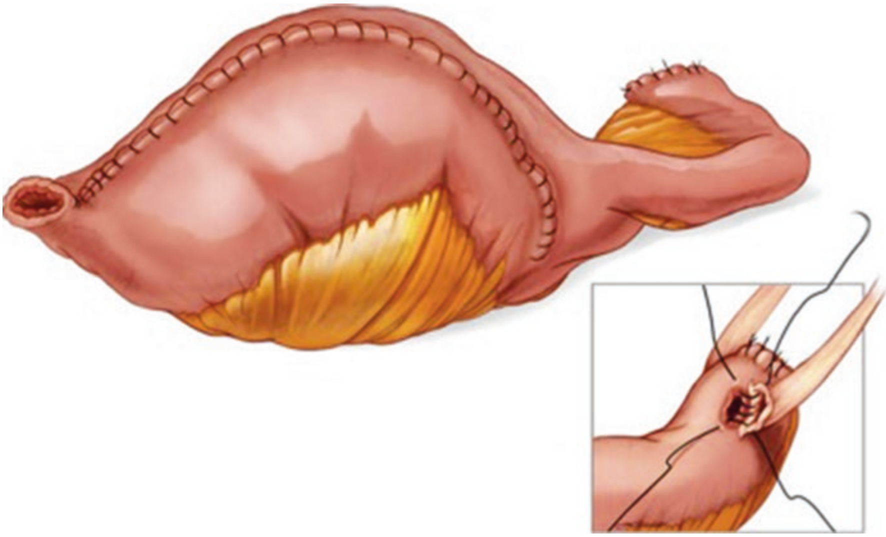


Fig. 2.6 Ureteroileal anastomosis

created at the most mobile and dependent portion of the reservoir as originally described by Studer. Although thought to decrease folding that can occur at the neck of the bladder leading to functional obstruction, urinary retention rates appear to be similar with both techniques [10]. Each ureter is spatulated and a standard bilateral end-to-side ureteroileal anastomosis is performed using interrupted 4-0 polyglycolic acid suture (Fig. 2.6). The reservoir is anastomosed to the urethra using the previously placed urethral sutures (Fig. 2.7).

Perioperative Management

Radical cystectomy and urinary diversion remains one of the most complex urologic operations. Most patients are elderly and have significant comorbidities including long-term tobacco use. Thorough preoperative evaluation and counseling is critical in ensuring optimal outcomes and reducing complications. Many patients will require cardiac clearance particularly if there is a significant smoking history. We adhere to the principles of enhanced recovery after surgery (ERAS) and have implemented a postoperative pathway that has led to a dramatic decrease in hospital length of stay to a median of 4 days [11]. We no longer recommend mechanical or antibiotic bowel preparation which leads to dehydration, alteration of normal bowel flora and electrolyte disturbances. Patients undergoing a preoperatively planned continent cutaneous reservoir using the colon however are given a mechanical bowel preparation in order to decrease the amount of stool present in the colonic segment being used. Several studies have shown no benefit to bowel preparation prior to radical cystectomy including gastrointestinal complications [12]. A meta-analysis on the utility of bowel preparation prior to colorectal surgeries showed no

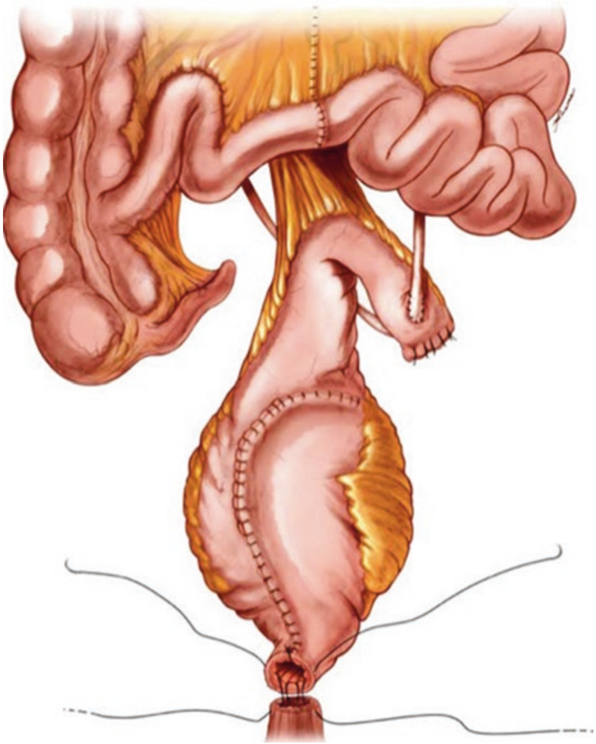


Fig. 2.7 Urethral anastomosis

difference in rates of wound infection, peritonitis, re-operation, or mortality [13]. In same token, nasogastric tube decompression is not necessary and in fact may increase complication rates rather than prevent aspiration or bowel leak [14]. In one study Inman et al. showed NGT decompression was actually associated with a prolonged time to gastrointestinal recovery and length of hospital stay [15]. Other studies have confirmed these findings, and in high volume centers, it is generally accepted that bowel resection can be safely performed without the use of postoperative nasogastric tube decompression [16, 17]. The meta-analysis performed by Cheatham et al. over 20 years ago confirmed the same findings in over 4000 and actually demonstrated a higher incidence of pulmonary complications with no clinical benefit [18]. Fasting and adhering to a clear liquid diet prior to surgery has again been the dogmatic approach to patients undergoing bowel resection and urinary diversion. Fasting however leads to insulin resistance and dehydration and in fact can increase postoperative complication rates. In fact evidence suggests that preoperative carbohydrate loading plays an important role in decreasing hospital stay by reducing insulin resistance [19]. We recommend use of high-protein, high-carbohydrate liquid drinks starting a few days prior to surgery. A regular diet is continued up until the night prior to surgery as per routine non-bowel surgery. Patients are directed toward a preoperative "cystectomy class" whereby they learn more about managing the various aspects of their upcoming surgery. Nurse specialists are involved and may be able to detect psychosocial barriers that may impede early recovery.

Patients are given alvimopan in the preoperative holding area about 1 h prior to surgery. Alvimopan is a mu opioid receptor antagonist that has been shown in multiple randomized trials to accelerate the return of bowel function following bowel resection. There are 5 multicenter double-blind randomized placebo-controlled trials including 1877 patients which have shown a decreased time to bowel function and hospital length of stay [20]. In patients undergoing radical cystectomy and urinary diversion a phase IV double-blind, placebo-controlled study again demonstrated the same benefit in decreasing time to bowel recovery leading to shorter hospital length of stay with a significant decrease in rates of ileus in the Alvimopan group (8.4% vs 29.1%; $p < 0.001$) [21].

Patients are also given subcutaneous heparin starting preoperatively in order to reduce the risk for venous thromboembolism. Patients are maintained on thrice daily subcutaneous heparin during the postoperative period and then discharged on prophylactic low molecular weight heparin. Intraoperatively, fluid intake is minimized and judicious use of colloids helps maintain intravascular volume. Every effort is made to minimize time under anesthesia and to decrease intraoperative blood loss including use of tissue sealants and fibrin products. Patients are given intravenous acetaminophen acetate as well as ketorolac (if adequate renal function) and opioid use is kept to a minimum. At the conclusion of the case, patients are transferred to a ward on telemetry unless there is an indication for admission to the ICU.

Postoperative Management

As previously mentioned we have adopted and evidence-based multimodal postoperative care pathway (enhanced recovery after surgery – ERAS) aimed at decreasing gastrointestinal complication rates and hospital length of stay. The pathway focuses on carbohydrate loading preoperatively, no bowel preparation, no postoperative nasogastric tube, focus on non-narcotic pain management, peripheral mu receptor opioid antagonist (alvimopan), use of neostigmine, and early feeding and ambulation. Sips of liquids (including high-carbohydrate, high-protein fluids) are started early on the afternoon or evening of surgery if tolerated up to a limit of 500 cc. Patients are started on a regular diet on postoperative day one provided they have no nausea, vomiting, or abdominal distention regardless of gas passage or bowel movement. Our "cystectomy diet" is designed for patients to improve tolerance post-surgery and to provide a high level of nutrients for healing. Foods known to cause bloating such as milk, raw fruits and vegetables, and high-fat foods are not included. Alvimopan is continued postoperatively and neostigmine and bisacodyl suppositories are administered to facilitate bowel function recovery. All of these medications are discontinued once the patient has a bowel movement. Additionally, a magnesium-based lactulose is started if there is no bowel function recovery by postoperative day 3. Proton pump inhibitor and H2 receptor blockers are used routinely for stress ulcer prevention and ondansetron and/or metoclopramide is administered for nausea and vomiting prophylaxis. Patients are asked to ambulate three times a day starting on postoperative day one.

If the patient has small volume emesis but is otherwise clinically stable and non-distended, we continue the same regimen but ask the patient to decrease their oral intake. Nasogastric tube decompression is only used for large volume, or repeated emesis or significant distention. If the patient is not tolerating oral food by 1 week postoperatively and/or there is no bowel activity, parenteral nutrition is considered.

Pain Management

Patients are given ketorolac (if renal function allows) and acetaminophen intravenously intraoperatively at the conclusion of the case. Para-incisional subfascial catheters are placed intraoperatively by the surgeon (positioned between the rectus muscle and the posterior rectus sheath) with constant local anesthetic (0.2% ropivacaine) release. Intramuscular ketorolac and oral acetaminophen are continued postoperatively for 48 h with opioid medication given for breakthrough pain. Use of postoperative opioids is minimized (while maintaining adequate pain control to reduce the chance of ileus). Opioid receptors are distributed throughout the gastrointestinal tract, and most opiates have mu receptor activity that inhibits gut motility and delays emptying [22]. As previously mentioned alvimopan helps to block these mu receptors and decrease ileus rates. We do use oral opioid pain medications starting postoperative day 1 with most patient being transitioned to oral analgesics only by POD 3–4.

Discharge and Postoperative Care

Discharge criteria include bowel activity, adequate pain control with oral medication, ability to ambulate, normal electrolytes, and adequate oral intake of at least 1 l in 24 h. Prophylactic antibiotics are also used for 3 weeks postoperatively although there is a lack of evidence for their efficacy. Patients are discharged on oral sodium bicarbonate replacement if there are signs of early hyperchloremic metabolic acidosis. Patients are generally sent home with the catheter and the drain with instructions to irrigate the catheter 3–4 times a day. They have a schedule postoperative follow-up 7–10 days following discharge for a check-up and laboratories. In order to ensure adequate hydration during the early post-discharge period and to decrease readmission for dehydration and electrolyte abnormalities, we arrange for patients to receive 1 l of intravenous fluid therapy at home through a short peripherally inserted central line. All patients are seen at 3 weeks postoperatively for removal of catheters, drains and stents, and pouch training.

Urinary Functional Outcomes

Urinary diversion with an orthotopic ileal neobladders provides a reservoir that most closely resembles the native bladder in capacity and function. However there orthotopic diversion involves is associated with variable continence rates. In general bladder stretch reflexes and filling sensation are no longer present, and most patients will need to empty based on timed voiding using voluntary sphincter relaxation, Valsalva maneuvers, and Crede maneuvers.

Daytime continence rates vary widely in the literature but are generally excellent, ranging from 80% to 98% [7, 8, 23–27]. Nighttime continence in these same studies range from 72% to 80%; however, almost all of these studies are retrospective in nature and rely on physician reported outcomes. We recently reported our continence outcomes in a prospective study of 188 male patients using a previously validated pictorial pad usage questionnaire. There were 351 continence questionnaires completed over a 3-year period with the majority of the patients undergoing a modified Studer type of diversion. Daytime continence peaked at 92% at 12–18 months postoperatively, while nighttime continence peaked at 51% at 18–36 months. Nearly half of patients were fully continent at both day and night by 18–36 months. Age over 65 and diabetes were associated with worse daytime continence. Only 10% of the patients reported clean intermittent catheterization at any time point in the postoperative period [10]. While the nighttime continence rates were lower than previously reports (including our own prior published work), the results are far more realistic and in line with what patients report. Further efforts are needed to understand mechanisms involved in nighttime continence and whether interventions (such as pelvic floor rehabilitation, use of medications) can possibly improve outcomes. It is important however to keep in mind that most patients who wear pads at night are satisfied with their continence since most report their pads are “almost dry” or “slightly wet.” Given its safety, efficacy and avoidance of external appliances and catheterization requirement, we believe the orthotopic neobladder offers the best overall functional outcome for patients undergoing cystectomy and urinary diversion.

Orthotopic Urinary Diversion in the Elderly

Elderly patients face a number of unique challenges in the selection, construction, and care of continent urinary diversion. Many patients over age 65 or 70 are not offered orthotopic diversion due to ambiguous reasons. Studies have shown that younger patients undergo continent urinary diversions at a significantly high rate than the elderly regardless of their preexisting medical condition. These factors contribute to rate of incontinent urinary diversion following radical cystectomy for the elderly that exceeds 80% nationwide [28]. Advanced age is often associated with an increased postoperative complication rate in most surgical disciplines; however, there are ample data available to suggest carefully selected elderly patients have similar outcomes to younger patient undergoing continent diversion [29–31]. When assessing for candidacy, consideration should be made for the physiologic, rather than chronologic, age. Advanced age in and of itself should not be a contraindication for orthotopic diversion, and many elderly patients can still enjoy the benefits of a continent reservoir. Lack of experience and misconception regarding complication rates and continence rates in the elderly lead many surgeons to suggest an incontinent diversion to elderly patients. In fact, elderly patients undergoing orthotopic diversion have no significant difference in early complications, late complications, or operative mortality than those undergoing incontinent diversion [32]. Complications of urinary diversion are covered in another chapter and are generally not any different for elderly patients, although the elderly generally do have lower physiologic reserves and are more prone to anorexia and malnutrition.

Continence data specifically for elderly neobladders patients is sparse but in selected patients appears to be similar to the younger group of patients [29–31]. Previous studies have reported that increasing age may be associated with inferior daytime continence due to a weakened urethral sphincter complex, impaired pelvic sensation, and decreased vigilance [33]. However, more recent data from centers of excellence has shown similar urinary function scores among carefully selected elderly patients undergoing neobladder when compared to their younger counterparts. Additionally, measures of urinary bother (odor, leakage, dysuria, hematuria) following neobladder reconstruction have also been shown to be equivalent across wide age range [34].

We recently reported our results on 221 elderly men who underwent a neobladder following radial cystectomy for bladder cancer. Complications directly related attributable to the neobladder occurred in approximately 10% of patients. During the daytime 62% were completely dry or leaked small amount less than once per day, while at night, 45% were completely dry or leaked less than once per night, which was comparable to the younger cohort [35]. As with any complex procedure, surgeon selection and patient participation are critical to long-term success.

Orthotopic Neobladder Reconstruction Following Prior Radical Prostatectomy

Radical cystectomy and orthotopic diversion following pelvic surgery poses a significant challenge for surgeons. Patients who have undergone prior radical prostatectomy have pelvic adhesions, and the urethral sphincter complex may already be compromised from the prior surgery. For better delineation of the urethrovesical junction, we advance a flexible cystoscopy during the bladder neck dissection in order to facilitate complete resection of bladder while preserving the remaining external sphincter. There are very few reports of orthotopic diversion following prior radical prostatectomy. In 2012, we reported on 24 patients who had a neobladder performed following prior radical prostatectomy. The types of neobladders reconstruction were Kock neobladder in 3, sigmoid reservoir in 1, Studer neobladder in 12, and T pouch ileal neobladder in 8 patients. Nineteen patients had adequate perioperative data available of whom 11 (57.9%) had good continence (0–1 pad/day) and regained the preoperative level of urinary control within 1 year. Four patients had an AUS placed at the time of cystectomy, while another 4 patients (20%) required placement of an artificial urethral sphincter (AUS) due to severe incontinence of whom 2 had significant baseline incontinence. Importantly, there were no neobladder neck anastomotic strictures [36]. Therefore, select patients who have undergone prior radical prostatectomy are still candidates for orthotopic diversion, and adequate results can be achieved.

Conclusion

There has been a significant improved understanding of factors influencing patient selection and outcomes following orthotopic diversion over the past decade. Majority of patients are candidates for orthotopic diversion and should be counseled or referred accordingly. In order to ensure optimal outcomes and patient satisfaction, patients should undergo thorough preoperative counseling, have realistic expectations and ideally have their surgery performed at an experienced center.

References

1. Hautmann RE, Abol-Enein H, Lee CT, Mansson W, Mills RD, Penson DF, et al. Urinary diversion: how experts divert. Urology. 2015;85(1):233–8.
2. Daneshmand S, Bartsch G. Improving selection of appropriate urinary diversion following radical cystectomy for bladder cancer. Expert Rev Anticancer Ther. 2011;11(6):941–8.
3. Ashley MS, Daneshmand S. Factors influencing the choice of urinary diversion in patients undergoing radical cystectomy. BJU Int. 2010;106(5):654–7.
4. Suriano F, Daneshmand S, Buscarini M. Use of nonabsorbable staples for urinary diversion: a step in the wrong direction. Urol Int. 2013;90(2):125–9.
5. Hautmann RE. Surgery illustrated – surgical atlas ileal neobladder. BJU Int. 2010;105(7):1024–35.
6. Hautmann RE, Volkmer BG, Schumacher MC, Gschwend JE, Studer UE. Long-term results of standard procedures in urology: the ileal neobladder. World J Urol. 2006;24(3):305–14.
7. Lee KS, Montie JE, Dunn RL, Lee CT. Hautmann and Studer orthotopic neobladders: a contemporary experience. J Urol. 2003;169(6):2188–91.
8. Studer UE, Burkhard FC, Schumacher M, Kessler TM, Thoeny H, Fleischmann A, et al. Twenty years experience with an ileal orthotopic low pressure bladder substitute –lessons to be learned. J Urol. 2006;176(1):161–6.
9. Stein JP, Skinner DG. Surgical atlas: the orthotopic T-pouch ileal neobladder. BJU Int. 2006;98(2):469–82.
10. Clifford TG, Shah SH, Bazargani ST, Miranda G, Cai J, Wayne K, et al. Prospective evaluation of continence following radical cystectomy and orthotopic urinary diversion using a validated questionnaire. J Urol. 2016;196(6):1685–91.
11. Daneshmand S, Ahmadi H, Schuckman AK, Mitra AP, Cai J, Miranda G, et al. Enhanced recovery protocol after radical cystectomy for bladder cancer. J Urol. 2014;192(1):50–5.
12. Raynor MC, Lavien G, Nielsen M, Wallen EM, Pruthi RS. Elimination of preoperative mechanical bowel preparation in patients undergoing cystectomy and urinary diversion. Urol Oncol. 2013;31(1):32–5.
13. Guenaga KF, Matos D, Wille-Jorgensen P. Mechanical bowel preparation for elective colorectal surgery. Cochrane Database Syst Rev. 2011;9:CD001544.
14. Maffezzini M, Campodonico F, Canepa G, Gerbi G, Parodi D. Current perioperative management of radical cystectomy with intestinal urinary reconstruction for muscle-invasive bladder cancer and reduction of the incidence of postoperative ileus. Surg Oncol. 2008;17(1):41–8.
15. Inman BA, Harel F, Tiguert R, Lacombe L, Fradet Y. Routine nasogastric tubes are not required following cystectomy with urinary diversion: a comparative analysis of 430 patients. J Urol. 2003;170(5):1888–91.
16. Park HK, Kwak C, Byun SS, Lee E, Lee SE. Early removal of nasogastric tube after cystectomy with urinary diversion: does postoperative ileus risk increase? Urology. 2005;65(5):905–8.
17. Vermeulen H, Storm-Versloot MN, Busch OR, Ubbink DT. Nasogastric intubation after abdominal surgery: a meta-analysis of recent literature. Arch Surg. 2006;141(3):307–14.

18. Cheatham ML, Chapman WC, Key SP, Sawyers JL. A meta-analysis of selective versus routine nasogastric decompression after elective laparotomy. Ann Surg. 1995;221(5):469–76. discussion 76-8
19. Ljungqvist O, Nygren J, Thorell A. Insulin resistance and elective surgery. Surgery. 2000;128(5):757–60.
20. Vaughan-Shaw PG, Fecher IC, Harris S, Knight JS. A meta-analysis of the effectiveness of the opioid receptor antagonist alvimopan in reducing hospital length of stay and time to GI recovery in patients enrolled in a standardized accelerated recovery program after abdominal surgery. Dis Colon Rectum. 2012;55(5):611–20.
21. Lee CT, Chang SS, Kamat AM, Amiel G, Beard TL, Fergany A, et al. Alvimopan accelerates gastrointestinal recovery after radical cystectomy: a multicenter randomized placebo-controlled trial. Eur Urol. 2014;66(2):265–72.
22. Barletta JF, Asgeirsson T, Senagore AJ. Influence of intravenous opioid dose on postoperative ileus. Ann Pharmacother. 2011;45(7–8):916–23.
23. Stein JP, Dunn MD, Quek ML, Miranda G, Skinner DG. The orthotopic T pouch ileal neobladder: experience with 209 patients. J Urol. 2004;172(2):584–7.
24. Hautmann RE, de Petriconi R, Gottfried HW, Kleinschmidt K, Mattes R, Paiss T. The ileal neobladder: complications and functional results in 363 patients after 11 years of follow-up. J Urol. 1999;161(2):422–7. discussion 7-8.
25. Steven K, Poulsen AL. The orthotopic Kock ileal neobladder: functional results, urodynamic features, complications and survival in 166 men. J Urol. 2000;164(2):288–95.
26. Abol-Enein H, Ghoneim MA. Functional results of orthotopic ileal neobladder with serous-lined extramural ureteral reimplantation: experience with 450 patients. J Urol. 2001;165(5):1427–32.
27. Daneshmand S. Orthotopic urinary diversion. Curr Opin Urol. 2015;25(6):545–9.
28. Gore JL, Saigal CS, Hanley JM, Schonlau M, Litwin MS. Variations in reconstruction after radical cystectomy. Cancer. 2006;107(4):729–37.
29. Sogni F, Brausi M, Frea B, Martinengo C, Faggiano F, Tizzani A, et al. Morbidity and quality of life in elderly patients receiving ileal conduit or orthotopic neobladder after radical cystectomy for invasive bladder cancer. Urology. 2008;71(5):919–23.
30. Saika T, Suyama B, Murata T, Manabe D, Kurashige T, Nasu Y, et al. Orthotopic neobladder reconstruction in elderly bladder cancer patients. Int J Urol. 2001;8(10):533–8.
31. Takenaka A, Soga H, Terakawa T, Kumano M, Furukawa J, Muramaki M, et al. Assessment of voiding function of orthotopic neobladders in elderly patients with long-term survival. BJU Int. 2009;103(7):927–30.
32. Clark PE, Stein JP, Groshen SG, Cai J, Miranda G, Lieskovsky G, et al. Radical cystectomy in the elderly: comparison of clinical outcomes between younger and older patients. Cancer. 2005;104(1):36–43.
33. Madersbacher S, Mohrle K, Burkhard F, Studer UE. Long-term voiding pattern of patients with ileal orthotopic bladder substitutes. J Urol. 2002;167(5):2052–7.
34. Ahmadi H, Skinner EC, Simma-Chiang V, Miranda G, Cai J, Penson DF, et al. Urinary functional outcome following radical cystoprostatectomy and ileal neobladder reconstruction in male patients. J Urol. 2013;189(5):1782–8.
35. Daneshmand S, Ashley MS. Continent urinary diversion in the elderly. Curr Geriatr Rep. 2015;4(1):1–6.
36. Huang EY, Skinner EC, Boyd SD, Cai J, Miranda G, Daneshmand S. Radical cystectomy with orthotopic neobladder reconstruction following prior radical prostatectomy. World J Urol. 2012;30(6):741–5.

3 Orthotopic Urinary Diversion in Women

Georgios Gakis

Anatomical Considerations for Orthotopic Bladder Substitution in Women

In order to understand the oncological and functional aspects of orthotopic urinary diversion in women, a profound knowledge about the anatomy of the female pelvic floor is important which is briefly described in this subchapter.

The female urethral sphincter consists of the internal urethral sphincter (IUS) and external urethral sphincter (EUS). The EUS consists of striated muscle fibers which are innervated by the pudendal nerve and can be divided into two portions. The superior horseshoe-like section covers the anterolateral aspects of the superior urethra and is opened at its dorsal part. The inferior part exhibits large "muscular wings" which cover both the lateral part of the inferior urethra and the lateral portion of the anterior vagina. Both parts of the EUS are not attached to the bony pelvis. Instead, a tendinous connection of the inferior EUS to medial portion of the levator ani muscle (LAM) exists. This "muscle-to-muscle" connection has implications for maintenance of sufficient urethral closing pressure.

The IUS consists of smooth muscle and covers basically circumferentially the superior urethra. It is thickest at its dorsal part. At the inferior urethral level, it covers only the anterolateral part but does not extend as far caudally as the inferior EUS. The superior EUS is covered laterally by a tendinous arch to the pelvic fascia which surrounds the puborectal muscle of the LAM. At its dorsal side, the superior EUS is connected to the anterior vaginal wall via connective tissue. As a result, proper function of the EUS for contraction and competent urethral closure depends on the integrity of the LAM. Contraction of the LAM results in a force that pulls the rectum and vagina (the

The author declares no conflicts of interest in relation to the contents of this book chapter.

G. Gakis, MD, FEBU
Department of Urology, Eberhard-Karls University Tuebingen, University Hospital of Tübingen, Hoppe-Seyler Street 3, D-72076 Tuebingen, Germany
e-mail: georgios.gakis@gmail.com

S. Daneshmand (ed.), *Urinary Diversion*, DOI 10.1007/978-3-319-52186-2_3

so-called rectovaginal complex) anteriorly and superiorly which, in turn, results in a compression of the dorsal aspect of the superior urethra. Simultaneous contraction of the EUS results in a force that compresses the urethra inferiorly and posteriorly. These forces bend the urethra in its mid part as the contraction of the EUS and LAM exerts parallel forces on different urethral levels. When the LAM is functionally impaired (i.e., its attachments to the pelvic wall), the fixation spots of the EUS become displaced, and dysfunction of the EUS can result [1]. By contrast to the EUS which is innervated by the pudendal nerve, the LAM has a dual somatic innervation by the levator ani nerve (LAN) as its constant and main supply with communicating branches between the levator ani nerve and pudendal nerve in half of the cases [2]. These basic anatomical considerations are of particular importance for urethral dissection during radical cystectomy (RC).

Oncological Prerequisites for Orthotopic Urinary Diversion in Women

At the end of the 1980s, OBS began to emerge as a modality of urinary diversion for men undergoing RC for bladder cancer [3]. Yet, at that time, it was not considered to be a viable option for women. Skepticism that persisted during that time was that the remaining urethral length was considered to be too short to provide sufficient urethral closing pressure. In addition, tumor multifocality and the anatomical proximity to the urethra and pelvic floor raised concerns about the risk of uncontrolled local disease in case of urethral recurrence.

Due to the pioneering efforts of urologic surgeons in the 1990s [4, 5], orthotopic ileal neobladder is nowadays considered an established option for women treated with RC [6]. Yet, risk assessment for tumor recurrence involving the neobladder outlet or urethra is still an important issue for preoperative counseling and clinical decision-making. Primary tumor location and local staging are the critical determinants for assessing the oncological safety of OBS in women. It has been demonstrated that location of the primary tumor at the bladder neck increases the risk of a positive urethral margin at RC [7]. Thus, women with bladder neck involvement at RC are nowadays counseled for a non-orthotopic bladder substitute when preoperative biopsy of the bladder neck reveals malignancy [8]. Yet, the question that derives from this, admittedly, well-accepted clinical practice is whether bladder neck involvement is an absolute contraindication for an OBS or the exact level of urethral dissection should rather dictate the intraoperative clinical decision-making for an OBS. Essentially, this question remains unanswered until today as robust evidence on this issue is absent. In order to accurately assess the distal urethral margin, frozen section analysis (FSA) may provide useful information. An important prerequisite for accurate diagnosis of malignancy on FSA is that the specimen was obtained by full-thickness biopsy in order to allow for a circumferential and in-depth assessment of the urothelial margin [6]. In women, urethral frozen sections were found to exhibit a high accuracy of 90% with a specificity of 99% when compared to the final histological result [9]. On the other hand, a previous histoanatomical study on female cystectomy specimens demonstrated that the degree of concordance between malignancy at the bladder neck and the level of urethral dissection was only 40% [7]. Urethral tumors were exclusively found in the proximal and mid-urethra, whereas the distal third was found to be free. Location of the primary tumor at the bladder neck correlated with higher grade and stage as well as with concomitant urethral malignancy. In addition, with increasing distance from the bladder neck, the risk of recurrence drops considerably. In a retrospective, multicenter series, the risk of urethral recurrence was assessed in 297 women who were treated with RC and OBS [10]. Women were excluded from OBS when primary tumors that were staged cT4b and/or cN3 or preoperatively showed involvement of the bladder neck or a positive urethral margin as intraoperatively assessed by FSA. Based on these selection criteria, the rate of solitary (0.8%) or concomitant urethral recurrence (1.6%) was very low, and the only risk factor associated with urethral recurrence was found to be a positive final urethral margin status at RC. Histological tumor and nodal stage were determinants for all-cause mortality but not for urethral recurrence. None of the patients with bladder trigone involvement developed urethral recurrence after a median of 64 months. These findings are in line with previous results from single-center studies with reported rates of urethral recurrence ranging between 0.8% and 1.2% [11, 12]. Therefore, based on the available evidence, it seems justified to consider an OBS even in women with trigonal involvement or non-bulky lymph node disease provided the urethral margin on frozen section is negative.

Functional Prerequisites for Orthotopic Urinary Diversion in Women

Ileal OBS aims to store urine at low pressure while enabling spontaneous micturition and continence. Besides oncological parameters, women scheduled for orthotopic bladder substitution need to be critically assessed for various functional criteria. Renal function should be investigated by estimation of glomerular filtration rate (eGRF) or measurement of 24 h creatinine clearance in equivocal cases. A GFR above 60 ml/min is generally accepted for replacing the bladder with an OBS [13–15]. Uncontrolled diabetes mellitus does not only increase the odds for postoperative complications after major surgery but may contribute to the long-term development of metabolic acidosis after ileal neobladder [16]. Baseline hypertension and episodes of acute pyelonephritis were found to independently increase the risk of renal deterioration after urinary diversion [17]. Therefore, measures should be taken for optimized management of perioperative blood pressure and antibiotic treatment in patients with preoperative upper urinary tract infections. Besides renal function, an unrestricted hepatic function is crucial to prevent uncontrollable hematuria postoperatively [18]. Increased post-void residual urine may result in metabolic acidosis and impaired renal function, especially in the early period after OBS. Therefore, it is mandatory to preoperatively exclude the presence of physical or mental disorders which would preclude the ability of patients to catheterize their reservoir if retention occurs. Likewise, women who suffer from severe stress urinary incontinence due to external sphincter deficiency and wish to preserve postoperative continence should rather be offered a heterotopic form of continent diversion [19]. Patient factors (i.e., biological age, prior radiotherapy) and the selection of the appropriate type of diversion are also important for optimized functional outcomes and quality of life after orthotopic ileal neobladder [6].

Considerations and Technique of Nerve-Sparing Radical Cystectomy in Women

Optimized functional results in women with OBS depend on the extent of preservation of neurovascular structures which are critical for an intact innervation of the urethra, vagina, and pelvic floor [20]. In women, the standard extent of RC encompasses the removal of the tumor-bearing bladder, uterus, adnexa, and anterior vaginal wall [21]. The urethra and most distal part of the anterior vaginal wall are in closest anatomical proximity (Fig. 3.1). Innervation and vascularization occurs via nerves and vessels which traverse along the anterior and lateral aspects of the vagina [20]. When oncologically safe, preservation of these structures will result in superior functional outcomes [22]. As outcomes of orthotopic urinary diversion depend strongly on the technique of cystectomy, a detailed description of a technique encompassing nerve-sparing radical cystectomy with posterior neobladder support is outlined:

1st: Longitudinal midline abdominal incision between the pubic symphysis and the umbilicus with incision of the fascia and dissection of rectus abdominis muscle.

2nd: Opening of the transversal fascia and blunt dissection of Retzius space to enter the paravesical space bilaterally.

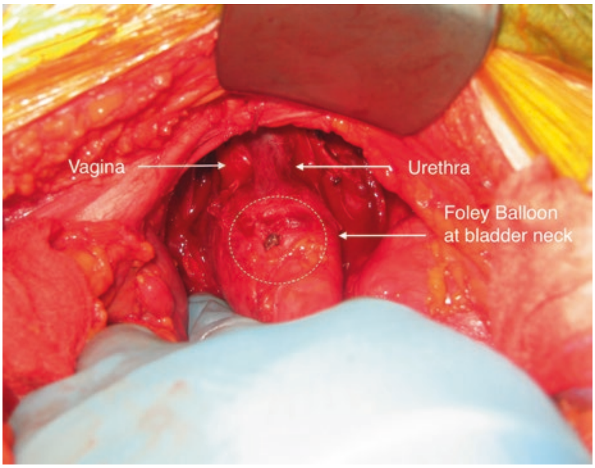


Fig. 3.1 Demonstration of the location of the cather ballon in relation to the pelvic floor and vagina *(Courtesy of Siamak Daneshmand, M.D.)*

3rd: V-shaped incision of the bladder peritoneum followed by dissection and ligation of the round ligament.
Landmark: Round Ligament
(Info: Preservation of maximal length of the round ligaments for suspension of the vagina later on.)

4th: Continuation of the peritoneal incision along the external and common iliac vessels up to the promontorium.

5th: Performance of pelvic lymphadenectomy up to the crossing of the ureters with common iliac vessels.
Landmark: Ureter
(Info: In case of normal findings on cross-sectional imaging lymph node dissection in the presacral region is discouraged to avoid injury of autonomous nerve fibers which traverse along the interval iliac artery and its branches to the cervix and vaginal walls [23]).

6th: Lateral division with identification of the ureters at their crossing with the common iliac vessels.
(Info: In order to preserve blood supply to the ureters, their fascial sheet should stay intact. This can be achieved by mobilization of all the tissue adjacent to the peritoneum toward the ureter.)

7th: Preparation of the ureters toward the bladder and ligation ca. 2–3 cm proximally to the ureteral orifice. A circumferential biopsy of both ureteral stumps should be sent to frozen section analysis [21].
(*Info: Clipping of distal end of ureters results in temporary hydrodistention which facilitates ureteroileal anastomosis later on.)*

8th: Ligation of the anterior pedicles as distally as possible (if oncologically possible) to minimize dissection of neurovascular structures with traverse along the branches of the internal iliac artery.
Landmark: Sacrouterine Ligament

9th: Identification of the lateral vaginal walls and posterior vaginal fornix.
(Info: Compression of the posterior vaginal fornix by an intravaginally placed curved sponge facilitates its anatomical identification.)

Landmark: Cul-de-Sac
10th: Identification and incision of the vaginal fornix at the level of cul-de-sac.

Info: Compression of the posterior vaginal fornix by an intravaginally placed curved sponge facilitates its anatomical identification (Fig. 3.2).

11th: Opening of the posterior vaginal fornix and identification of the cervix (Fig. 3.3).
Landmark: Cul-de-Sac and Cervix

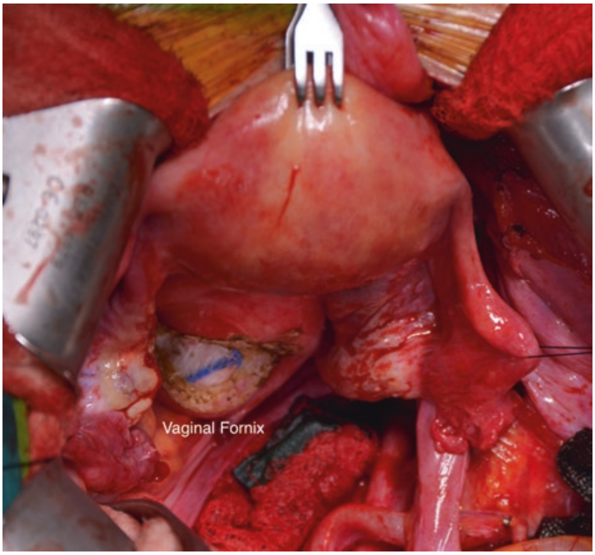


Fig. 3.2 View at the vaginal fornix after incision at the level of cul-de sac *(Courtesy of Siamak Daneshmand, M.D.)*

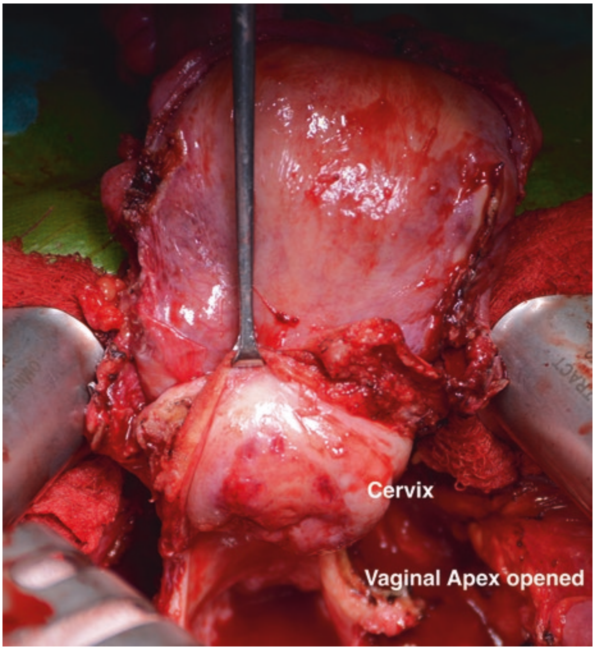


Fig. 3.3 This illustration shows the cervix and opened vaginal apex during dissection of the lateral vaginal wall *(Courtesy of Siamak Daneshmand, M.D.)*

12th: Continued dissection of the anterior from the lateral vaginal walls.
(Info: Identification and separation of the lateral vaginal walls from the bladder wall can be facilitated by continuous digital replacement of the catheter balloon during dissection. Ligation and dissection of the lateral from the anterior vaginal

wall using hook clamps are preferred; electrocautery should be avoided whenever possible as it may result in damage of autonomic nerve fibers.)

13th: When dissection of the anterior vaginal wall has reached the bladder neck on both sides, a hook clamp is introduced posteriorly to the bladder neck and gently crossed to the opposite side.

(Info: Retraction of balloon catheter toward distal aids in the identification of the bladder neck.)

14th: Transverse transection of the distal end of the anterior vaginal wall.

(*Info: A distance of at least 1.5–2 cm proximal to the level of urethral dissection should be met in order to prevent overlapping of the suture lines and decrease the risk of a neobladder-vaginal fistula formation. In vaginal-sparing cystectomy, the bladder is carefully separated from the anterior vaginal wall after opening the posterior vaginal fornix (Fig. 3.4).)*

15th: Visualization of the endopelvic fascia.

(*Info: Dissection should be avoided below the level of the endopelvic fascia.)*

16th: Ligation of the pubovesical complex by passing a clamp underneath the plexus and anteriorly to the urethra.

17th: Sharp dissection of the pubovesical complex from the bladder neck. Now the anterior aspect of the bladder neck and urethra can be visualized.

18th: Removal of the catheter slowly in order to accurately identify the transition area between the bladder neck and urethra.

19th: A smooth clamp is placed at the level of urethral dissection and the procedure completed by sharp dissection of the anterior and posterior urethra (Fig. 3.5).

(*Info*: A full-thickness biopsy of the urethra should be sent to frozen section analysis.)

20th: Closure of the anterior vaginal wall is performed initially by anchoring the long remnants of the round ligaments to the most lateral aspect of the vaginal opening.

(*Info: This approach suspends the vaginal neofornix cranially and serves as anchoring point for the omental flap which will be placed later on onto the anterior vaginal wall to prevent backfall of the reservoir.)*

21st: The vagina is closed symmetrically in a traverse manner using locked polyglactin sutures.

(*Info: This technique will avoid narrowing the vaginal lumen and decrease the risk of postoperative dyspareunia.)*

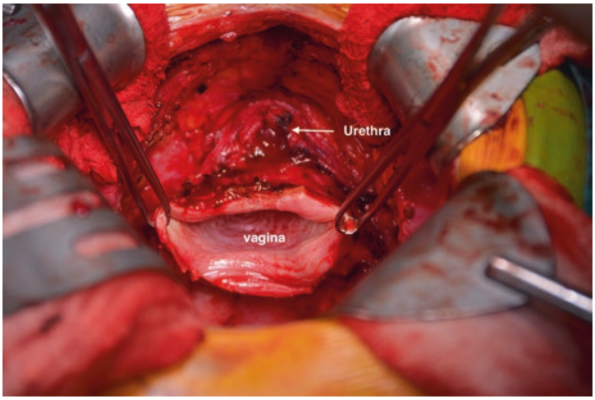


Fig. 3.4 Intrapelvic view demonstrating the level of urethral and anterior vaginal dissection. Please note anatomical distance between the two levels *(Courtesy of Siamak Daneshmand, M.D.)*

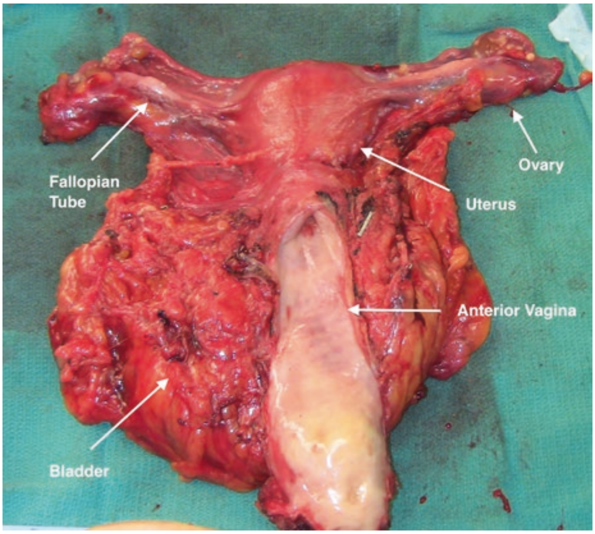


Fig. 3.5 Longitudinal view on the en bloc specimen comprising bladder, uterus, anterior vagina, ovaries and fallopian tubes *(Courtesy of Siamak Daneshmand, M.D.)*

22nd: Isolation of an adequate ileal length with ileoileal anastomosis and formation of an I-Pouch neobladder reservoir (or creation of other ileal neobladder reservoirs according to other techniques [24–28]).

23rd: Mobilization of an omental flap (if available) along the left paracolic trough into the pelvis with fixation to the round ligament and anterior vaginal wall.

(Info: Preservation of vascular supply of the omental flap is mandatory.)

24th: Creation of an opening in the most dependent part of the omental flap at the urethral opening.

(*Info: This approach helps to further separate the suture lines of the vaginal reconstruction and urethro-ileal anastomosis, thereby preventing fistula formation.)*

25th: After performance of urethro-ileal anastomosis, closure of the lateral leafs of the omental flap anteriorly to the neobladder is performed (if abundant omentum available).

(*Info: This approach will create an interlayer which may also prevent adhesion of the neobladder to the pelvic wall.)*

Genital-Sparing Cystectomy in Women with Bladder Cancer

In the era of increased awareness of organ preservation and quality of life issues in lower urinary tract cancer treatment [29], variations to the standard extent of nerve-sparing RC in women that include the preservation of the anterior vaginal wall with or without hysterectomy and/or ovariectomy have been proposed [30, 31]. As a result, markedly improved functional outcomes have been reported with day- and nighttime continence rates ranging between 77–100% and 77–92%, respectively [30, 31]. These studies were conducted in highly selected young women with a median age between 37 and 42 years. The improved functional outcomes need to be weighted against the possible oncological risk of a positive soft tissue surgical margin at RC. In this regard, a recent retrospective study on 160 women found that only women with tumor location at the bladder floor and neck, with an intraoperative palpable posterior mass or clinical lymphadenopathy, exhibited female pelvic organ involvement at RC [32]. In addition, among 180 women treated with standard RC for bladder cancer, only two (1%) had uterine infiltration on final examination [33]. These results suggest that preservation of the internal genital organs at RC offers a high chance for preservation of postoperative continence and sexual function in the majority of carefully selected women. Therefore, genital-sparing cystectomy has the potential to improve functional outcomes and quality of life in women with muscle-invasive bladder cancer without endangering oncological outcomes. Clinical expertise and optimal patient selection will be the critical factors in order to implement genital-sparing cystectomy for improved functional outcomes without compromising oncological safety. Prospective trials are encouraged for standardization of the inclusion criteria and the technical approach.

Treatment of Women with Functional Impairments After Orthotopic Bladder Substitution

Various types of ileal neobladder are currently used for OBS, and all of these have shown satisfactory functional and oncological outcomes [24–28, 34]. A relevant consideration for neobladder reconstruction is its propensity for postoperative complications. Although long-term preservation of renal function is crucial for any technique of OBS, uncertainty persists about the functional superiority of an antirefluxive over a refluxive ureteral implantation technique. In this regard, current evidence does not support an antirefluxive implantation technique for the protection of the upper tract. A randomized study compared both techniques with regard to long-term changes in renal function [35]. An antirefluxive ureteral implantation technique using serous-lined extramural troughs did not prevent postoperative decrease in renal function, as measured by 99 m-Tc-MAG3 scintigraphy. Likewise, pouch-related complication rates were shown to be higher in neobladders with complex antirefluxive ureteral implantation technique [25, 35]. Yet, in absolute figures, the rates of ureteral stricture between neobladder using an antirefluxive and non-refluxive ureteral implantation technique were shown to be similar [24, 26, 34]. Another important aspect on the management of patients with ileal neobladder is the easiness for accessing the upper tract during oncological surveillance after cystectomy [24]. In summary, current evidence does not strictly support the construction of a neobladder with antirefluxive ureteral implantation technique. Importantly, facilitating access to the upper tract should be also taken into account for straightforward surveillance of the upper tracts after cystectomy.

Another main problem after OBS in women is the risk of urinary retention and the need for postoperative clean intermittent catheterization (CIC). In women, the rates of CIC have shown to widely range between 20% and 58% [12, 36, 37]. The causes can be either functional, anatomical, or multifactorial [38]. Apart from oncological causes (i.e., urethral recurrence [10]), anatomical causes include an "ileal valve" of the neobladder outlet and a lack of posterior support resulting in neocystocele or urethral kinking. Hypercapacity of the neobladder can also result due to excessive length of ileum used for creation of the reservoir ("floppy bag") or preservation of the bladder neck during RC [39]. Functional causes comprise untreated or inadequately treated urinary tract infections or the failure to relax the pelvic floor for initiation of voiding and inability to develop and maintain sufficient intra-abdominal pressure during micturition. Basic work-up of patients with urinary retention or increased post-void residual urine volume includes a detailed history with voiding diary, clinical examination and urine analysis, sonography of the kidney and neobladder, and measurement of post-void residual urine volume. Further diagnostic management consists of urethropouchoscopy, dynamic investigations with voiding pouchogram, dynamic magnetic resonance imaging of the pelvic floor, and urodynamic assessment. Formation of a neobladder-vagina fistula using a transvaginal approach with Martius or omental flap was shown to provide high success rates but may still necessitate secondary procedures for satisfactory restoration of urinary continence [40]. In one of the largest series reporting on 12 women with post-cystectomy urinary incontinence, six had undiscovered urethrovaginal fistula [38]. The use of bulking agents showed a low long-term efficacy and carried also the risk of fistula formation. Likewise, placement of a tension-free sling had only a low efficacy, and continence was only achieved with the use of obstructing slings. In summary, it has to be stated that data on surgical treatment of women with urinary incontinence after ileal neobladder reconstruction are scarce.

Conclusions

As a result of an increased awareness of clinicians and patients alike, replacing the urinary bladder with an orthotopic bladder substitute has become the diversion of choice in many academic centers of expertise. Orthotopic bladder substitution can safely be performed in women with invasive bladder cancer provided a carefully obtained bladder neck biopsy or intraoperative frozen sectional analysis of the distal urethral margin excludes malignancy. The extent of preservation of female genital structures impacts on functional outcomes of women with orthotopic bladder substitutes.

References

1. Wallner C, Dabhoiwala NF, DeRuiter MC, Lamers WH. The anatomical components of urinary continence. Eur Urol. 2009;55(4):932–43.
2. Wallner C, van Wissen J, Maas CP, Dabhoiwala NF, DeRuiter MC, Lamers WH. The contribution of the levator ani nerve and the pudendal nerve to the innervation of the levator ani muscles; a study in human fetuses. Eur Urol. 2008;54(5):1136–42.
3. Hautmann RE, Egghart G, Frohneberg D, Miller K. The ileal neobladder. J Urol. 1988;139(1):39–42.
4. Stenzl A, Colleselli K, Poisel S, Feichtinger H, Pontasch H, Bartsch G. Rationale and technique of nerve sparing radical cystectomy before an orthotopic neobladder procedure in women. J Urol. 1995;154(6):2044–9.
5. Stenzl A, Draxl H, Posch B, Colleselli K, Falk M, Bartsch G. The risk of urethral tumors in female bladder cancer: can the urethra be used for orthotopic reconstruction of the lower urinary tract? J Urol. 1995;153(3 Pt 2):950–5.
6. Gakis G, Stenzl A. Considerations for orthotopic diversions in women. Curr Opin Urol. 2015;25(6):550–4.
7. Stein JP, Cote RJ, Freeman JA, Esrig D, Elmajian DA, Groshen S, et al. Indications for lower urinary tract reconstruction in women after cystectomy for bladder cancer: a pathological review of female cystectomy specimens. J Urol. 1995;154(4):1329–33.
8. Mills RD, Studer UE. Female orthotopic bladder substitution: a good operation in the right circumstances. J Urol. 2000;163(5):1501–4.
9. Osman Y, Mansour A, El-Tabey N, Abdel-Latif M, Mosbah A, Hekal I, et al. Value of routine frozen section analysis of urethral margin in male patients undergoing radical cystectomy in predicting prostatic involvement. Int Urol Nephrol. 2012;44(6):1721–5.
10. Gakis G, Ali-El-Dein B, Babjuk M, Hrbacek J, Macek P, Burkhard FC, et al. Urethral recurrence in women with orthotopic bladder substitutes: A multi-institutional study. Urol Oncol. 2015;33(5):204. e17–23.
11. Stenzl A, Jarolim L, Coloby P, Golia S, Bartsch G, Babjuk M, et al. Urethra-sparing cystectomy and orthotopic urinary diversion in women with malignant pelvic tumors. Cancer. 2001;92(7):1864–71.
12. Jentzmik F, Schrader AJ, de Petriconi R, Hefty R, Mueller J, Doetterl J, et al. The ileal neobladder in female patients with bladder cancer: long-term clinical, functional, and oncological outcome. World J Urol. 2012;30(6):733–9.
13. Hautmann RE, Abol-Enein H, Davidsson T, Gudjonsson S, Hautmann SH, Holm HV, et al. ICUD-EAU International Consultation on Bladder Cancer 2012: urinary diversion. Eur Urol. 2013;63(1):67–80.
14. Stenzl A, Cowan NC, De Santis M, Kuczyk MA, Merseburger AS, Ribal MJ, et al. Treatment of muscle-invasive and metastatic bladder cancer: update of the EAU guidelines. Eur Urol. 2011;59(6):1009–18.
15. Witjes JA, Comperat E, Cowan NC, De Santis M, Gakis G, Lebret T, et al. EAU guidelines on muscle-invasive and metastatic bladder cancer: summary of the 2013 guidelines. Eur Urol. 2014;65(4):778–92.
16. Kim KH, Yoon HS, Yoon H, Chung WS, Sim BS, Ryu DR, et al. Risk factors for developing metabolic acidosis after radical cystectomy and ileal neobladder. PLoS One. 2016;11(7):e0158220.

17. Nishikawa M, Miyake H, Yamashita M, Inoue TA, Fujisawa M. Long-term changes in renal function outcomes following radical cystectomy and urinary diversion. Int J Clin Oncol. 2014;19(6):1105–11.
18. Oderda M, Mondino P, Lucca I, Fiorito C, Gillo A, Zitella A, et al. Fatal haematuria in a patient with an orthotopic neobladder and chronic liver failure. Urol Int. 2009;83(3):368–9.
19. Al Hussein Al Awamlh B, Wang LC, Nguyen DP, Rieken M, Lee RK, Lee DJ, et al. Is continent cutaneous urinary diversion a suitable alternative to orthotopic bladder substitute and ileal conduit after cystectomy? BJU Int. 2015;116(5):805–14.
20. Hinata N, Murakami G, Abe S, Honda M, Isoyama T, Sejima T, et al. Detailed histological investigation of the female urethra: application to radical cystectomy. J Urol. 2012;187(2):451–6.
21. Gakis G, Efstathiou J, Lerner SP, Cookson MS, Keegan KA, Guru KA, et al. ICUD-EAU International Consultation on Bladder Cancer 2012: radical cystectomy and bladder preservation for muscle-invasive urothelial carcinoma of the bladder. Eur Urol. 2013;63(1):45–57.
22. Colleselli K, Stenzl A, Eder R, Strasser H, Poisel S, Bartsch G. The female urethral sphincter: a morphological and topographical study. J Urol. 1998;160(1):49–54.
23. Miocinovic R, Gong MC, Ghoneim IA, Fergany AF, Hansel DE, Stephenson AJ. Presacral and retroperitoneal lymph node involvement in urothelial bladder cancer: results of a prospective mapping study. J Urol. 2011;186(4):1269–73.
24. Gakis G, Abdelhafez MF, Stenzl A. The "I-Pouch": results of a new ileal neobladder technique. Scand J Urol. 2015;49(5):400–6.
25. Skinner EC, Fairey AS, Groshen S, Daneshmand S, Cai J, Miranda G, et al. Randomized trial of studer pouch versus T-pouch orthotopic ileal neobladder in patients with bladder cancer. J Urol. 2015;194(2):433–9.
26. Abol-Enein H, Ghoneim MA. Functional results of orthotopic ileal neobladder with serous-lined extramural ureteral reimplantation: experience with 450 patients. J Urol. 2001;165(5):1427–32.
27. De Sutter T, Akand M, Albersen M, Everaerts W, Van Cleynenbreugel B, De Ridder D, et al. The N-shaped orthotopic ileal neobladder: functional outcomes and complication rates in 119 patients. Springerplus. 2016;5:646.
28. Mischinger J, Abdelhafez MF, Todenhofer T, Schwentner C, Aufderklamm S, Stenzl A, et al. Quality of life outcomes after radical cystectomy: long-term standardized assessment of Studer Pouch versus I-Pouch. World J Urol. 2015;33(10):1381–7.
29. Gakis G, Witjes JA, Comperat E, Cowan NC, De Santis M, Lebret T, et al. EAU guidelines on primary urethral carcinoma. Eur Urol. 2013;64(5):823–30.
30. Ali-El-Dein B, Mosbah A, Osman Y, El-Tabey N, Abdel-Latif M, Eraky I, et al. Preservation of the internal genital organs during radical cystectomy in selected women with bladder cancer: a report on 15 cases with long term follow-up. Eur J Surg Oncol J Eur Soc Surg Oncol Br Assoc Surg Oncol. 2013;39(4):358–64.
31. Moursy EE, Eldahshoursy MZ, Gamal WM, Badawy AA. Orthotopic genital sparing radical cystectomy in pre-menopausal women with muscle-invasive bladder carcinoma: A prospective study. Indian J Urol J Urol Soc India. 2016;32(1):65–70.
32. Gregg JR, Emeruwa C, Wong J, Barocas DA, Chang SS, Clark PE, et al. Oncologic outcomes after anterior exenteration for muscle invasive bladder cancer in women. J Urol. 2016;196(4):1030–5.
33. Ali-El-Dein B. Oncological outcome after radical cystectomy and orthotopic bladder substitution in women. Eur J Surg Oncol J Eur Soc Surg Oncol Br Assoc Surg Oncol. 2009;35(3):320–5.
34. Hautmann RE, Volkmer BG, Schumacher MC, Gschwend JE, Studer UE. Long-term results of standard procedures in urology: the ileal neobladder. World J Urol. 2006;24(3):305–14.
35. Harraz AM, Mosbah A, El-Assmy A, Gad H, Shaaban AA. Renal function evaluation in patients undergoing orthotopic bladder substitution: a systematic review of literature. BJU Int. 2014;114(4):484–95.

36. Pichler R, Zangerl F, Leonhartsberger N, Stohr B, Horninger W, Steiner H. Orthotopic bladder replacement in women: focus on functional results of a retrospective, single-centre study. Scand J Urol. 2013;47(4):295–301.
37. Stein JP, Dunn MD, Quek ML, Miranda G, Skinner DG. The orthotopic T pouch ileal neobladder: experience with 209 patients. J Urol. 2004;172(2):584–7.
38. Bailey GC, Blackburne A, Ziegelmann MJ, Lightner DJ. Outcomes of surgical management in patients with stress urinary incontinence and/or neovesicovaginal fistula after orthotopic neobladder diversion. J Urol. 2016;196(5):1478–83.
39. Hautmann RE, de Petriconi R, Kleinschmidt K, Gottfried HW, Gschwend JE. Orthotopic ileal neobladder in females: impact of the urethral resection line on functional results. Int Urogynecol J Pelvic Floor Dysfunct. 2000;11(4):224–9. discussion 30.
40. Carmel ME, Goldman HB, Moore CK, Rackley RR, Vasavada SP. Transvaginal neobladder vaginal fistula repair after radical cystectomy with orthotopic urinary diversion in women. Neurourol Urodyn. 2016;35(1):90–4.

Continent Cutaneous Urinary Diversion

4

Jonathan N. Warner and Kevin G. Chan

Introduction

Continent cutaneous urinary diversion (CCUD) utilizes an intestinal segment to create a low-pressure urinary reservoir and a catheterizable continence mechanism. It provides a urinary tract reconstruction option for patients who are not candidates for continent orthotopic urinary diversion and in patients with whom an ileal conduit is not desirable. The ideal candidate for a CCUD is the same patient who would be considered for orthotopic neobladder but may not have a usable urethra.

At our institution, we counsel female patients undergoing cystectomy toward CCUD if they desire a continent reconstruction. Incontinence in women with orthotopic urinary diversion is reported to be 30–40% and may carry with it a negative impact on health-related quality of life [1, 2]. If urinary incontinence is encountered, unlike in men, successful treatment options are very limited [3].

Advantages of a continent cutaneous urinary diversion include a relatively immediate and predictable continence without the need for an external appliance bag. It allows patients a more physically active lifestyle than that with an external appliance. The potential disadvantages are that it (1) requires a longer anesthesia time when compared to an ileal conduit, (2) carries a higher complication rate than ileal conduit [4], (3) requires the manual dexterity necessary to catheterize a stoma, and (4) requires the mental aptitude to perform catheterizations on a fairly rigid schedule.

Most surgeons' choice of CCUD is influenced by their belief of whether a freely refluxing urinary reservoir is safe in the presence of urine colonized with bacteria. The concern regarding a refluxing cutaneous urinary diversion is that the

J.N. Warner, MD • K.G. Chan, MD (✉)
City of Hope Cancer Center, Duarte, CA, USA
e-mail: kchan@coh.org

S. Daneshmand (ed.), *Urinary Diversion*, DOI 10.1007/978-3-319-52186-2_4

transmission of high pressures and/or the reflux of infected urine can lead to renal deterioration. Kristjansson et al. evaluated the effect of refluxing versus anti-refluxing anastomoses in continent and incontinent cutaneous urinary diversions and did not find a significant difference in the fall of glomerular filtration rate between the two groups [5]. The risk of reflux is balanced against the potentially higher risk of ureteral obstruction with the various anti-refluxing modalities, whether it is an anti-refluxing afferent limb or anti-refluxing ureteral-intestinal anastomosis [6, 7]. Surgeons performing a freely refluxing cutaneous urinary diversion feel that the reduced chance of reoperation for obstruction is a more important factor than the risk from urinary reflux.

In this chapter, we describe the most commonly used continent cutaneous urinary diversions with the primary differences being the anti-reflux and continence mechanisms. The Indiana pouch utilizes freely refluxing ureterocolonic anastomoses or tunneled non-refluxing anastomoses and the ileocecal valve as the continence mechanism. The right colon pouch utilizes the same segment of colon and ileum as the Indiana pouch but utilizes the ileocecal valve as the anti-reflux mechanism and the Mitrofanoff principle for the continence mechanism. The double T-pouch utilizes two separate 20-cm segments of ileum in a subserosal tunnel to create a non-refluxing afferent limb and a continent, catheterizable efferent limb.

Patient Selection

Patients must demonstrate the ability and willingness to self-catheterize in a regimented fashion. Inability or unwillingness to perform self-catheterization can lead to perforations, stones, upper tract deterioration, and infections. Patients with impaired manual dexterity, neurologic decline such as dementia, or renal dysfunction should be counseled toward ileal conduit urinary diversion. The International Consultation on Bladder Cancer recommended against continent diversion in patients with a glomerular filtration rate (GFR) <50 ml/min or a serum creatinine >150 μmol/l [8].

Preoperative workup should include a past medical and surgical history to assess pre-existing neurologic disease, renal disease, liver disease, and prior abdominal operations, particularly colon surgery and small bowel surgery. Patients being considered for CCUD may desire to undergo a preoperative colonoscopy to rule out colonic disease.

Laboratory testing should be performed to ensure appropriate renal function and nutritional reserves. As above, patients with renal dysfunction should be counseled toward ileal conduit. Preoperative nutrition consultation can also restore albumin and prealbumin levels to appropriate levels to minimize complications.

Imaging should include computerized tomography to assess anatomy and identify any anomalies. Nuclear medicine scan with mercaptoacetyltriglycine can be used to assess baseline renal function, but is not mandatory.

Surgical Preparation

All patients should undergo a mechanical and antibiotic bowel preparation. A marking by stomal nurse should be utilized in all patients, as there may be a need to convert to an ileal conduit for any unforeseen intraoperative findings. The location of a catheterizable stoma is more flexible than an ileal conduit as no appliance is required. Placement within a skin fold or below a bikini line is reasonable if requested by the patient. The umbilicus is also a choice of stoma location preferred by some surgeons.

Indiana Pouch

The Indiana pouch offers a distinct advantage over other forms of combined ileum and colon continent diversions in that it utilizes the natural continence mechanism of the ileocecal valve. Another advantage is that it is more easily fashioned in the obese patient because any length of terminal ileum may be prepared for the catheterizable segment. Continence rates of Indiana pouches have been reported to be 93–97% [9, 10].

Once the cystectomy has been completed, the right colon is completely mobilized distal to the hepatic flexure. The terminal ileum is divided 10–15 cm proximal to the ileocecal valve with a bowel stapler in addition to an additional 5–8 cm of mesentery along the avascular plane of Treves using a vessel-sealing device or suture ligatures. The right colon is divided at the junction of the right and middle colic arteries using a bowel stapler. A general guide is 31 cm for the right colon segment (Fig. 4.1).

Bowel continuity is restored in a side-to-side fashion using a bowel stapler. The mesenteric defect is closed using a running 3-0 polyglactin suture.

The colonic segment is opened using electrocautery along its antimesenteric border beginning at the excised distal staple line to the base of the appendix, which is also excised (Fig. 4.2).

The ileal segment is then tapered. A 12 French catheter is placed into the ileum and passed through the ileocecal valve. Allis clamps are placed along the antimesenteric side of the ileum (Fig. 4.3).

A stapler passed under the Allis clamps and the bowel lumen is narrowed (Fig. 4.4a, b). The stapler is pressed down against the red Robinson catheter to taper the lumen as narrow as possible. Redundancy can create difficulty in catheterizing stoma. Two or three staple loads are usually required to complete tapering of the 15-cm segment of ileum. Care must be taken to ensure the stapler stays completely antimesenteric so as not to include the mesentery in the staple line.

The final 1–2 cm near the ileocecal valve is not stapled. Instead, imbricating sutures are placed to taper the lumen at this level (Fig. 4.5). This is performed with interrupted 3-0 silk Lembert sutures at the superior, anterior, and inferior base of the ileocecal valve. Once this is completed, one should demonstrate that a 16Fr red Robinson catheter passes easily through the ileal segment and ileocecal valve.

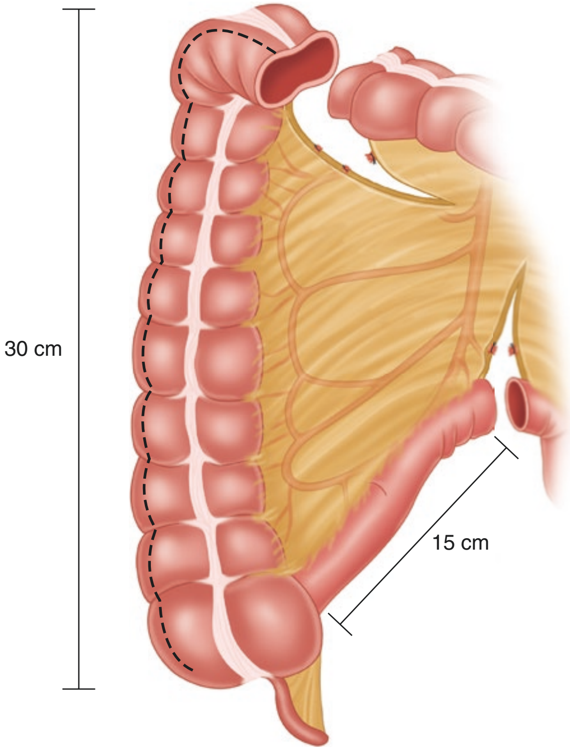


Fig. 4.1 Isolation of the ileal-colonic segment used for the Indiana pouch [17]

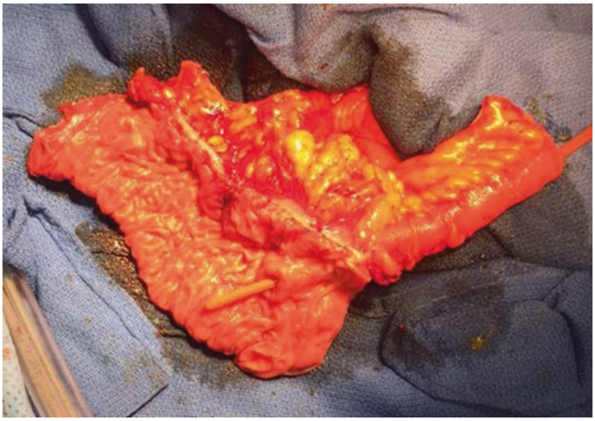


Fig. 4.2 The colonic segment has been opened along its antimesenteric border down to the base of the appendix. The red robinson catheter is shown traversing the ileocecal valve

The colonic pouch is then closed by folding the appendiceal edge of the cecum up to the distal colonic edge. This allows of the ileal segment to face anteriorly. This is closed with a running 3-0 polyglactin suture.

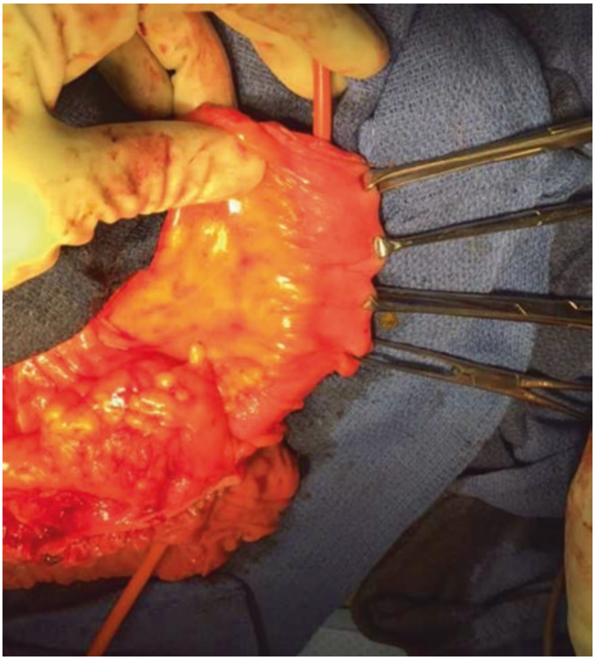


Fig. 4.3 A 12Fr red robinson catheter and a series of allis clamps are used to facilitate ileal tapering

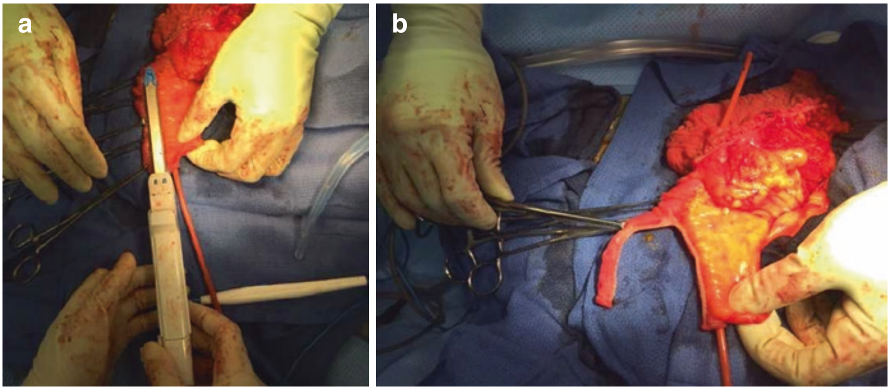


Fig. 4.4 (**a**, **b**) Multiple loads of a GIA stapler are utilized to taper the ileal segement down to the base of the ileocecal valve

Once the pouch is closed, the right end/corner of the colonic suture line has a natural tendency to rotate 90° counterclockwise toward the pelvis. With the pouch in this final resting position, the appropriate site for ureteral anastomosis is selected and performed. The colonic suture line acts as a longitudinal median determining right and left. The left ureter is anastomosed to the antimesenteric portion of colon pouch inferiorly and left of the suture line. The right ureter is anastomosed to an antimesenteric portion of colon pouch inferiorly and right of the suture line. Putting the pouch into this natural position for the ureteral anastomosis sites prevents sharp

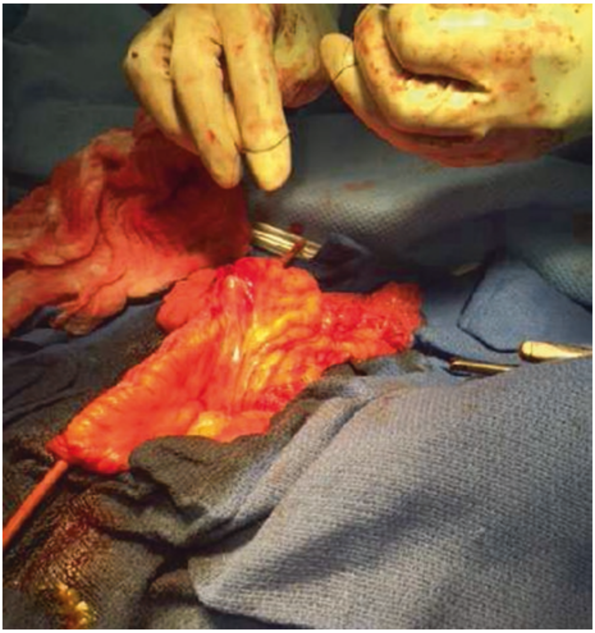


Fig. 4.5 3-0 Silk imbricating sutures are placed at the base of the ileocecal valve

angles to the anastomosis, which can occur if the ureteral anastomosis is performed prior to rotating the pouch into the appropriate location.

A number of ureterocolonic anastomoses have been described for colonic pouches. At our institution, we perform a direct, end-to-side, spatulated freely refluxing anastomosis. We use interrupted 4-0 polyglactin sutures using a cutting needle. Our ureteral anastomoses also utilize four 4-0 chromic mucosal-everting sutures at the enterotomy in the colon. We believe this facilitates a better mucosa-to-mucosa re-approximation. The anastomoses are stented with 7Fr single J urinary diversion stents that are brought out through a small opening on the right side of the pouch (secured with a purse-string plain gut suture) and exit the skin through a small 5-mm incision inferior to the stoma location. This stent location should be well below the stoma to accommodate an external appliance bag that is used to collect the urine from the stents.

Once the ureteral anastomoses are complete, a pouchostomy tube site is selected in the right upper portion of the pouch. Using a 24F Foley or Malecot catheter, we bring the tube from outside through the abdominal wall and into the pouch where it is secured with two sets of concentric 2-0 polyglactin purse-string sutures. The purpose of the catheter is primary drainage of the pouch until the patient begins catheterizing pouch 3 weeks postoperatively.

A 1-cm ellipse of skin is removed at the desired stoma location. A tunnel is made through the subcuticular fat, fascia, and peritoneum. The tapered ileum is passed through the defect and pulled through as much as possible to limit redundant length to the limb. Once the limb has been pulled through as much as possible, the excess ileum is resected leaving 1 cm above the skin level, and the cutaneous stoma is matured at the skin with interrupted 2-0 polyglactin sutures. The shorter limb will result in fewer long-term catheterization issues.

Extracorporeal Variation for Indiana Pouch in Robotic Radical Cystectomy

If cystectomy is performed in a laparoscopic or robot-assisted laparoscopic fashion, the left ureter is tunneled under the sigmoid mesentery, and the left and right ureters are tagged with 9-in. polyglactin sutures for identification. Using the existing robotic ports, laparoscopic mobilization of the ascending colon and the hepatic flexure is performed. Alternatively, the low midline specimen extraction incision can be made, and a Gelport® (Applied Medical, Rancho Santa Margarita, USA) can be used to perform a hand-assisted colon mobilization. The existing robotic ports are utilized so no new port sites are placed. Once the specimen is retrieved, an Alexis wound protector (Applied Medical, California, USA) is placed into the wound. The ureters labeled with preplaced dyed and undyed polyglactin are oriented at the wound, and ileal-colonic segment is delivered through the wound. The Indiana pouch is then constructed as described previously.

Right Colon Pouch

A common approach for surgeons who feel strongly about the need for a non-refluxing continent cutaneous urinary diversion is the use of a right colon pouch where the ileocecal valve remains intact and the distal 10–15-cm segment of terminal ileum is used as the afferent limb where the ureters are anastomosed. The anti-reflux mechanism is the native ileocecal valve originally described by Zinman [11]. The common choice of continence mechanism in this setting is utilizing the Mitrofanoff principle using the appendix or a Yang-Monti channel. Stein et al. reported continence rates with right colon pouches to be 100% [12].

The right colon pouch with embedded appendix in the submucosa has been well described in the literature as an alternative to the Indiana pouch. Several modifications have been described leading to the following technique as described by Stein et al. [12] In this technique the procedure is initiated in a similar fashion to the Indiana pouch with complete mobilization of the small bowel, cecum, and ascending and transverse colon. This can be performed laparoscopically if indicated. Thirty to forty centimeters of ascending and transverse colon is isolated, along with 5–10 cm of the terminal ileum.

The ileal mesenteric division is made at the avascular plane of Treves between the terminal branches of the ileum and the ileocolic artery. Minimal distal colonic mesenteric division is necessary.

The appendix is then assessed for suitability as an efferent catheterizable limb. Generally, the appendix must be 5–6 cm in length and should accommodate a 12 Fr catheter. If the appendix is deemed appropriate, the appendix and mesoappendix are

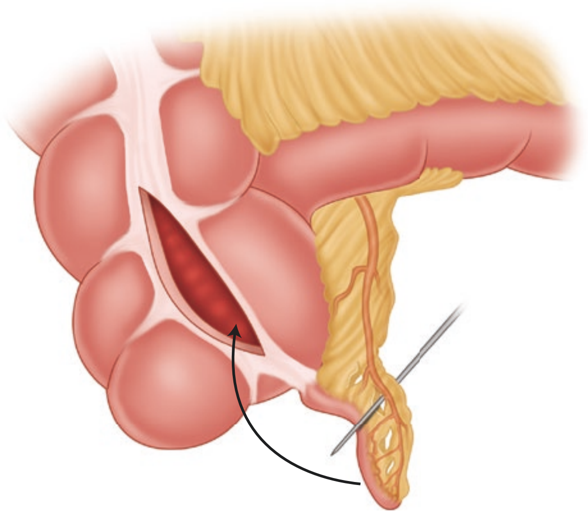


Fig. 4.6 A channel in the tenia of the cecum is created that will hold the proximal appendix [12]

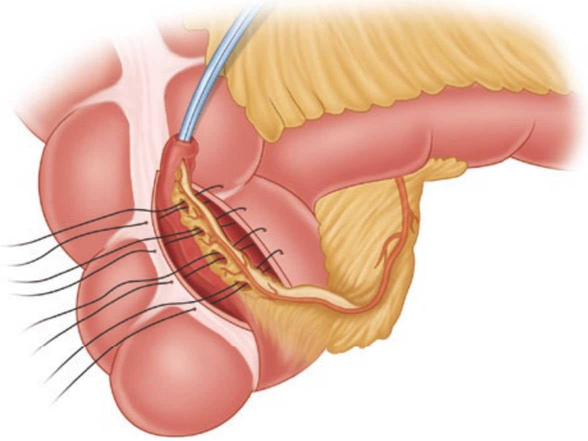


Fig. 4.7 The edges of the tenia serosa are reapproximated through the appendiceal mesenteric windows using 3-0 silk sutures [12]

carefully mobilized in order to preserve blood supply. The distal edge of the appendix is incised and cannulated with a 12 Fr catheter.

Several mesenteric windows are created through the appendiceal mesentery adjacent to the serosa of the appendix. Care is taken to avoid injuring the blood supply to the appendix. Next, a 4–5-cm longitudinal incision is made through the anterior tenia of the cecum to the level of the mucosa, allowing the mucosa to bulge into the incision without violating the mucosa. This provides the channel in which the appendix will rest (Fig. 4.6).

The appendix is then flipped into the channel, and 3-0 silk sutures are used to re-approximate the lateral edges of the incised tenia passing each suture through the mesenteric windows that were previously created in a U-stitch fashion. Using a Penrose drain passed through the mesenteric window will facilitate passage of the suture (Fig. 4.7).

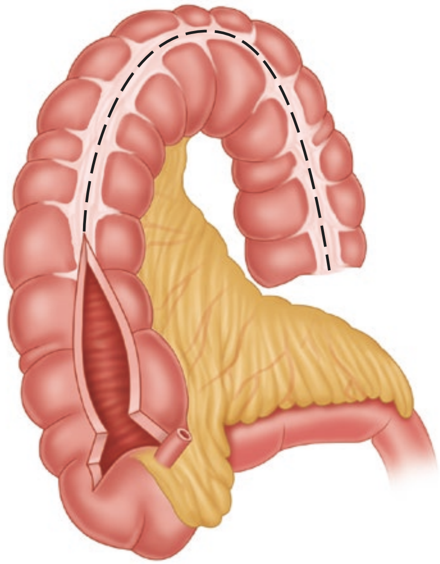


Fig. 4.8 The colonic segment is detubularized along its antimesenteric border [12]

Once all sutures are passed, they will then be tied down. This will embed the appendix into the seromuscular layer while preserving the blood supply through the mesentery. Three to four centimeters of the appendix should be buried into the tenia to create an adequate continence mechanism.

Next, the isolated colon is incised along the antimesenteric border from the transverse colon to the cecum; as the appendix is approached, the incision is deviated away from the appendix (Fig. 4.8).

The distal edge of the medial colon is then rotated medially and inferiorly to the medial edge of the divided cecum creating an inverted "U." The posterior edge is then sewn together with an absorbable suture (Fig. 4.9).

Bringing the top of the inverted "U" to the cecum and closing the edges with absorbable suture complete the pouch.

A bilateral end-to-side ureteroileal anastomosis is performed over a stent into the short segment of the terminal ileum. The stents can be double J stents and tied to the pouchostomy tube via a suture or can be passed through the ileocecal valve and then externalized via the appendix or a separate pouchostomy site (Fig. 4.10).

The stoma site is selected on the anterior abdominal wall. At that site, absorbable sutures are placed on either side of the stoma in a horizontal fashion through the posterior rectus fascia and then passed through the cecum. The appendix is passed through the abdominal wall, and the previously placed stay sutures are tied down, securing the cecum to the anterior abdominal wall. The distal appendix is matured.

When the appendix is not available or is unsuitable for an efferent limb, an alternative option is to create a Yang-Monti channel [13]. In this approach, an additional 2–3-cm segment of proximal small bowel is isolated (Figs. 4.11 and 4.12), detubularized on the antimesenteric border, and retubularized creating a narrow lumen channel.

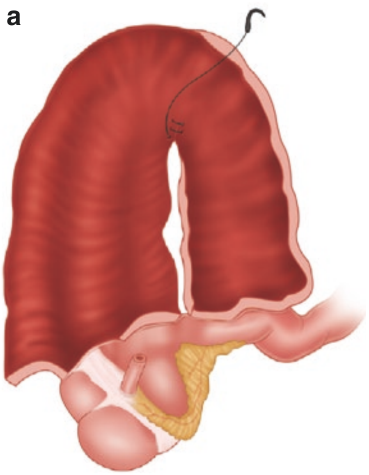
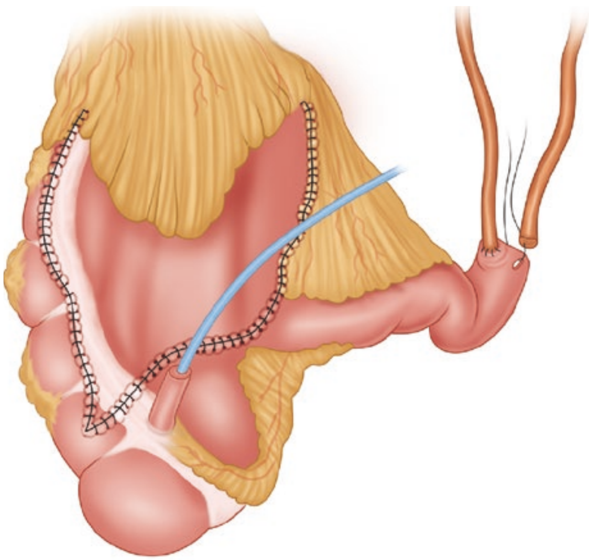


Fig. 4.9 The backwall of the colonic pouch is reapproximated with a running 3-0 polyglactin suture. The pouch is then closed in a Heineke-Mikulicz fashion with a runnig 3-0 polyglactin suture [12]

Fig. 4.10 Here is the completed right colon pouch with the uretero-ileal anastomoses completed, ready for maturation of the stoma at the skin [12]



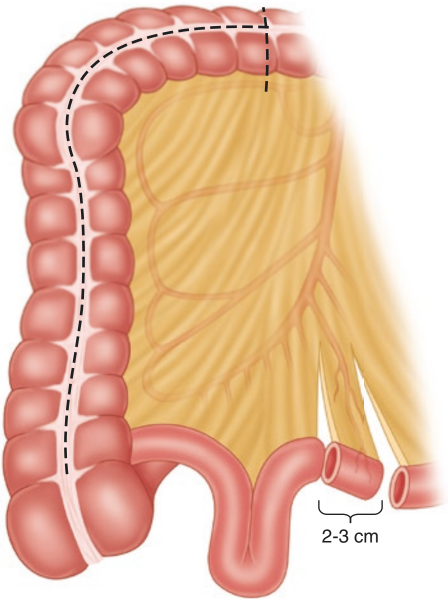


Fig. 4.11 For the Yang-Monti channel, a 2–3 cm segment small bowel, proximal to the initial ileal division is utilized [13]

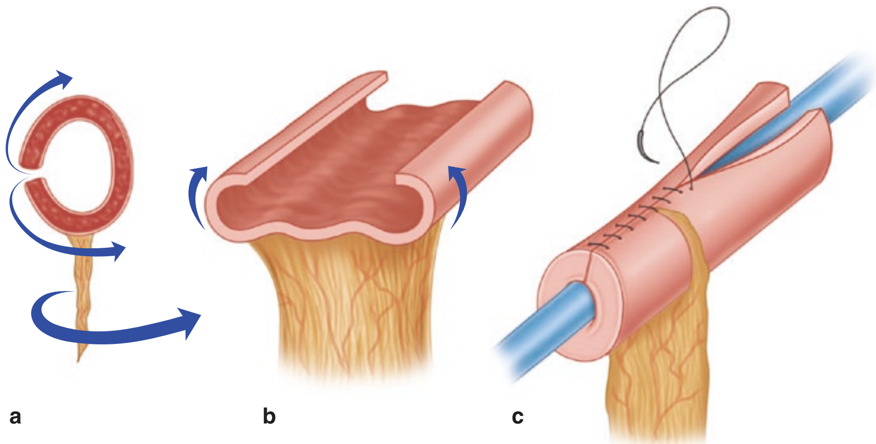


Fig. 4.12 Creation of the Yang-Monti channel is shown here [13]. (**a**) The 2–3 cm ileal segment is detublarized half-way to its antimesenteric border to allow more tubular distance on one side of the mesentery. (**b**) The detubularized segment is now ready to be rolled on its perpendicular axis. (**c**) The re-oriented ileal segment is re-tubularized with 3-0 absorbable suture

The right colon is detubularized, and a pouch is created as previously described. The proximal cecal tenia is again selected for the site of insertion of the channel. A 4-cm trough is created, and the base of the trough is opened for the Yang-Monti channel to be anastomosed and then buried into the trough creating an antimesenteric pouch (Fig. 4.13).

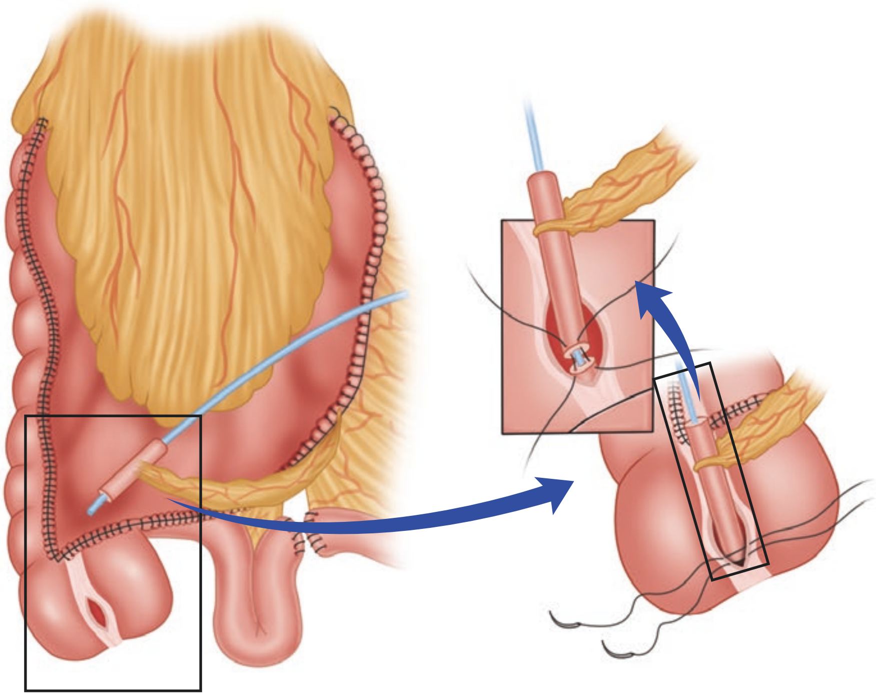


Fig. 4.13 The Yang-Monti channel is buried in a trough created in the anterior tenia, creating a flap-valve mechanism [13]

Double T-Pouch

The double T-pouch was devised as a means of creating a continence and anti-refluxing mechanism using exclusively small bowel while limiting complications seen with the Kock pouch. Several techniques were modified to lead to the following technique described by Stein and Skinner in 2001 [14]. Continence rates for the double T-pouch have been reported as high as 95% [15].

Seventy centimeters of terminal ileum is isolated, sparing the distal 15 cm of terminal ileum. The proximal 10-cm segment of the 70-cm segment is isolated and will serve as the anti-reflux mechanism and the site for ureteroenteric anastomosis. The distal 15-cm segment is isolated and rotated and will serve as the cutaneous continence mechanism (Fig. 4.14a). The remaining ileum is configured into a "W" (Fig. 4.14b). Each leg of the "W" is approximately 11 cm. The afferent anti-refluxing mechanism is created by opening the windows through the mesentery near the bowel wall between the vascular arcades along the distal 3–4 cm as described previously for the mesoappendix. Similarly the efferent limb mesentery is opened between the vascular arcades for 7–8 cm (Fig. 4.14c). A Penrose drain can be placed through each window to facilitate passage of the 3-0 silk sutures, thrown in a horizontal mattress fashion through the serosa of the appropriate "W" limb (Fig. 4.14d).

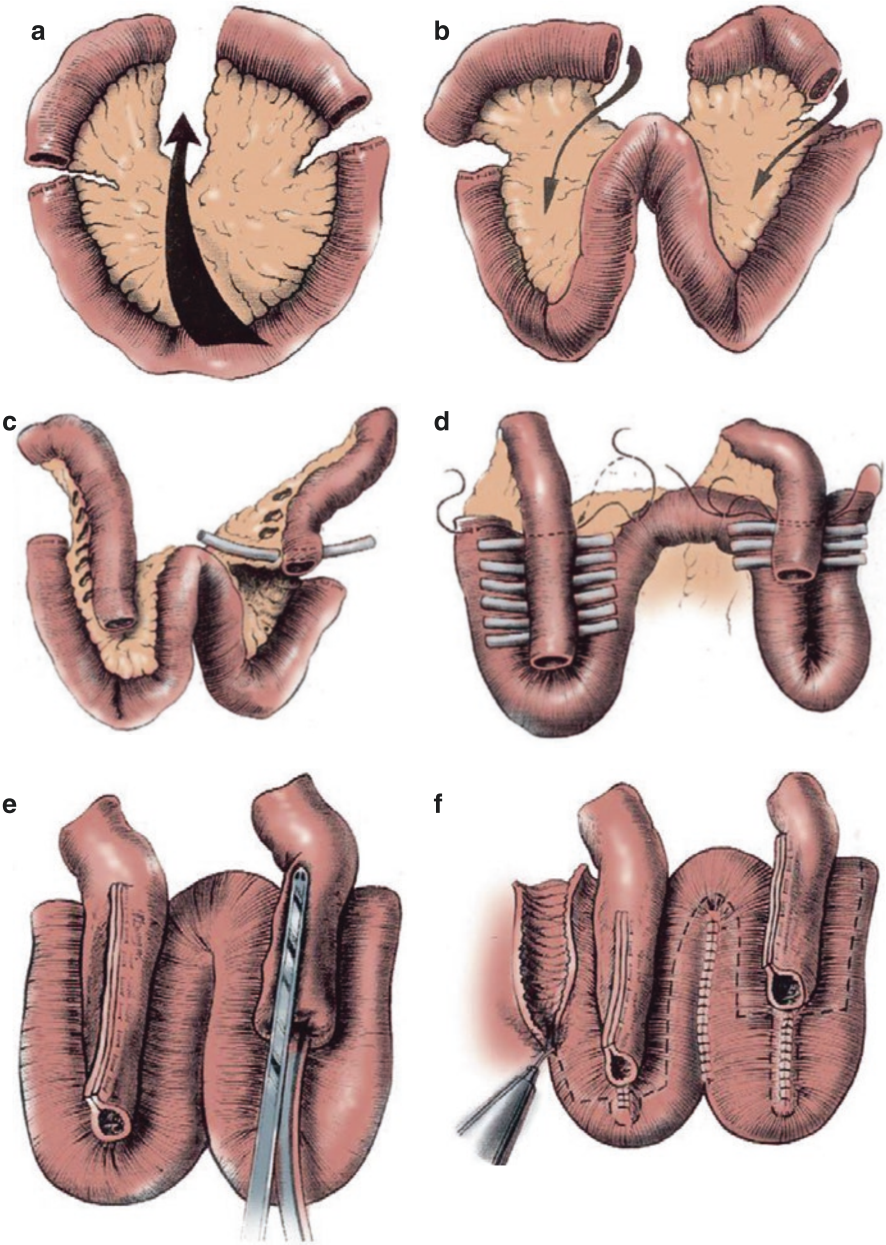


Fig. 4.14 Steps in the creation of the Double-T pouch [18]. (**a**) The 10 cm proximal segment, 45 cm middle segment, and 15 cm distal segment of the 70 cm ileal segment is divided and prepared. (**b**) The 45 cm segment is placed in a "W" configuration, and the proximal and distal ileal segments are rotated into their respective troughs of the "W." (**c**) Windows in the mesentery, just under proximal and distal ileal segments are made and marked with short penrose drains. (**d**) The windows for the efferent limb extend 7–8 cm while the windows for the afferent limb span 3–4 cm. (**e**) Using a bowel stapler tapering of the efferent limb is performed over a 16 Fr catheter and tapering of the afferent limb is performed over a 30 Fr catheter. (**f**) The tapering of the efferent limb has a funneled path for ease of catheterization. The bowel of the "W" segment detubularized along it's mesenteric boader as delineated by the dotted line.

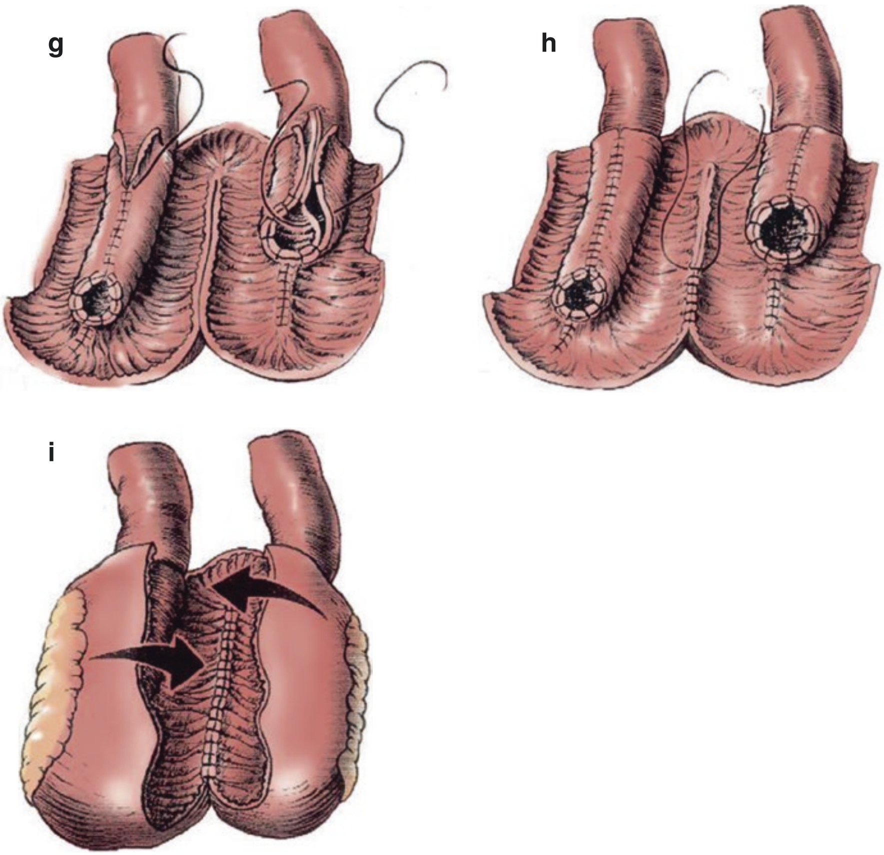


Fig. 4.14 (continued) (**g**) The cut edges of the "W" segment overlaying the efferent and afferent limbs are re-approximated. (**h**) The back wall of the "W" is re-approximated. (**i**) The pouch is folded and closed by re-approximating the remaining cut edges

Once secured, the proximal 3–4-cm afferent limb is tapered over a 30 Fr catheter, while the 7–8 cm of the efferent limb is tapered over a 16 Fr catheter (Fig. 4.14e). The tapering is completed with a bowel stapler. The efferent limb must be tapered gradually to prevent the catheter from hitting a ridge. Rather, the catheter should have a funneled path to the pouch.

Each limb of the "W" is sewn together with an absorbable suture. The bowel is then opened on the antimesenteric border (Fig. 4.14e). Near the medial suture lines of the trough, the incision is kept near the suture lines. The cut edge of the bowel is sewn over the efferent and afferent limbs, while the remaining incised bowel is sewn to the lumen of each channel (Fig. 4.14g). The medial limb of the "W" is sewn together (Fig, 4.14h), and finally the lateral edges of each limb of the "W" are secured (Fig. 4.14i), completing the pouch. Two end-to-side ureteral-ileal anastomoses are performed, and the distal aspect of the efferent limb is matured as a stoma.

Postoperative Care

Most institutions follow an enhanced recovery after surgery protocol. No nasogastric tube is utilized. A liquid diet is started postoperative day 0 or 1. Continent cutaneous urinary diversions remain maximally decompressed for 3 weeks with a large bore catheter acting as pouchostomy, a catheter in efferent stoma, and stents externalized or sutured to the pouchostomy catheter. It is imperative to irrigate the pouch regularly at every 4–6 hour intervals to ensure patency of the catheter and ensure maximal decompression. At our institution, the stoma is not catheterized, and the pouch is decompressed with only the pouchostomy and stents. A large closed-suction drain is utilized in the pelvis and adjacent to the pouch and ureterointestinal anastomoses. Externalized stents are removed when the patient is tolerating a regular diet, and the drain output is not a characteristic of urine. Drains are typically removed prior to discharge from the hospital but not until the output is less than 400 ml/day.

Patients are discharged to home when tolerating a regular diet and bowel function has returned. They are followed weekly until week 3 when a pouchogram is performed to confirm an intact pouch. At this visit, the patient undergoes "pouch training." The patient is instructed on pouch catheterization and placed on an every 2-hour schedule for catheterization. The interval between catheterizations is gradually increased weekly until the patient is catheterizing every 4–6 h. The stoma is dressed with a small bandage that helps prevent mucous from staining the patient's clothing.

Complications

The complication rate in CCUD has been reported to be as high as 89–94%, although most of these complications are Clavien grade II or less [9, 16]. We also found that CCUD tends to carry a higher complication rate than ileal conduit or orthotopic urinary diversion [4]. Early complications include pouch leak, ileus, urinary tract infection, and stomal necrosis. Later complications include ureteral anastomotic strictures, renal insufficiency, pouch stones, stomal incontinence, and stomal stenosis.

Conclusion

For the properly selected patients, a CCUD offers a viable alternative to orthotopic and ileal conduit urinary diversion. While complications of CCUD are generally higher than that of other diversion types, the high predictability of continence makes this an attractive urinary diversion option to many patients.

References

1. Bartsch G, Daneshmand S, Skinner EC, Syan S, Skinner DG, Penson DF. Urinary functional outcomes in female neobladder patients. World J Urol. 2014;32:221–8.
2. Zahran MH, El-Hefnawy AS, Zidan EM, El-Bilsha MA, Taha DE, Ali-El-Dein B. Health-related quality of life after radical cystectomy and neobladder reconstruction in women: impact of voiding and continence status. Int J Urol. 2014;21:887–92.

3. Bailey GC, Blackburne A, Ziegelmann MJ, Lightner DJ. Outcomes of surgical management of patients with stress urinary incontinence and/or neovesicovaginal fistula after orthotopic neobladder diversion. J Urol. 2016;196(5):1478–83.
4. Nazmy M, Yuh B, Kawachi M, et al. Early and late complications of robot-assisted radical cystectomy: a standardized analysis by urinary diversion type. J Urol. 2014;191:681–7.
5. Kristjansson A, Wallin L, Mansson W. Renal function up to 16 years after conduit (refluxing or anti-reflux anastomosis) or continent urinary diversion. 1. Glomerular filtration rate and patency of uretero-intestinal anastomosis. Br J Urol. 1995;76:539–45.
6. Wilson TG, Moreno JG, Weinberg A, Ahlering TE. Late complications of the modified Indiana pouch. J Urol. 1994;151:331–4.
7. Webster C, Bukkapatnam R, Seigne JD, et al. Continent colonic urinary reservoir (Florida pouch): long-term surgical complications (greater than 11 years). J Urol. 2003;169:174–6.
8. Hautmann RE, Abol-Enein H, Davidsson T, et al. ICUD-EAU International Consultation on Bladder Cancer 2012: urinary diversion. Eur Urol. 2013;63:67–80.
9. Torrey RR, Chan KG, Yip W, et al. Functional outcomes and complications in patients with bladder cancer undergoing robotic-assisted radical cystectomy with extracorporeal Indiana pouch continent cutaneous urinary diversion. Urology. 2012;79:1073–8.
10. Rowland RG, Mitchell ME, Bihrle R, Kahnoski RJ, Piser JE. Indiana continent urinary reservoir. J Urol. 1987;137:1136–9.
11. Zinman L, Libertino JA. Ileocecal conduit for temporary and permanent urinary diversion. J Urol. 1975;113:317–23.
12. Stein JP, Daneshmand S, Dunn M, Garcia M, Lieskovsky G, Skinner DG. Continent right colon reservoir using a cutaneous appendicostomy. Urology. 2004;63:577–80. discussion 80–1.
13. Wagner M, Bayne A, Daneshmand S. Application of the Yang-Monti channel in adult continent cutaneous urinary diversion. Urology. 2008;72:828–31.
14. Stein JP, Skinner DG. T-mechanism applied to urinary diversion: the orthotopic T-pouch ileal neobladder and cutaneous double-T-pouch ileal reservoir. Tech Urol. 2001;7:209–22.
15. Abol-Enein H, Ghoneim MA. Surgical atlas. A continent cutaneous ileal neobladder using the serous-lined extramural valves. BJU Int. 2006;98:1125–37.
16. Holmes DG, Thrasher JB, Park GY, Kueker DC, Weigel JW. Long-term complications related to the modified Indiana pouch. Urology. 2002;60:603–6.
17. Simmons MN, Campbell SC. Continent cutaneous urinary diversion: right colonic reservoirs. In: Montague D, Gill I, Angermeier K, and Ross JH (Eds). Textbook of Reconstructive Urologic Surgery. Boca Raton, FL: Taylor and Francis. 2008. p. 378.
18. Decastro GJ, Mckiernan JM, and Benson MC. Cutaneous Continent Urinary Diversion. In: Alan J. Wein (Ed). Campbell-Walsh Urology, Chapter 98. 11th ed Philadelphia, PA: Elsevier. 2016.

Robot-Assisted Intracorporeal Urinary Diversion

5

Ahmed A. Hussein, Youssef E. Ahmed, and Khurshid A. Guru

Introduction

Radical Cystectomy (RC) with pelvic lymph node dissection represents the cornerstone for treatment of muscle invasive bladder cancer, as well as refractory non-muscle invasive disease. RC remains a major procedure that bears a high rate of complications and 5-year overall survival of 50–70% [1–3]. Ongoing attempts have been made with the aim of improving outcomes following RC, including use of neoadjuvant chemotherapy (NAC) and performing a more thorough lymph node dissection [4]. A robot-assisted approach to RC has gained much popularity in the last decade with a dramatic increase from <1% in 2004 to 13% in 2010. Robot-assisted radical cystectomy (RARC) offers advantages in terms of blood loss, transfusion rates, and potentially hospital stay, in addition to improved ergonomics and visualization without jeopardizing oncological outcomes [4].

The choice of urinary diversion after RC is dependent on multiple factors including the patient's quality of life (QoL), preference, and associated short- and long-term complications [5]. Deciding the most appropriate method of urinary diversion is usually individually tailored according to the patient's choice and disease characteristics [6]. Surgeon experience and training also have a substantial influence in the presentation of the available options to patients and therefore significantly affect the decision for urinary diversion as previously described in this book [6].

A.A. Hussein, MD
Department of Urology, Roswell Park Cancer Institute,
Elm & Carlton St, Buffalo, NY 14263, USA

Department of Urology, Cairo University, Giza, Egypt
e-mail: Ahmed.Aly@roswellpark.org

Y.E. Ahmed, MD • K.A. Guru, MD (✉)
Department of Urology, Roswell Park Cancer Institute,
Elm & Carlton St, Buffalo, NY 14263, USA
e-mail: Youssef.Ahmed@roswellpark.org; Khurshid.Guru@roswellpark.org

S. Daneshmand (ed.), *Urinary Diversion*, DOI 10.1007/978-3-319-52186-2_5

Although orthotopic bladder substitution (OBS) may represent the new gold standard, ileal conduit (IC) remains the most popular diversion method in the United States (>80%) [7]. OBS gained more popularity as it offers the potential for normal voiding without an abdominal stoma. However, it is not feasible for all patients, especially for those with compromised renal function (serum creatinine 150–200 mmol/l) and severe hepatic disease. Other relative contraindications include the presence of urethral stricture, intellectual disability, or the lack of manual dexterity [8]. After RARC, urinary diversion is mostly performed extracorporeally [9]. In this chapter we will discuss and describe a step-by-step approach to intracorporeal urinary diversion.

Preoperative Preparation

Patients undergoing RARC should provide an informed consent after being thoroughly counseled and fully understand the risks, benefits, and possible complications. The patient should also be counseled about their future lifestyle changes including stoma management and the possibility of self-catheterization. Working with the stoma therapist in the preoperative and postoperative period represents a crucial part for the success of the procedure.

A complete preoperative anesthesiology assessment including cardiac testing, renal and hepatic function, and correction of modifiable medical disease should be performed. Careful consideration of the patient's pulmonary functions is vital to tolerate the steep Trendelenburg position, especially with the prolonged operative duration of the intracorporeal diversion. The "fast track" combines innovative aspects such as limited bowel preparation and allowing clear liquid diet up to 12 h before surgery. Scant evidence supports bowel preparation, and a simple cleaning enema the night before surgery as part of fast track seems to be sufficient [10].

Thromboembolic complications are not uncommon after RC [11]. Mechanical methods (as compression stockings and intermittent pneumatic compression devices) and low molecular weight heparin are important for measures for thromboembolic prophylaxis [12]. Broad-spectrum intravenous antibiotics are preferably administered 1 h before the start of the procedure.

Positioning and Port Placement

The patient is positioned in the Trendelenburg position with the feet higher than the head with around 10–15°. This position provides more working space by displacing the intestinal loops upward. The abdomen is insufflated using the Veress needle or Hassan technique. After placing the camera port, all ports are placed under direct vision. Ports should be placed more cephalad to facilitate bowel maneuvering and performing extended pelvic lymph node dissection. A standard 6-port transperitoneal approach is used with an additional 12-mm-short suprapubic port placed later to facilitate bowel anastomosis.

Intracorporeal Ileal Conduit (The "Marionette" Technique)

Marionette Stitch and Identification of the Bowel Segment

After RARC, the left ureter is crossed to the right side by incising the sigmoid mesentery. After identification of the ileocecal valve, a 12-cm ileal segment is measured at least 15–20 cm from the ileocecal valve. The "Marionette" stitch is made using a 60-cm silk suture on a Keith needle to suspend the bowel loop from the anterior abdominal wall. The Keith needle is passed through the hypogastrium of the anterior abdominal wall, the distal end of the bowel segment, and then brought back through the same location on the anterior abdominal wall. The stitch is not tied but held in position with a clamp. This allows raising and lowering of the bowel segment (similar to moving a marionette) to facilitate bowel manipulation.

Isolation of the Bowel Segment

The mesentery is stretched by putting the Marionette under tension. Two mesenteric windows are created using the hook cautery making sure an adequate width of its base is maintained. The mesenteric fat is incised in a progressive fashion rather than deep cuts to avoid injury to adjacent structures. Care should be taken to avoid stretch injury of the mesenteric vessels. The mesenteric vessels can be controlled by hook cautery, bipolar grasper, hem-o-lok clips, vascular stapler, or ligature.

Once the two mesenteric windows are created, an Endo GIA stapler is introduced through the 15-mm assistant port to divide and isolate the ileal conduit. An enterotomy on the distal end of the conduit is made for the introduction of the ureteral stents using the hook cautery. Two other enterotomies on either side of the proximal end are also made for the ureteroileal anastomosis. A 0-silk suture is taken to approximate the two bowel ends to ensure proper orientation and avoid malrotation.

Ureteroileal Anastomosis

The ureters are anastomosed to the isolated bowel segment either using Wallace or Bricker technique. Appropriate length of the ureters can be ensured by aligning the ureteric ends with their corresponding enterotomies. The distal ureter should be excised if scarred or with questionable vascularity, until the healthy end is encountered to avoid ureteroileal narrowing. Ensuring a wide, tension-free, and water-tight anastomosis is crucial to avoid stricture or leakage. During the Wallace anastomosis, the ureters joined together at their posterior walls and are sutured into single enterotomy on the conduit. In the Bricker anastomosis, the left ureteroileal anastomosis is performed first. The fourth arm can be used to steadily hold the ureteral end. The ureter is partially transected and spatulated for a wide anastomosis. The marionette stitch is manipulated to align the conduit with the ureter to facilitate the anastomosis. A single armed 4-0 absorbable suture (5 cm long) is used for an interrupted anastomosis. The first anchoring stitch is placed in an "outside-in" manner on the ureter side at the angle of the spatulation and then "inside out" on the conduit side, perpendicular to the proximal staple line. Then, the fourth arm is used to approximate the ureteral end to the conduit before tying the suture for a tension-free mucosa-to-mucosa anastomosis.

Once the posterior wall of the anastomosis is completed, the ureteral stent is placed. A metal laparoscopic suction tube is gently advanced through the distal enterotomy up to the anastomosis, guided by the robotic needle driver, to allow passage of stent into the ureter. A 90-cm, 8.5-French, single-J ureteral stent with a guidewire is passed through the suction tip and fed into the ureter. Once the stent is pushed all the way, the suction is removed while holding the stent in place. A 3-0 chromic suture on SH needle is used to secure the stent to the conduit to prevent dislodgement. The guide wire is removed and the anterior half of the anastomosis is completed. The anastomosis of the right side is performed in similar fashion. After placement of right stent, the distal ends of both the stents are left in the 15-mm side port.

Bowel-to-Bowel Anastomosis

Continuity of the bowel is restored by performing a side-to-side anastomosis. An additional 12-mm port is placed in the hypogastrium, on the left side just lateral to the midline. In males, the port incision may be extended later or Pfannenstiel incision for specimen bag retrieval. The anti-mesenteric borders of the two bowel ends are incised just below the staple line to allow the jaws of a 60-mm Endo GIA stapler to pass through. The two bowel segments are aligned and properly oriented along the anti-mesenteric border. The stapler is passed through the hypogastric port and is fired. Another stapler is fired from the right assistant port to staple the open ends of the either bowel segments. The mesenteric window is closed with interrupted silk sutures.

Stoma

The bladder and lymph nodes specimen bag strings are retrieved from the hypogastric port (or transvaginally in female patients). A cruciate incision is made in the anterior rectus sheath, and the rectus muscle is split. Four stay sutures are placed in the sheath to anchor the conduit once it is exteriorized. Under vision, a vascular clamp is introduced through the stoma opening to grasp the marionette suture and the ends of the ureteral stents. These are pulled out through the stoma while avoiding twisting of the conduit.

Modified Studer Neobladder

First, the small bowel is assessed for the ease of approximation to the urethral stump for a tension-free ureteroileal anastomosis. The main difference between various techniques is the timing of performance of the ureteroileal anastomosis. The Karolinska group advocates early anastomosis, while others recommend performing the anastomosis after constructing the posterior plate of the neobladder

Neobladder-Urethral Anastomosis

The ileum is sufficiently mobilized to perform a tension-free neobladder-urethral anastomosis. Using robotic scissors, an enterotomy is made at the most dependent anti-mesenteric portion of the ileum. The continuous anastomosis is performed by the Van Velthoven technique. A silicone catheter is used to delineate the urethral stump in a fashion similar to urethral-vesical anastomosis during robot-assisted radical prostatectomy.

Various maneuvers can be used to facilitate approximation of the bowel to the urethral stump, reducing Trendelenburg position, using the Penrose drain for gentle stretching and traction, performing a release incision in the mesentery, stapling the medial/proximal portion of the mesentery taking care not to compromise the blood supply of the neobladder, and mobilizing the ileum around the ileocecal region.

Isolation of Bowel

A 40-cm segment of terminal ileum for the body of the neobladder and approximately 10–15 cm for the afferent limb are harvested. The ileal segment is isolated using a laparoscopic 60-mm bowel stapler. The bedside assistant can use the hybrid 15-mm port to insert the stapler for ease of alignment with the bowel. Side-to-side bowel re-anastomosed using a stapler is performed to restore bowel continuity.

Bowel Detubularization

The distal 40 cm of the isolated ileal segment is detubularized along the anti-mesenteric border, which is delineated by inserting a 24-Fr chest tube. A 10-cm proximal isoperistaltic afferent limb is left intact to anastomose the ureters.

Creation of the Modified Studer Neobladder

The posterior part of the Studer neobladder is closed using absorbable running sutures (2-0 or 3-0). After the posterior part is sutured, the distal half of the anterior part of the reservoir is also sutured in a similar fashion, leaving the proximal portion to be closed toward the end of the procedure.

Ureteral-Neobladder Anastomosis

The left ureter is tunneled to the right side through the sigmoid mesentery. The Bricker or the Wallace techniques can be used to complete the anastomosis over two single-J 40-cm ureteric stents similar to the ureteroileal anastomosis for the conduit. The ureters are anastomosed to the afferent isoperistaltic afferent limb of the Studer reservoir. The stents can be externalized or internalized (by using double J stents).

Closure of the Neobladder

The remaining part of the reservoir is closed toward the completion of the neobladder. The balloon of the indwelling catheter is filled with 10 cc of sterile water. The neobladder is checked for any anastomotic leakage. A Jackson-Pratt drain is placed in the pelvis away from the urethral-neobladder anastomosis

Outcomes

One of the major advantages of ileal conduits is the relatively simple surgical technique and the low rate of inherent postoperative complications. However, the presence of a visible stoma and its lifelong care and the related limitations in terms of social relationships, lifestyle, and leisure activities are well-recognized disadvantages. The advantages of intracorporeal ileal conduit urinary diversion include potentially faster postoperative recovery, early return of bowel function, and reduced analgesia requirements which also impact the overall hospital stay though there are no randomized studies to compare open versus robotic intracorporeal diversion.

Studies that compared different urinary diversions had some inherent limitations including non-standardized reporting of short- and long-term complications; they are mostly retrospective in nature with nonuniform patient selection and follow-up. This may explain that although technically simpler to perform, ileal conduit has not been associated with lower complications as patients who undergo this form of diversion are usually older, with multiple comorbidities, and unfavorable disease characteristics [13–15].

Conclusion

There has been a significant increase in radical cystectomies performed with robotic assistance. However, much of the lack of widespread dissemination of this technique has been attributed to longer operative times (especially with intracorporeal urinary diversion) [9]. Nevertheless, RARC and intracorporeal ileal conduit have been shown to be technically feasible with excellent outcomes [16]. Despite the potential benefits of earlier bowel recovery and improved pain scores, intracorporeal neobladders have been less popular and are limited to high-volume academic institutions worldwide. They are more technically challenging, time-consuming, and with a steep learning curve. Careful patient selection and thorough preoperative discussion and counseling with the patient, relatives, and the surgical oncology team are the key steps for satisfactory overall outcomes regardless of the urinary diversion chosen.

References

1. Johar RS, Hayn MH, Stegemann AP, Ahmed K, Agarwal P, Balbay MD, et al. Complications after robot-assisted radical cystectomy: results from the International Robotic Cystectomy Consortium. Eur Urol. 2013;64(1):52–7.
2. Raza SJ, Wilson T, Peabody JO, Wiklund P, Scherr DS, Al-Daghmin A, et al. Long-term oncologic outcomes following robot-assisted radical cystectomy: results from the International Robotic Cystectomy Consortium. Eur Urol. 2015;68(4):721–8.
3. Ghoneim MA, Abdel-Latif M, el-Mekresh M, Abol-Enein H, Mosbah A, Ashamallah A, et al. Radical cystectomy for carcinoma of the bladder: 2,720 consecutive cases 5 years later. J Urol. 2008;180(1):121–7.
4. Wilson TG, Guru K, Rosen RC, Wiklund P, Annerstedt M, Bochner BH, et al. Best practices in robot-assisted radical cystectomy and urinary reconstruction: recommendations of the Pasadena Consensus Panel. Eur Urol. 2015;67(3):363–75.
5. Lee RK, Abol-Enein H, Artibani W, Bochner B, Dalbagni G, Daneshmand S, et al. Urinary diversion after radical cystectomy for bladder cancer: options, patient selection, and outcomes. BJU Int. 2014;113(1):11–23.
6. Skinner EC. Choosing the right urinary diversion: patient's choice or surgeon's inclination? Urol Oncol. 2011;29(5):473–5.
7. Gore JL, Litwin MS, Urologic Diseases in America P. Quality of care in bladder cancer: trends in urinary diversion following radical cystectomy. World J Urol. 2009;27(1):45–50.
8. Hautmann RE, Abol-Enein H, Davidsson T, Gudjonsson S, Hautmann SH, Holm HV, et al. ICUD-EAU International Consultation on Bladder Cancer 2012: Urinary diversion. Eur Urol. 2013;63(1):67–80.
9. Leow JJ, Reese SW, Jiang W, Lipsitz SR, Bellmunt J, Trinh QD, et al. Propensity-matched comparison of morbidity and costs of open and robot-assisted radical cystectomies: a contemporary population-based analysis in the United States. Eur Urol. 2014;66(3):569–76.
10. Maffezzini M, Campodonico F, Canepa G, Gerbi G, Parodi D. Current perioperative management of radical cystectomy with intestinal urinary reconstruction for muscle-invasive bladder cancer and reduction of the incidence of postoperative ileus. Surg Oncol. 2008;17(1):41–8.
11. Dyer J, Wyke S, Lynch C. Hospital Episode Statistics data analysis of postoperative venous thromboembolus in patients undergoing urological surgery: a review of 126,891 cases. Ann R Coll Surg Engl. 2013;95(1):65–9.
12. Rice JP, Spier BJ, Soni A. Preoperative diagnosis of cholecystocolonic fistula on ERCP. N Z Med J. 2010;123(1311):69–72.
13. Madersbacher S, Schmidt J, Eberle JM, Thoeny HC, Burkhard F, Hochreiter W, et al. Long-term outcome of ileal conduit diversion. J Urol. 2003;169(3):985–90.
14. Gburek BM, Lieber MM, Blute ML. Comparison of studer ileal neobladder and ileal conduit urinary diversion with respect to perioperative outcome and late complications. J Urol. 1998;160(3 Pt 1):721–3.
15. Gudjonsson S, Davidsson T, Mansson W. Incontinent urinary diversion. BJU Int. 2008;102(9 Pt B):1320–5.
16. Hussein AA, Dibaj S, Hinata N, Field E, O'Leary K, Kuvshinoff B, et al. Development and validation of a quality assurance score for robot-assisted radical cystectomy: a 10-year analysis. Urology. 2016;97:124–9.

Complications of Ileal Conduit Diversion

6

Timothy F. Donahue and Bernard H. Bochner

In 1950 Bricker described the use of ileum for "bladder substitution" after pelvic exenteration [1], and to date it remains the most common form of urinary reconstruction after radical cystectomy [2] due to its simplicity and ease of construction. Despite six decades of experience and numerous advancements in surgical technique, ileal conduit urinary diversion remains associated with significant medical and surgical complications. In this chapter, we review the management of complications associated with ileal conduit urinary diversion.

Complications after ileal conduit surgery are generally separated into early (<90 days postop) versus late and those related to the conduit or stoma and those associated with the bowel anastomosis. Early complications are reported in up to 56% of patients [3] and include events such as bowel obstruction, enterocutaneous fistula formation, anastomotic leaks, wound infections, conduit necrosis, and pyelonephritis. Late complications occur in 28–81% of patients [3] and include bowel obstruction, ureterointestinal strictures, stomal prolapse, stomal stenosis, stomal retraction, parastomal hernias, calculi, and metabolic derangements. Jahnson and Pedersen reported 20-year data on 124 patients who underwent ileal conduit diversion and described early complications in 48%, including anastomotic leaks (both ureteroileal and ileoileal), urinary obstruction, bowel obstruction, wound dehiscence, wound infections, and major cardiovascular events. These authors described a 6% mortality rate in the early postoperative period, and late complications were seen in 52% of patients [4]. Singh and colleagues reported complication rates after ileal conduit diversion for 93 patients with an average follow-up of 5 years and noted stoma-related complications were the most frequently encountered (31%); 10% of patients developed clinical evidence of a parastomal hernia, 7% had ureterointestinal strictures, and 4.3% developed stomal stenosis and retraction [5].

T.F. Donahue, MD • B.H. Bochner, MD (✉)
Sidney Kimmel Center for Prostate and Urologic Cancers, Memorial Sloan Kettering Cancer Center, New York, NY, USA
e-mail: bochnerb@MSKCC.ORG

S. Daneshmand (ed.), *Urinary Diversion*, DOI 10.1007/978-3-319-52186-2_6

Selection of the site for the stoma is the first step toward a successful urinary reconstruction. The stoma should be located on a flat aspect of the abdomen and the suitability of the site confirmed with the patient in supine, sitting, and upright positions. Abdominal folds, creases, and the belt line should be avoided when selecting the stoma site. The stoma should be marked preoperatively to confirm the position is appropriate for the stomal appliance and offers the patient easy access to care for it. Stoma site marking preoperatively by a certified enterostomal therapist is associated with fewer postoperative stomal complications [3, 6] and is a routine part of our practice for all patients undergoing radical cystectomy.

Conduit urinary diversion can be constructed using either a portion of ileum or colon, typically either the transverse or sigmoid colon. The use of ileum is generally preferred due to the redundancy of small bowel available for reconstruction and because it is technically less challenging. Using large bowel for conduit diversion may be necessary when the use of ileum is not suitable, such as after abdominal radiation, in patients with short gut syndrome, or in those with inflammatory bowel disease. Another setting where the use of colon for conduit diversion may be considered is during a concurrent large bowel resection where a second bowel anastomosis could be avoided. Complication rates and types associated with ileal conduits and large bowel conduits are similar in appropriately selected patients [4, 5, 7, 8].

All patients at our institution are evaluated preoperatively by a wound-ostomy-certified nurse to mark the stoma location. We do not routinely have patients undergo bowel preparation with an oral PEG solution for an ileal conduit diversion; this is only used if a colon-based conduit is planned. Conduits are isolated from the ileum by standard techniques, and the decision to perform an end-stoma or Turnbull loop conduit is determined by surgeon preference. Typically, a length of 10–12 cm of ileum is selected for the conduit; in obese patients, those with a shorter mesentery, or those patients with a thicker abdominal wall, a longer segment of ileum may be required. After reestablishing bowel continuity and closing the mesenteric defect to prevent internal hernias, a circular segment of skin and subcutaneous fat at the predesignated stoma site is excised. A cruciate incision is made in the anterior rectus fascia, and the fibers of the rectus muscles are separated longitudinally to allow the passage of two fingers through a second incision in the posterior rectus fascia, although care must be taken not to widen the opening too much in order to decrease the chance of a parastomal hernia. The ileum is passed through the abdominal wall trephine, and maturation of the stoma is completed. The decision to place supporting sutures at the level of fascia is made according to surgeon preference. After stoma maturation, the intra-abdominal portion of the conduit should be inspected to make certain it is straight and that the ureteral anastomoses are not on tension. Securing the proximal end of the conduit to the retroperitoneum or sacrum can reduce tension on the ureterointestinal anastomoses. Drainage of the conduit is facilitated by placement of a segment of a 24 French red rubber catheter inserted below the level of the fascia and brought out through the stoma. This is left in place for the first 48–72 h after surgery when postoperative edema and stomal congestion are typically at its maximum. The use of ureterointestinal stents is performed according to surgeon preference.

Early complications after ileal conduit diversion are often related to the reconstructive portion of the surgery and specifically the bowel resection and anastomosis. These include such complications as paralytic ileus, bowel obstruction, anastomotic leaks, enterocutaneous fistulas, and conduit necrosis.

Postoperative ileus is one of the most common causes for delayed return of bowel function after radical cystectomy. Although there is no standard definition, postoperative ileus is generally defined as oral intake intolerance that persists beyond 5 days after surgery or by nausea and vomiting accompanied by abdominal distention that requires bowel rest with or without a nasogastric tube [9, 10]. It is characterized by abdominal distension, absent bowel sounds, delayed flatus, nausea, and vomiting and if persistent can prolong hospital stays and increase the risk of needing parenteral nutrition. The incidence of ileus varies greatly according to the definition used but typically approaches 20–30% in most series [11, 12]. In patients who are symptomatic or whose ileus lasts significantly longer than normal, the use of a nasogastric tube is warranted to decompress the stomach, accumulated gas, and secretions. Bowel obstruction must be ruled out and electrolyte abnormalities corrected in patients with a prolonged ileus. Parenteral nutrition may be necessary if the ileus persists longer than 7–10 days after surgery. The vast majority of patients will regain bowel function with these supportive measures alone.

The use of enhanced recovery programs for patients undergoing radical cystectomy has implemented evidence-based steps that focus on early return of gastrointestinal function. The avoidance of a bowel preparation, lack of a nasogastric tube after surgery, the use of nonnarcotic pain medications, and the use of a μ-receptor antagonist prior to surgery have been demonstrated to significantly decrease the time to gastrointestinal recovery and shorten hospital stays [12].

Bowel obstruction is an uncommon complication after ileal conduit surgery with reported rates ranging from 0.7 to 14.9% [8, 13]. It must be differentiated from a postoperative ileus, which can be challenging due to overlapping common symptoms during the initial phases of both processes. Both are associated with abdominal distension, abdominal pain, absent bowel sounds, lack of flatus, and nausea and vomiting. For patients with bowel obstruction, the abdominal pain may be intermittent and switch to constant if the bowel has been compromised. If the pain and tenderness localize to a specific region of the abdomen, one should be concerned about bowel obstruction, ischemia, and peritonitis. Radiographic imaging is often helpful in defining the location and degree of bowel obstruction. Plain radiographs of the abdomen taken in the supine and upright positions may identify multiple air fluid levels and lack of gas in the bowel distal to the point of obstruction; patients with an ileus may also have air fluid levels, but gas is typically seen throughout the entire gastrointestinal tract. Computed tomography with oral contrast has a sensitivity and specificity of over 90% in identifying small bowel obstruction [14] and is typically the study of choice to rule out its presence. Differentiating between complete and partial bowel obstruction is important since the management strategies vary greatly. Complete bowel obstruction occurs when there is a complete lack of passage of stool or flatus beyond an identified point of obstruction visualized on imaging. Some patients with an early complete bowel obstruction may continue to pass flatus for a short period of time if gas was present in the distal bowel prior to the obstruction. In general, patients with a partial bowel obstruction can be successfully managed with conservative measures, such as nasogastric tube decompression, fluid resuscitation, electrolyte replacement, and time. Upward of 90% of patients with a partial small bowel obstruction can be safely managed in this manner with two thirds of these bowel obstructions resolving within 7 days and the remainder within 14 days [15]. Supportive care during this period of obstruction is warranted, and consideration of reoperation should be entertained if there is not resolution by 2 weeks. Sullivan and colleagues reported on 336 patients undergoing ileal conduit construction after radical cystectomy, 6% of whom developed severe intestinal obstruction, and half of whom eventually required surgical intervention [8].

Enterocutaneous fistula is an abnormal communication between the bowel and the skin and is associated with mortality rates as high as 15%. Risk factors for developing an enterocutaneous fistula center around poor preoperative nutritional status, which leads to increased risk of anastomotic leak, wound infections, and poor healing after major surgery. Additionally, those patients with diabetes, renal failure, on chemotherapy, or who are on chronic steroids are at increased risk for fistula formation. The initial presentation for an enterocutaneous fistula often occurs between postoperative days 4 and 7 and is marked by signs and symptoms consistent with a wound infection: leukocytosis, fever, peri-incisional erythema and edema, and drainage of either pus or feculent material from the wound. The initial management of a fistula is not operative but rather supportive with attention directed toward managing the infection, correcting electrolyte and fluid losses, and providing adequate nutrition. Patients may require antibiotic and fluid support over the first few days after fistula presentation. Intra-abdominal abscesses should be ruled out and drained accordingly if present on cross-sectional imaging. Patients should be supported with parenteral nutrition, and oral intake should be minimized to decrease the volume of enteric secretions. Patients should be placed on either histamine (H2) receptor antagonists or proton pump inhibitors to reduce the risk of gastric ulcer formation and to decrease the volume of gastric secretions. Some patients may benefit from the use of somatostatin to decrease the volume of bowel secretions, which may in turn reduce the number of days until spontaneous fistula resolution [16]. If the fistula does not resolve after 6 weeks of appropriate nutritional support and no evidence of infection, spontaneous resolution is unlikely, and further management is based upon the volume of enteric losses through the fistula and whether the patient is at risk for continued sepsis [17]. Some small-volume enterocutaneous fistulas may be observed and managed nonoperatively over the long term.

Anastomotic bowel leak is a rare but devastating complication that has been reported in 1–5% of patients after ileal conduit urinary diversion [18]. Factors that may contribute to the risk of bowel anastomotic leak include poor preoperative nutrition, ischemia at the site of bowel anastomosis, history of radiation therapy, steroid use, excess tension on the anastomotic repair, and distal obstruction.

Anastomotic bowel leakage places the patient at risk for septic complications, abdominal abscesses, fistula formation, and wound dehiscence. Exploratory laparotomy, segmental bowel resection, reanastomosis, and proximal intestinal diversion are often required to address this severe complication.

Conduit necrosis develops secondary to acute ischemia of the segment of bowel forming the conduit and results from mesenteric compromise, twisting of the mesentery on its root, or due to a blood supply inadequate to support the limb from the time of initial resection [18]. Conduit necrosis must be distinguished from the typical postoperative edema that accompanies conduit construction observed over the first days to week after surgery. Venous congestion will give the stoma and distal conduit limb above the fascia a maroon, dusky appearance that resolves spontaneously over the first few days. Conversely, conduit necrosis often manifests with a progressively darkening stoma with retraction of the conduit away from the skin edges forming the border of the abdominal wall trephine. The conduit above and below the abdominal wall fascia will demonstrate vascular compromise, which can be visualized during endoscopy of the conduit. Patients with a nonviable conduit may present clinically with a septic picture, acidosis, hyperphosphatemia, and early shock [17]. Acute conduit necrosis is a surgical emergency and requires urgent abdominal exploration to inspect both the conduit and entire small bowel to look for vascular compromise followed by excision and replacement of the ischemic conduit.

Stomal complications remain the most common reason for reoperation after conduit surgery and include events such as stomal necrosis, stomal prolapse, stomal stenosis, stomal retraction, and parastomal hernia development. Bricker described the outcomes of 543 patients who had an ileal conduit urinary diversion and noted stomal complications were the cause of 26% of reoperations. Klein and colleagues reported on 319 patients who underwent conduit urinary diversion over 11 years at their institution. The overall complication rate was 8.5%, and 5% of all patients required stoma revision due to complications such as symptomatic parastomal hernias, stomal stenosis, stomal prolapse, stomal retraction, and conduit ischemia [19]. Cheung described the complications associated with 322 stoma patients, 123 of whom underwent ileal conduit diversion, with an average follow-up of 6 years. Stomal complications were noted in 63% of patients with an ileal conduit, specifically, clinical evidence of parastomal hernia in 28%, skin excoriation in 20%, stomal stenosis in 7%, and stomal prolapse in 4% [20]. In a series of 139 children with neuropathic bladders who underwent ileal conduit diversion, Cass and colleagues noted that stoma-related complications were the reason for over 50% of reoperations [21].

Stomal stenosis often results from factors such as chronic ischemia of the conduit, fascial narrowing, retraction of the stoma, or due to local skin changes from chronic irritation and dermatitis. When constructing the stoma, formation of a large nipple or stomal protrusion above the skin level allows for appropriate fit of the ostomy appliance and minimizes the local skin changes associated with leakage, skin irritation, and hyperkeratosis that can ultimately lead to stomal stenosis. Long-term sequelae of stomal stenosis may include urinary obstruction at the skin level, recurrent infections, and renal deterioration. Historic series describe stomal stenosis rates as high as 25%

for end-stomal ileal conduits and 10–20% for Turnbull loop stomas. More contemporary series, such as Frazier et al.'s report on 675 patients undergoing conduit diversion, describe stomal stenosis rates closer to 3% [22]. Compared to an end stoma, Turnbull loop stomas have been associated with significantly reduced rates of stomal stenosis [23] and should be considered in patients with a short mesentery and thick abdominal wall where an end-stoma approach may be not be feasible. Surgical repair of stomal stenosis may be as simple as a circumferential releasing incision; however, more complex repairs such as a Y-V plasty or intra-abdominal release of the conduit may be necessary depending on the severity and level of stenosis.

Stomal complications remain one of the major challenges with conduit urinary diversion and have been shown to negatively impact quality of life after radical cystectomy [24]. Although parastomal hernias remain one of the most frequent complications after stoma formation, accurate rates have been difficult to estimate. Quoted rates for the development of a parastomal hernia vary widely between 5 and 65% [25–31] depending on the length of follow-up and whether the diagnosis is made clinically or radiographically. Because of inconsistent definitions and variable lengths of follow-up, it is difficult to compare parastomal hernia rates between different series. Most studies have reported parastomal hernia rates based upon clinical exam, which can vary if the data is collected prospectively or retrospectively or if it is self-reported or documented by the surgical team. Most clinical definitions are based upon the finding of a protrusion in the vicinity of the stoma, but studies differ greatly in terms of how the examinations were performed, i.e., supine or upright with or without Valsalva maneuvers. Recently, several studies have used similar definitions for parastomal hernias and reported rates of approximately 27–50% after 12 months of follow-up [25, 32]. While parastomal hernias have been reported as late as 27 years after surgery [33], the majority occur within the first 2 years after surgery [34, 35]. A minimum follow-up of 12 months after the index operation is needed to accurately assess for the presence of a parastomal hernia [36]. The most appropriate clinical definition is any palpable defect or bulge adjacent to the stoma when the patient is supine with legs elevated or when straining when upright. If cross-sectional imaging is added to the clinical exam, a parastomal hernia can be defined as any intra-abdominal content protruding along the ostomy [37].

Radiologic evaluation of the stoma site with cross-sectional imaging has been used as an aid to clinical exam to improve detection rates of parastomal hernias. Radiographic criteria have the advantage of being objective, less impacted by physical factors such as body habitus, and reproducible in the retrospective setting. Additionally, cross-sectional imaging allows for objective measures of the sizes of the stoma aperture and hernia sac longitudinally over time. Moreno-Matias et al. described a classification system for radiographic evidence of parastomal hernias [38] that has been successfully applied in a randomized, controlled trial setting [39] and in multiple retrospective series [25, 40]. The classification system is based upon the relationship between the hernia sac and the bowel forming the stoma. A Type 1 parastomal hernia is defined as a hernia sac that contains prolapsed bowel forming the stoma, while a Type 2 contains abdominal fat or omentum herniating through the abdominal wall defect created by the stoma. A Type 3 hernia contains herniated loops of bowel other than that forming the stoma [38] (Fig. 6.1).

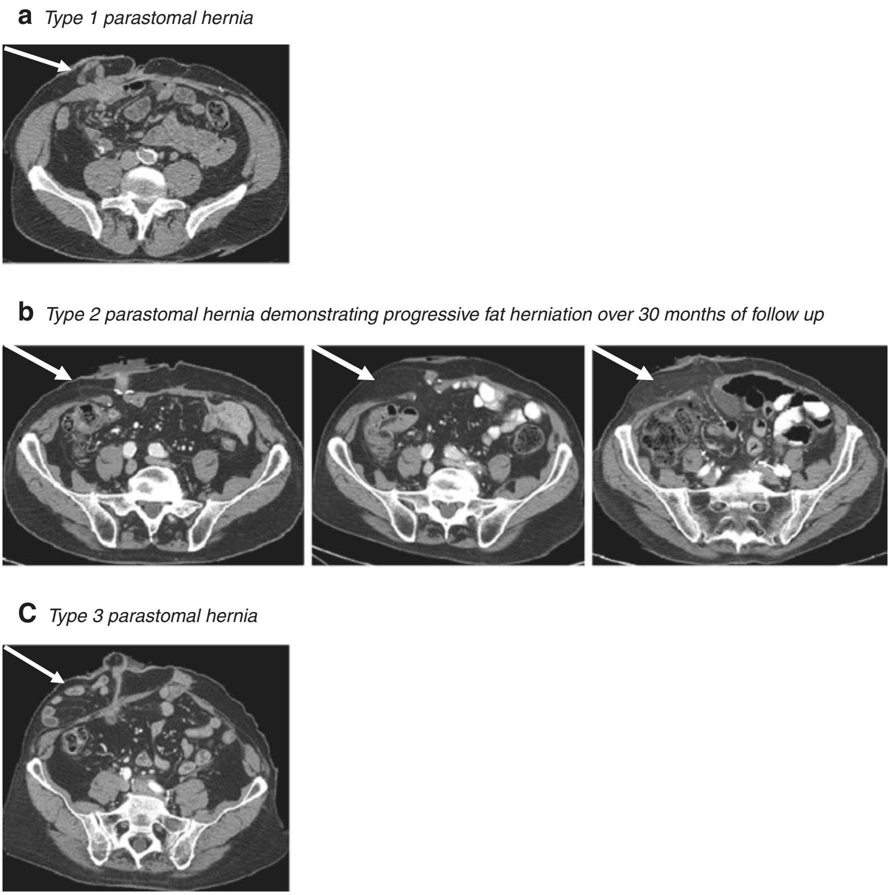


Fig. 6.1 (**a**) Type 1 parastomal hernia. (**b**) Type 2 parastomal hernia demonstrating progressive fat herniation over 30 months of follow up. (**c**) Type 3 parastomal hernia

One concern regarding radiographic classification systems for parastomal hernias is whether clinically insignificant hernias are being identified due to the increased sensitivity of cross-sectional imaging. Though experience with this radiographic classification system is limited, there appears to be good concordance between radiographically evident parastomal hernias and clinical symptoms. Seo et al. described the rates of clinical and radiographic parastomal hernias in 83 patients undergoing end colostomy. All patients with Type 3 radiographic parastomal hernia (n = 12) were clinically detectable and all were symptomatic; 80% of Type 2 radiographic hernias were clinically detectable, and 75% were symptomatic; and 60% of Type 1 hernias were clinically detectable with 63% being symptomatic [40]. In other series, radiographic Type 3 hernias have been universally identified on physical exam, while Type 2 hernias have a concordance rate of 60–80% with physical exam [25, 38, 40, 41].

The etiology of parastomal hernias is multifactorial and influenced by both technical and patient-related factors. Technical factors, such as the type of stoma created, the size and location of the stoma, the use of fascial anchoring sutures, and preoperative marking by a wound-ostomy nurse, may alter the risk of parastomal hernia development [23, 34, 40, 42–45]. Patient-related factors believed to be associated with parastomal hernia development include obesity, female gender, age, prior abdominal surgery, smoking, poor nutrition, emergency surgery, postoperative sepsis, corticosteroid use, and malignancy [25, 26, 34, 35, 40, 41, 46–48]. Obesity, female gender, poor nutrition, and stoma aperture size have been found on multivariable analyses to be independent risk factors for radiographic parastomal hernia development in retrospective series [25, 40–42].

While most patients with parastomal hernias are asymptomatic, up to a third will undergo surgical repair on an elective basis for bothersome symptoms or occasionally in emergent circumstances due to strangulation or bowel obstruction [35]. In a report of 782 ostomy patients with a median follow-up of 10.5 years, Ripoche et al. identified clinical evidence of parastomal hernias in 25.6% of patients. Only 24% of patients with a parastomal hernia denied the presence of symptoms, and in the three-quarters who were symptomatic, 46% reported pain, 37% stomal appliance problems, 36% leakage, 29% skin irritation, and 20% described psychological and aesthetic concerns secondary to the hernia. Stomal prolapse occurred in 18%, and at least one episode of obstruction was observed in 15% of patients [33]. Liu et al. reported a clinical parastomal hernia rate of 29% at a median follow-up of 29 months, 45% of whom underwent surgical repair for abdominal pain (58%), acute strangulation or bowel obstruction (15%), partial small bowel obstruction (15%), or for elective reasons (12%) [26]. In our own series of 384 consecutive patients undergoing radical cystectomy and ileal conduit diversion, we noted 24% of patients had parastomal hernias on physical exam, 40% of whom were symptomatic. Of the 93 patients with a clinically apparent hernia, an abdominal hernia belt or binder was prescribed for 75 patients (81%), and 16 (17%) were referred for possible surgical repair. Only eight patients (9%) with symptomatic parastomal hernias underwent surgical repair, two of which were performed emergently due to bowel strangulation. Three of the eight repairs developed a recurrent parastomal hernia a median of 13 months (range 10–22 months) later. The low rates of referral may reflect the need to balance the competing issues of advanced disease and short life expectancy in some patients with high recurrence rates and potential morbidity associated with the hernia repair [25].

The negative quality of life issues, morbidity of surgical repair, and relatively high recurrences rates have prompted surgeons to attempt to prevent parastomal hernias from the time of the index operation. There have been five prospective, randomized studies where mesh was placed at the time of stoma formation in an attempt to prevent parastomal hernias, all of which have demonstrated significant reductions in the clinical and radiographic parastomal hernia rates without associated postoperative complications or long-term morbidity [39, 49–51] (Table 6.1). Four studies used partially absorbable mesh, and the fifth was a phase I trial of a biologic mesh in patients undergoing loop ileostomy with planned reversal 6 months later (Fig. 6.2). The series with the longest follow-up comes from Janes et al. who reported short- and long-term results from their randomized trial. After both

Table 6.1 Randomized controlled trials of prophylactic mesh placement

Author	Type of stoma	Type of mesh	Placement technique	Number of patients	Median follow-up	Primary endpoint	PH rate	Mesh-related complications
Janes	Permanent end colostomy	Partially absorbable (Vypro)	Sublay	Mesh = 27 Control = 27	14 months (95% CI 12–17)	Clinical PH	At 12 months: Mesh: 0/16 (0%) Control: 8/18 (44.4%)	None reported
Serra-Aracil	Permanent end colostomy	Partially absorbable (Ultrapro)	Sublay	Mesh = 27 Control = 27	29 months (range, 13–49)	Clinical PH Radiographic PH	At 29 months (median) *Clinical PH* Mesh: 4/27 (14.8%) Control: 11/27 (40.7%) *Radiographic PH* Mesh: 6/27 (22.2%) Control: 12/27 (44.4%)	None reported
Hammond	Loop stoma	Xenogenic collagen	Sublay	Implant = 10 Control = 10	6.5 months	Clinical PH	At 12 months: Implant: 0/10 (0%) Control: 3/10 (33.3%)	None reported
Lambrecht	Permanent end colostomy	Polypropylene	Sublay	Mesh = 32 Control = 26	40 months (range, 3–87)	Clinical PH	At 24 months: Mesh: 2/32 (6.3%) Control: 12/26 (46.2%)	None reported
Vierimaa	Permanent end colostomy	Partially absorbable (Dyna-Mesh IPOM)	Intraperitoneal onlay	Mesh = 35 Control =35	12 months	Clinical PH Radiographic PH	At 12 months: *Clinical PH* Mesh: 5/35 (14.3%) Control: 12/32 (32.3%) *Radiographic PH* Mesh: 18/35 (51.4%) Control: 17/32 (53.1%)	None reported

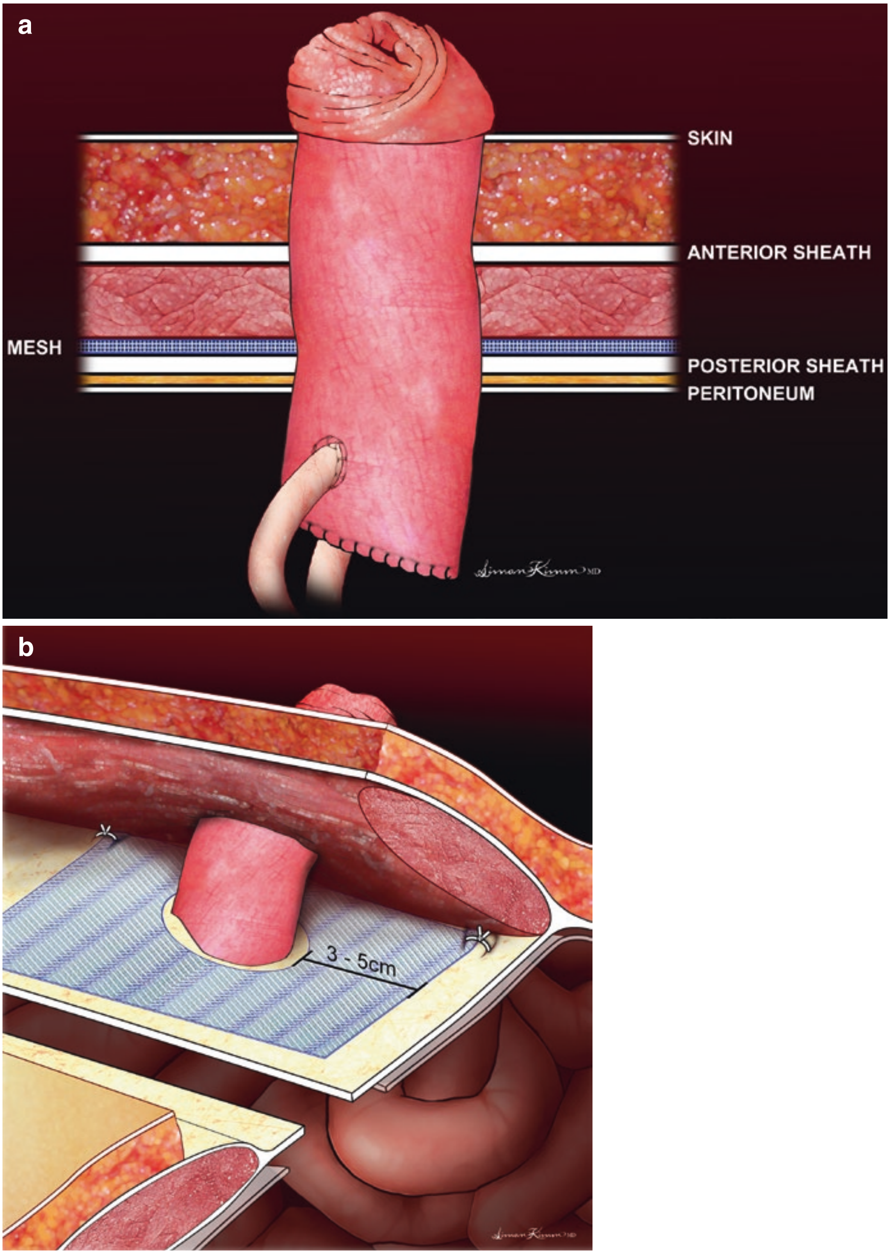


Fig. 6.2 Example of placement of prophylactic mesh in the sublay (retrorectus) position at the time of conduit creation. (**a**) Cross sectional view of the layers of the abdomen illustrating the mesh is placed immediately posterior to the rectus muscle. (**b**) The mesh is placed anterior the posterior rectus sheath and posterior to the rectus muscle. The mesh is tailored to a size that allows for a 3–5 cm circumferential margin around the conduit

12-month and 5-year follow-up for patients in their randomized trial, they reported significant reductions in the rates of parastomal hernias for patients receiving prophylactic mesh compared to standard surgery [49, 52]. At a minimum of 5-year follow-up, the parastomal hernia rate for those alive with mesh was 13% compared to 81% who had standard surgery ($p < 0.001$). Over a mean of 72 months of follow-up, no fistulas, strictures, and mesh infections were noted, and no patient has required mesh removal [52].

Not all randomized trials of prophylactic mesh placement at the time of stoma formation have demonstrated equivalent results. Vierimaa et al. reported on 83 patients randomized to have a dual layer mesh placed in the intraperitoneal onlay position at the time of laparoscopic end-colostomy formation versus traditional stoma formation. The primary end points for the trial were to measure both clinical and radiographic parastomal hernia rates with secondary end points being stoma-related morbidity and need for surgical parastomal hernia repair. The authors noted a significant reduction in clinical parastomal hernias for those receiving mesh compared to those having standard surgery (14.3% versus 32.3%; $p = 0.049$); however, the rates of radiographic parastomal hernias as assessed by CT imaging were not different (51.4% versus 53.1%; $p = 1.00$) [53].

Non-randomized series of consecutive patients receiving prophylactic mesh at the time of index surgery have recently been published. Styrke reported a single institution, 10-year consecutive series of 114 patients having prophylactic mesh placed in the sublay (retrorectus) position at the time of open radical cystectomy and ileal conduit formation. After a median follow-up of 35 months, they reported a clinical parastomal hernia rate of 14% in 58 evaluable patients and no mesh-related complications [54]. In contrast to other investigators, Nikberg et al. did not identify a difference in clinical or radiographic parastomal hernia rates after introducing prophylactic sublay mesh for all patients undergoing end colostomy at their institution beginning in 2007. When compared to matched patients having traditional surgery ($n = 135$) between 1997 and 2007, those having prophylactic mesh ($n = 71$) after 2007 had the exact same clinical parastomal hernia rates (25%; $p = 0.953$) and radiographic parastomal hernia rates (53%; $p = 0.176$). The degree of herniation on cross-sectional imaging (containing omentum or bowel in the hernia sac) was similar for those having mesh placed and those having standard surgery (80% versus 61%; $p = 0.155$). On multivariable analysis, these authors found BMI to be an independent risk factor for development of parastomal hernia (HR = 1.09, 95% CI = 1.00–1.18) [55]. Ultimately, the degree to which placement of prophylactic mesh at the time of ileal conduit construction reduces parastomal hernia rates should be established in the setting of a randomized controlled trial.

There is significant debate regarding whether the ureterointestinal anastomoses should be constructed in a non-refluxing or refluxing manner. The principle behind constructing non-refluxing anastomoses is to protect the kidneys and upper tracts from sustained high pressures and to prevent ascending bacteriuria. This was particularly relevant for patients undergoing ureterosigmoidostomy, which diverts the urine into a high-pressure system, but has become less of a concern with the development of lower pressure, high-capacity continent reservoirs and for patients undergoing conduit urinary diversion. There appears to be a greater risk of gradual renal deterioration from ureterointestinal anastomotic strictures than from reflux of urine into the upper tracts. Non-refluxing anastomoses are associated with twice the rate of strictures than refluxing anastomoses, irrespective of the type of bowel segment used. Rates of ureterointestinal strictures with a refluxing anastomotic repair range from 1.7 to 3.6% compared to the 13–29% described with the LeDuc non-refluxing anastomosis technique [56]. Approximately half of patients with strictures will require surgical intervention, leading some surgeons to conclude that the greater risk to the upper tracts is ureterointestinal anastomotic stricture rather than reflux. In a group of 126 patients followed over 25 years with Kock reservoirs, Jonnson and colleagues concluded that the type of diversion does not significantly impact long-term kidney function as long as any potential strictures are recognized and treated [57]. Refluxing anastomoses are technically simpler to complete and have not been associated with significant rates of upper tract deterioration, thus making them the procedure of choice for ureterointestinal anastomoses [58–62].

Ureterointestinal strictures occur in 3–29% of patients depending on the anastomotic technique used and the length of follow-up reported. Most strictures are felt to be due to ureteral ischemia and will occur within the first 1–2 years after surgery irrespective of the type of anastomosis performed. These strictures are typically asymptomatic and only identified by changes in creatinine levels over time or on surveillance imaging studies [63–66]. Minimizing mobilization and devascularization of ureters is of paramount importance in reducing the risk of postoperative strictures. Care must be taken in routing the left ureter under the descending colon or through an avascular segment of its mesentery, which should be considered when passing the ureter beneath the colon might cause excessive angulation or place the anastomosis on tension.

Antegrade and retrograde endoscopic as well as open surgical approaches have been described to address ureterointestinal strictures. Both endoscopic or antegrade dilation and incision of strictures have been described with success rates of 20.0% to 50.0% versus 44.4% to 63.0%, respectively. The best results with endoscopic management have been seen with short (< 2 cm) distal strictures in kidneys with preserved renal function at the time of intervention; endoscopic treatment of strictures in renal units with less than 25% differential function is associated with poorer outcomes [66–71]. At 3 years follow-up, endoscopic management of ureterointestinal strictures has a reported continued success rate of only 32% [72]. Open surgical approaches have success rates approaching 90% but are the most invasive and technically challenging. It is important to evaluate the excised segment of stenotic ureter and bowel for the presence of malignancy when performing an open repair.

Ileum and colon are associated with the fewest electrolyte disturbances, have the greatest amount of redundancy, are easily mobilized to any portion of the abdomen or pelvis, and have excellent blood supplies. Both segments have the same metabolic abnormalities due to the absorption of ammonium chloride resulting in a hyperchloremic metabolic acidosis. Patients with impaired renal function can develop lethargy, anorexia, weight loss, and long-term risk for bone demineralization leading to osteopenia. Symptomatic metabolic acidosis can be treated with alkalinizing agents, maintaining good hydration, and minimizing dwell time of urine in the conduit. The terminal ileum is responsible for absorption of bile salts, fat-soluble vitamins (K, A, D, and E), and the absorption of vitamin B-12. If excessive lengths of ileum are used for diversion, patients can develop steatorrhea, vitamin B-12 deficiency, and dehydration.

The use of the terminal ileum for construction of either a continent cutaneous reservoir or orthotopic neobladder can place the patient at risk for vitamin B-12 deficiency. Ideally, the segment of ileum utilized for the conduit should be taken from an area proximal to the terminal ileum to avoid this complication. Vitamin B-12 absorption occurs primarily in the terminal ileum, and deficiency can result in irreversible neurologic and hematologic derangements. From baseline levels vitamin B-12 depletion is a slowly occurring event after loss of the terminal ileum, often taking 3–5 years to drop to a level sufficiently low enough to produce symptoms [73–76]. It is our practice to monitor B-12 levels on an annual basis and to replace on a yearly basis beginning at year 3 after urinary diversion.

Chronic acidosis after urinary diversion occurs in 5.5–13.3% of patients at a mean follow-up of 51 months and can result long term in bone demineralization and osteomalacia [77]. Decreased intestinal absorption of calcium can occur with resection of longer segments of ileum. Bone minerals, such as calcium and carbonate, act as buffers against hydrogen ions, leading to decreased skeletal calcium content. Chronic acidosis will induce vitamin D deficiency, resulting in bone mineralization defects, and finally the acidic environment activates resorption of bone by osteoclasts [78–81]. Laboratory values may show elevated alkaline phosphatase and reduced serum calcium and phosphate levels [79, 82]. Patients can present with a variety of issues related to bone demineralization ranging from being asymptomatic to pain in weight bearing joints to having fractures. Women and those patients undergoing urinary diversion at a young age when bone growth is not yet complete appear to be at highest risk for the complications associated with bone demineralization. Patients with impaired renal function are at risk for acidosis which may be worsened after urinary diversion. Radiographic evidence of bone demineralization may take years to develop. Serial measurements of bone mineral density by DEXA scan may demonstrate subtle alterations over time, but this needs to be further studied in prospective manner. Symptomatic patients should have their acid-base status corrected as a first step, which may also result in remineralization of the bone; however, those failing to respond should be managed with calcium supplements and vitamin D [83–85]. Oral sodium bicarbonate should be considered for patients with a base deficit of −2.5 mmol/l to reduce the likelihood of developing bone sequelae from chronic acidosis.

Despite six decades of experience with ileal conduit urinary diversion, medical and surgical complications are common and can negatively impact patients' quality of life. Urologists must have a thorough understanding of the principles of urinary diversion, meticulous attention to detail during the index operation, and comprehensive long-term follow-up to help reduce the early and late complications associated with this urinary reconstruction.

References

1. Bricker EM. Bladder substitution after pelvic evisceration. Surg Clin North Am. 1950;30:1511.
2. Hautmann RE, Abol-Enein H, Lee CT, et al. Urinary diversion: how experts divert. Urology. 2015;85:233.
3. Killeen KP, Libertino JA. Management of bowel and urinary tract complications after urinary diversion. Urol Clin North Am. 1988;15:183.
4. Jahnson S, Pedersen J. Cystectomy and urinary diversion during twenty years –complications and metabolic implications. Eur Urol. 1993;24:343.
5. Singh G, Wilkinson JM, Thomas DG. Supravesical diversion for incontinence: a long-term follow-up. Br J Urol. 1997;79:348.
6. Bass EM, Del Pino A, Tan A, et al. Does preoperative stoma marking and education by the enterostomal therapist affect outcome? Dis Colon Rectum. 1997;40:440.
7. Madersbacher S, Schmidt J, Eberle JM, et al. Long-term outcome of ileal conduit diversion. J Urol. 2003;169:985.
8. Sullivan JW, Grabstald H, Whitmore Jr WF. Complications of ureteroileal conduit with radical cystectomy: review of 336 cases. J Urol. 1980;124:797.
9. Shabsigh A, Korets R, Vora KC, et al. Defining early morbidity of radical cystectomy for patients with bladder cancer using a standardized reporting methodology. Eur Urol. 2009;55:164.
10. Ramirez JA, McIntosh AG, Strehlow R, et al. Definition, incidence, risk factors, and prevention of paralytic ileus following radical cystectomy: a systematic review. Eur Urol. 2013;64:588.
11. Winer AG, Sfakianos JP, Puttanniah VG, et al. Comparison of perioperative outcomes for epidural versus intravenous patient-controlled analgesia after radical cystectomy. Reg Anesth Pain Med. 2015;40:239.
12. Djaladat H, Daneshmand S. Gastrointestinal complications in patients who undergo radical cystectomy with enhanced recovery protocol. Curr Urol Rep. 2016;17:50.
13. Remigailo RV, Lewis EL, Woodard JR, et al. Ileal conduit urinary diversion. Ten-year review. Urology. 1976;7:343.
14. Donckier V, Closset J, Van Gansbeke D, et al. Contribution of computed tomography to decision making in the management of adhesive small bowel obstruction. Br J Surg. 1998;85:1071.
15. Pickleman J, Lee RM. The management of patients with suspected early postoperative small bowel obstruction. Ann Surg. 1989;210:216.
16. Boike GM, Sightler SE, Averette HE. Treatment of small intestinal fistulas with octreotide, a somatostatin analog. J Surg Oncol. 1992;49:63.
17. Kanofsky JA, Guilherme G, Taneja SS. Complications of conduit urinary diversion. In: Taneja SS, editor. Complications of urologic surgery: prevention and management. 4th ed. Philadelphia: WB Saunders; 2010. p. 533–46.
18. Gitlin JT. Complications of conduit urinary diversion. In: Taneja SS, Smith RB, Ehrlich RM, editors. Complications of urologic surgery: prevention and management. 3rd ed. Philadelphia: WB Saunders; 2001. p. 437–53.
19. Klein EA, Montie JE, Montague DK, et al. Stomal complications of intestinal conduit urinary diversion. Cleve Clin J Med. 1989;56:48.
20. Cheung MT. Complications of an abdominal stoma: an analysis of 322 stomas. Aust N Z J Surg. 1995;65:808.
21. Cass AS, Luxenberg M, Gleich P, et al. A 22-year followup of ileal conduits in children with a neurogenic bladder. J Urol. 1984;132:529.
22. Frazier HA, Robertson JE, Paulson DF. Complications of radical cystectomy and urinary diversion: a retrospective review of 675 cases in 2 decades. J Urol. 1992;148:1401.
23. Emmott D, Noble MJ, Mebust WK. A comparison of end versus loop stomas for ileal conduit urinary diversion. J Urol. 1985;133:588.
24. Gerharz EW, Mansson A, Hunt S, et al. Quality of life after cystectomy and urinary diversion: an evidence based analysis. J Urol. 2005;174:1729.

25. Donahue TF, Bochner BH, Sfakianos JP, et al. Risk factors for the development of parastomal hernia after radical cystectomy. J Urol. 2014;191:1708.
26. Liu NW, Hackney JT, Gellhaus PT, et al. Incidence and risk factors of parastomal hernia in patients undergoing radical cystectomy and ileal conduit diversion. J Urol. 2014;191:1313.
27. Farnham SB, Cookson MS. Surgical complications of urinary diversion. World J Urol. 2004;22:157.
28. Kouba E, Sands M, Lentz A, et al. Incidence and risk factors of stomal complications in patients undergoing cystectomy with ileal conduit urinary diversion for bladder cancer. J Urol. 2007;178:950.
29. Wood DN, Allen SE, Hussain M, et al. Stomal complications of ileal conduits are significantly higher when formed in women with intractable urinary incontinence. J Urol. 2004;172:2300.
30. Bloom DA, Grossman HB, Konnak JW. Stomal construction and reconstruction. Urol Clin North Am. 1986;13:275.
31. Fontaine E, Barthelemy Y, Houlgatte A, et al. Twenty-year experience with jejunal conduits. Urology. 1997;50:207.
32. Janes A, Cengiz Y, Israelsson LA. Experiences with a prophylactic mesh in 93 consecutive ostomies. World J Surg. 2010;34:1637.
33. Ripoche J, Basurko C, Fabbro-Perray P, et al. Parastomal hernia. A study of the French federation of ostomy patients. J Visc Surg. 2011;148:e435.
34. Martin L, Foster G. Parastomal hernia. Ann R Coll Surg Engl. 1996;78:81.
35. Marimuthu K, Vijayasekar C, Ghosh D, et al. Prevention of parastomal hernia using preperitoneal mesh: a prospective observational study. Color Dis. 2006;8:672.
36. Israelsson LA. Parastomal hernias. Surg Clin North Am. 2008;88:113.
37. Janes A, Weisby L, Israelsson LA. Parastomal hernia: clinical and radiological definitions. Hernia. 2011;15:189.
38. Moreno-Matias J, Serra-Aracil X, Darnell-Martin A, et al. The prevalence of parastomal hernia after formation of an end colostomy. A new clinico-radiological classification. Color Dis. 2009;11:173.
39. Serra-Aracil X, Bombardo-Junca J, Moreno-Matias J, et al. Randomized, controlled, prospective trial of the use of a mesh to prevent parastomal hernia. Ann Surg. 2009;249:583.
40. Seo SH, Kim HJ, Oh SY, et al. Computed tomography classification for parastomal hernia. J Korean Surg Soc. 2011;81:111.
41. Hong SY, Oh SY, Lee JH, et al. Risk factors for parastomal hernia: based on radiological definition. J Korean Surg Soc. 2013;84:43.
42. Hotouras A, Murphy J, Power N, et al. Radiological incidence of parastomal herniation in cancer patients with permanent colostomy: what is the ideal size of the surgical aperture? Int J Surg. 2013;11:425.
43. Pilgrim CH, McIntyre R, Bailey M. Prospective audit of parastomal hernia: prevalence and associated comorbidities. Dis Colon Rectum. 2010;53:71.
44. McGrath A, Porrett T, Heyman B. Parastomal hernia: an exploration of the risk factors and the implications. Br J Nurs. 2006;15:317.
45. Pisters AL, Kamat AM, Wei W, et al. Anterior fascial fixation does not reduce the parastomal hernia rate after radical cystectomy and ileal conduit. Urology. 2014;83:1427.
46. Carne PW, Frye JN, Robertson GM, et al. Parastomal hernia following minimally invasive stoma formation. ANZ J Surg. 2003;73:843.
47. Sjodahl R, Anderberg B, Bolin T. Parastomal hernia in relation to site of the abdominal stoma. Br J Surg. 1988;75:339.
48. Gogenur I, Mortensen J, Harvald T, et al. Prevention of parastomal hernia by placement of a polypropylene mesh at the primary operation. Dis Colon Rectum. 2006;49:1131.
49. Janes A, Cengiz Y, Israelsson LA. Randomized clinical trial of the use of a prosthetic mesh to prevent parastomal hernia. Br J Surg. 2004;91:280.
50. Hammond TM, Huang A, Prosser K, et al. Parastomal hernia prevention using a novel collagen implant: a randomised controlled phase 1 study. Hernia. 2008;12:475.

51. Lambrecht RJ, Larsen GS, Reiertsen O, et al. Prophylactic mesh at end-colostomy construction reduces parastomal hernia rate: a randomised trial. Color Dis. 2015;17(10):O191–7.
52. Janes A, Cengiz Y, Israelsson LA. Preventing parastomal hernia with a prosthetic mesh: a 5-year follow-up of a randomized study. World J Surg. 2009;33:118.
53. Vierimaa M, Klintrup K, Biancari F, et al. Prospective, randomized study on the use of a prosthetic mesh for prevention of parastomal hernia of permanent colostomy. Dis Colon Rectum. 2015;58:943.
54. Styrke J, Johansson M, Granasen G, et al. Parastomal hernia after ileal conduit with a prophylactic mesh: a 10 year consecutive case series. Scand J Urol. 2015;49:1.
55. Nikberg M, Sverrisson I, Tsimogiannis K, et al. Prophylactic stoma mesh did not prevent parastomal hernias. Int J Color Dis. 2015;30:1217.
56. Stein JP, Stenzl A, Grossfeld GD, et al. The use of orthotopic neobladders in women undergoing cystectomy for pelvic malignancy. World J Urol. 1996;14:9.
57. Hobisch A, Tosun K, Kinzl J, et al. Quality of life after cystectomy and orthotopic neobladder versus ileal conduit urinary diversion. World J Urol. 2000;18:338.
58. Hautmann RE, de Petriconi R, Gottfried HW, et al. The ileal neobladder: complications and functional results in 363 patients after 11 years of followup. J Urol. 1999;161:422.
59. Henningsohn L, Steven K, Kallestrup EB, et al. Distressful symptoms and well-being after radical cystectomy and orthotopic bladder substitution compared with a matched control population. J Urol. 2002;168:168.
60. Hart S, Skinner EC, Meyerowitz BE, et al. Quality of life after radical cystectomy for bladder cancer in patients with an ileal conduit, cutaneous or urethral kock pouch. J Urol. 1999;162:77.
61. Mansson A, Caruso A, Capovilla E, et al. Quality of life after radical cystectomy and orthotopic bladder substitution: a comparison between Italian and Swedish men. BJU Int. 2000;85:26.
62. Bihrle R. The Indiana pouch continent urinary reservoir. Urol Clin North Am. 1997;24:773.
63. Hautmann RE. Urinary diversion: ileal conduit to neobladder. J Urol. 2003;169:834.
64. Pantuck AJ, Han KR, Perrotti M, et al. Ureteroenteric anastomosis in continent urinary diversion: long-term results and complications of direct versus nonrefluxing techniques. J Urol. 2000;163:450.
65. Schwaibold H, Friedrich MG, Fernandez S, et al. Improvement of ureteroileal anastomosis in continent urinary diversion with modified Le Duc procedure. J Urol. 1998;160:718.
66. Roth S, van Ahlen H, Semjonow A, et al. Does the success of ureterointestinal implantation in orthotopic bladder substitution depend more on surgeon level of experience or choice of technique? J Urol. 1997;157:56.
67. Abol-Enein H, Ghoneim MA. Functional results of orthotopic ileal neobladder with serous-lined extramural ureteral reimplantation: experience with 450 patients. J Urol. 2001;165:1427.
68. De Carli P, Micali S, O'Sullivan D, et al. Ureteral anastomosis in the orthotopic ileal neobladder: comparison of 2 techniques. J Urol. 1997;157:469.
69. Kristjansson A, Bajc M, Wallin L, et al. Renal function up to 16 years after conduit (refluxing or anti-reflux anastomosis) or continent urinary diversion. 2. Renal scarring and location of bacteriuria. Br J Urol. 1995;**76**:546.
70. Studer UE, Danuser H, Thalmann GN, et al. Antireflux nipples or afferent tubular segments in 70 patients with ileal low pressure bladder substitutes: long-term results of a prospective randomized trial. J Urol. 1996;156:1913.
71. Osman Y, Abol-Enein H, Nabeeh A, et al. Long-term results of a prospective randomized study comparing two different antireflux techniques in orthotopic bladder substitution. Eur Urol. 2004;45:82.
72. Wolf Jr JS, Elashry OM, Clayman RV. Long-term results of endoureterotomy for benign ureteral and ureteroenteric strictures. J Urol. 1997;158:759.
73. McDougal WS. Metabolic complications of urinary intestinal diversion. J Urol. 1992;147:1199.
74. Yakout H, Bissada NK. Intermediate effects of the ileocaecal urinary reservoir (Charleston pouch 1) on serum vitamin B12 concentrations: can vitamin B12 deficiency be prevented? BJU Int. 2003;91:653.

75. Sagalowsky AI, Frenkel EP. Cobalamin profiles in patients after urinary diversion. J Urol. 2002;167:1696.
76. Pfitzenmaier J, Lotz J, Faldum A, et al. Metabolic evaluation of 94 patients 5 to 16 years after ileocecal pouch (Mainz pouch 1) continent urinary diversion. J Urol. 2003;170:1884.
77. Alcini E, D'Addessi A, Racioppi M, et al. Results of 4 years of experience with bladder replacement using an ileocecal segment with multiple transverse teniamyotomies. J Urol. 1993;149:735.
78. Bettice JA, Gamble Jr JL. Skeletal buffering of acute metabolic acidosis. Am J Phys. 1975;229:1618.
79. McDougal WS, Koch MO, Shands 3rd C, et al. Bony demineralization following urinary intestinal diversion. J Urol. 1988;140:853.
80. Lee SW, Russell J, Avioli LV. 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol: conversion impaired by systemic metabolic acidosis. Science. 1977;195:994.
81. Arnett TR, Dempster DW. Effect of pH on bone resorption by rat osteoclasts in vitro. Endocrinology. 1986;119:119.
82. Mundy AR, Nurse DE. Calcium balance, growth and skeletal mineralisation in patients with cystoplasties. Br J Urol. 1992;69:257.
83. Hossain M. The osteomalacia syndrome after colocystoplasty; a cure with sodium bicarbonate alone. Br J Urol. 1970;42:243.
84. Siklos P, Davie M, Jung RT, et al. Osteomalacia in ureterosigmoidostomy: healing by correction of the acidosis. Br J Urol. 1980;52:61.
85. Perry W, Allen LN, Stamp TC, et al. Vitamin D resistance in osteomalacia after ureterosigmoidostomy. N Engl J Med. 1977;297:1110.

7 Use of Regenerative Tissue for Urinary Diversion

Nikolai A. Sopko, Max Kates, Anirudha Singh,
Gary D. Steinberg, Norm D. Smith,
Mark P. Schoenberg, and Trinity J. Bivalacqua

Introduction

There is a large interest in developing tissue-engineered urinary diversions (TEUDs) in order to reduce the significant morbidity that results from utilization of the alimentary tract in the urinary system. The gastrointestinal tract has been used for urinary diversion for over 150 years with the first reported ureteroproctostomy by Simon in 1858 [1]. Although it is also a tubular structure designed for material transport, the absorptive qualities of the alimentary tract result in significant morbidity when exposed to urinary waste. Invariably, some degree of metabolic disequilibrium and anorexia develop, in addition to the operative sequela of bowel surgery. Additional long-term sequela may include urolithiasis, infection, disruption of the enterohepatic circulation, anemia, and chronic metabolic acidosis. Furthermore, incorporated bowel segments do not have the mechanical properties and innervation necessary to recapitulate the complex function of coordinated urinary storage and emptying.

Given the clear need for a new approach, it is no surprise that reconstruction of the urinary tract has been sought after since the early years of tissue engineering [2, 3].

N.A. Sopko, MD, PhD • M. Kates • A. Singh
The James Buchanan Brady Urological Institute and Department of Urology, The Johns Hopkins School of Medicine, 800 Orleans Street, Marburg 420, Baltimore, MD 21287, USA
e-mail: nas@jhmi.edu

G.D. Steinberg, MD • N.D. Smith, MD
Department of Urology, University of Chicago, Chicago, IL, USA

M.P. Schoenberg, MD
Department of Urology, Albert Einstein College of Medicine, New York, NY, USA

T.J. Bivalacqua (✉)
Department of Urology, The Johns Hopkins Hospital, Baltimore, MD, USA

S. Daneshmand (ed.), *Urinary Diversion*, DOI 10.1007/978-3-319-52186-2_7

There are four essential components of any tissue engineering program to replace a whole organ:

1. Identification of the most appropriate biomaterial
2. Identification of a cell type for seeding of the biomaterial/scaffold
3. Creation of a stimulus from host microenvironment or from implanted cells
4. Identification of a blood supply to bring nutrients, oxygen, and growth factors for the tissue-engineered organ to maturate and regenerate

Studies continue to identify novel scaffold materials and cell populations that are combined to generate TEUDs. Scaffold composition ranges from synthetic material to decellularized bladder tissue. Cell types vary from fully differentiated adult populations such as smooth muscle cells isolated from the bladder to stem cell populations including mesenchymal stem cells and induced pluripotent stem cells. Each scaffold and cell type has its advantages and disadvantages with no clear superior component having been identified. Recent clinical trials have been disappointing, supporting the need for additional investigation. The successful marriage of these components into a biologically successful tissue-engineered organ is challenging. The various types of scaffolds and cells that are currently showing clinical promise in urinary diversion strategies will be reviewed.

Scaffolds

As its name implies, scaffolds provide the backbone for TEUDs. Cells grown in culture do not have enough structural integrity to be used by themselves, although sheets of cells have been used to treat injury to native bladder tissues [4, 5]. The ideal scaffold provides mechanical support for cells to engraft, completely degrades over time, and elicits minimal to no foreign body reaction while performing the complex physiological task of storing and voiding urine [6]. Cells can be seeded or migrate in from neighboring host tissues. To do so, they need the proper cues to aid cells in differentiating and organizing themselves to serve their physiological function, i.e., urothelium to form on the luminal surface and smooth muscle within the walls [7]. These cues can come from the inherent properties of the material used or from growth factors incorporated into the scaffold [8]. For example, collagens comparable to those that make up the basement membrane of the bladder can be used in guiding urothelial cell attachment and expansion [9].

Biomaterials for TEUDs can be organized into three general categories:

1. Acellular tissue matrices, such as bladder and small intestinal submucosa
2. Natural materials, such as collagen, alginate, and silk
3. Synthetic polymers, such as poly(glycolic acid) (PGA) and poly(lactic acid) (PLA)

There are advantages and disadvantages to each. Acellular tissue matrices maintain the complicated microstructure organization of the extracellular matrix optimized by nature for cell engraftment. They contain the natural mixture of structural proteins including laminin, collagens I and IV, glycosaminoglycans, and embedded bioactive proteins including transforming growth factor beta 1, vascular endothelial growth factor, and fibroblast growth factor [8, 10–12]. Their drawbacks include tissue harvesting and the inherent complications and cost thereof from cadavers or animals. This also makes the material heterogenic, which may affect their structural integrity and how consistently the products are implemented. They often do not have sufficient rigidity and collapse when used in tubular applications [13]. Acellular matrices can also induce a significant inflammatory reaction, which is influenced by the source of material and how it is processed [14].

Scaffolds derived from natural materials can be fabricated to fit a particular application. Materials are chosen based on the ease of their manipulation and their similarity to the extracellular matrix they are replacing. The most commonly used materials for TEUDs are collagen, alginate, and silk, with collagen being the most common of the three (Fig. 7.1). Structural strength and cell seeding ability are greatly impacted by how the scaffolds are constructed and often are competing variables. A tightly woven collagen lattice may have excellent tensile strength but may be suboptimal for cell implantation, which require porosity to allow for cellular movement and nutrient diffusion [15–19]. Scaffolds can be engineered to have a mix of substrates (such as collagen I and elastin) to further modify the mechanical properties as well as incorporate various growth factors to promote cell incorporation [20].

Synthetic scaffolds can be precisely constructed given the consistency and predictability of the synthetic polymers they are derived from. This lends a high degree of consistency between scaffolds [16, 21]. The most commonly used synthetic polymers are PGA, PLA, polyanhydrides, poly(ortho esters), and poly(lactic co-glycolic acid) (PLGA). PGA, PLA, and PLGA are FDA approved and have been used in the clinical arena for decades as suture material [22]. Synthetic scaffolds can incorporate growth factors and a variety of building components including natural materials

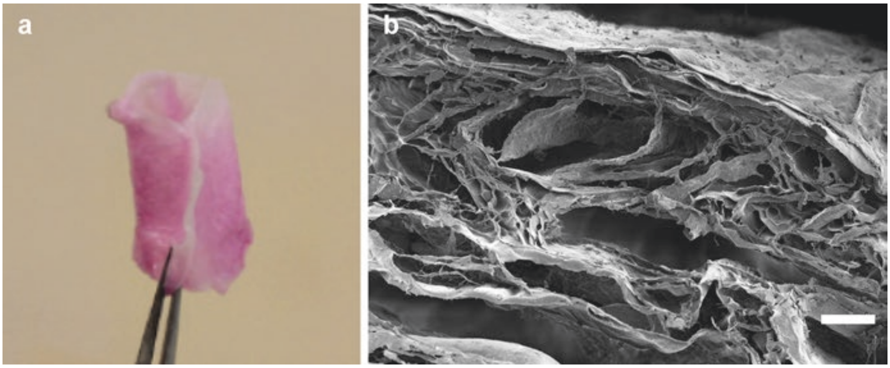


Fig. 7.1 (**a**) Collagen I-based scaffold molded into a tube. (**b**) Scanning electron microscopy cross section of molded collagen scaffold demonstrating laminar organization of collagen filaments. Scale bar represents 20 μM

(i.e., collagen and elastin) to augment their physical and cell engraftment properties. Synthetic scaffolds can elicit a foreign body reaction. This is due, in part, to the release of acidic byproducts when they are degraded [23]. New materials that do not form acidic by products are being actively investigated. No ideal scaffold material or combination of materials has been identified. This is a quickly evolving field, and many of the issues encountered are likely to be addressed by advances in material science and greater understanding of what cells need to successfully engraft TEUDs.

Why Are Cells Needed?

Early studies in animals demonstrated the importance of incorporating cells into implanted scaffolds [24, 25]. In a rabbit model of urethral replacement, unseeded tubular collagen matrices were uniformly structured, whereas collagen matrices seeded with autologous bladder cells did not. Histological analysis of the seeded grafts demonstrated a normal urethral architecture 1 month following implantation including intact innervation and the capacity for contractility in organ bath studies [24]. Similarly, bladder augmentation in rats with unseeded scaffolds was shown to have reduced overall cellularity and lack of complete epithelialization compared to grafts seeded with fibroblasts [25]. Although incorporating cells adds challenges of tissue harvest, cell expansion, and risk of rejection if using allogenic material, there are important benefits to integrating cells into TEUDs [26]. The seeded cells “jump-start” the process of replacing injured tissue when compared to unseeded scaffolds (Fig. 7.2). Incorporated cells facilitate neoangiogenesis, protect the graft from caustic urinary waste, and signal and facilitate incorporation of host tissues into the graft [25, 27].

Characteristics of the Ideal Cell Type

No ideal cell type has been identified for use in TEUDs. This is, in part, due to the unique properties required by the chosen cell type. Indeed, it is likely that one cell type may not suffice but a combination of cells will be used to recapitulate the human urothelial tract. The two main cell types that constitute the bulk of native human urothelium are (1) urothelial cells (UCs), which are epithelial in origin and form an impermeable barrier to allow for the transport and storage of toxic urinary waste, and (2) smooth muscle cells (SMCs), which provide structure and strength and allow for contraction and relaxation of genitourinary structures. Other important cell types include neurons, fibroblasts, and immune cells. In addition to performing these physiological functions, the cell type(s) must be amenable for tissue engineering. Specifically, they must be (1) simple to obtain, (2) have proliferative potential allowing expansion in culture, and (3) elicit little to no immune response when applied in recipient tissues. These multifaceted characteristics often juxtapose each other, i.e., performing a differentiated physiological function while being expandable in culture, which has made identification of the ideal cell type(s) difficult.

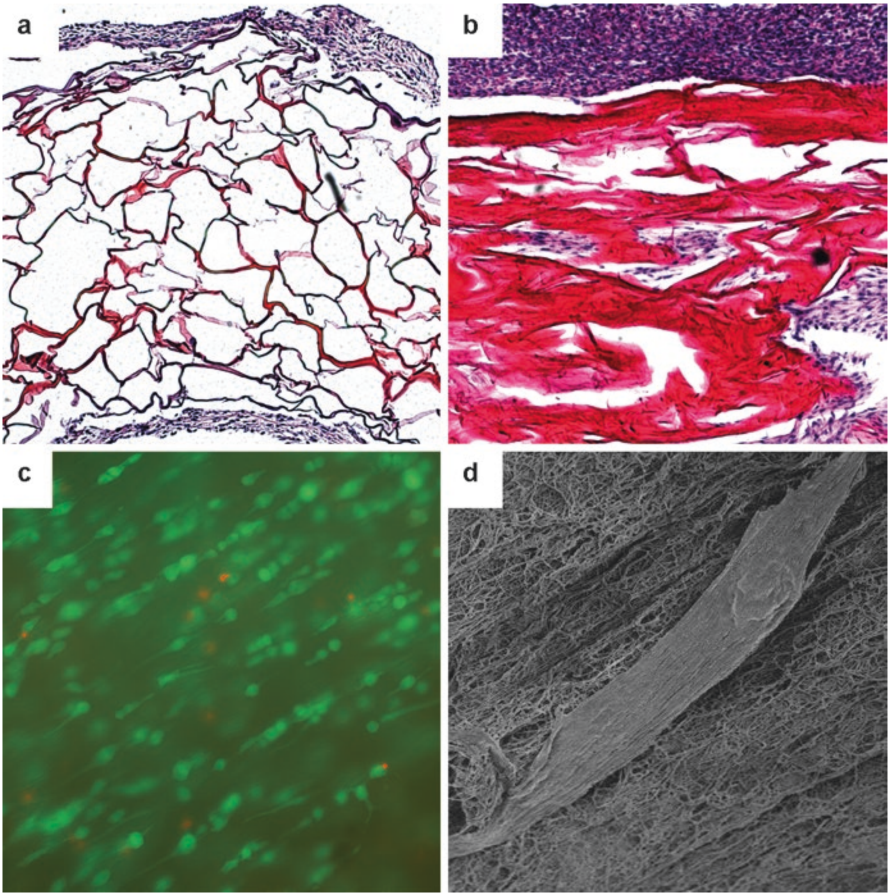


Fig. 7.2 Seeded collagen scaffolds. (**a**) Hematoxylin and eosin (HE) staining of seeded collagen scaffold showing cellular layering on exterior surfaces of scaffold after 3 days of seeding (40×). (**b**) HE staining demonstrating layering of cells on external and internal surfaces of collagen-based scaffold following 7 days of seeding (100×). (**c**) Membrane dye immunoflourescent imaging of adipose-derived stem cells (ADSCs) growing on a collagen-based scaffold. *Green* demonstrates viable cells; *red* demonstrates nonviable cells (100×). (**d**) Scanning electron microscopy of ADSC on the surface of a collagen-based scaffold. Scale bar represents 10 μM

Ideally, engineered tissues would arise from the recipient in order to avoid tissue rejection and to mitigate the risk of disease transmission. However, harvesting tissue from the recipient imposes several limitations. There is the availability and morbidity associated with tissue harvest. A significant proportion of urinary diversion procedures are in context of urothelial cancer. In this setting, it is not acceptable to use recipient urothelial tissues. Additionally, tissue expansion prior to implementation requires significant effort and time. This adds to treatment complexity by requiring coordination of tissue harvest, ex vivo TEUD development, and definitive surgical repair, therefore precluding off-the-shelf availability.

Importantly, not all recipients are the same nor is the quality of their tissues. Inherent patient characteristics including age, common comorbidities, such as diabetes and cardiovascular disease, tobacco use, and genetic abnormalities may reduce engineering tissue capacity, introducing variability in TEUD quality and reducing successful implementation [28–32].

Cell proliferative capacity is both an inherent function of the cell and influenced by culturing conditions. Differentiated cells such as UCs and SMCs have a limited replication potential in culture. However, manipulation of culturing conditions including serum-free media and enzyme-free techniques has allowed culturing of human UCs to 16 passages allowing the expansion in culture of a biopsy-sized specimen to that of a football field [18, 33–35]. Although they expressed differentiation markers consistent with urothelium, such as cytokeratin 7, they had a non-barrier-forming phenotype suggestive of a progenitor cell-like state [35]. They formed multiple layers consistent with fully differentiated uroepithelium when seeded onto scaffolds, which were implanted into animals. Stem cells are characterized by their ability to self-renew, potential to differentiate into various tissue types, and ability to form clonal populations without difficulty [36]. They have been under intense investigation for their use in TEUDs given their inherent characteristics. The various cell populations will be expanded upon below.

Cellular immunogenicity plays a critical role in tissue engineering applications. With or without cells, scaffolds can elicit an immune response, which the incorporated cell population can further exacerbate or attenuate. Autologous cells produce minimal to no immune response and do not trigger tissue rejection. Allogenic differentiated tissues harbor major histocompatibility complexes (MHCs), similar to organ transplantation, and are subject to the same rejection process. Several stem cell populations, most notably mesenchymal stem cells (MSCs), have been shown to have an immune modulatory capability and are immune evasive allowing allogenic transplantation without the need for powerful antirejection medications [37]. This has been shown to be in part to expression of inducible nitric oxide synthase (iNOS in mouse MSCs), indoleamine 2,3-dioxygenase 9 (IDO in human MSCs), prostaglandin-E2, interleukin-10, hemeoxygenase-1, and programmed cell death 1 ligand [38]. However, host antibodies against allogenic MSCs have been shown to develop, and it is unclear how these will play a role in MSC-seeded TEUDs that become a permanent part of the host [37]. MSCs have been shown to lose their immune-privileged status with differentiation, which has been attributed to altered expression including upregulation of interleukin-6 and altered expression of their MHCs [39, 40].

Cell Types

Urothelial Cells

Urothelial cells have been cultured for well over 40 years [41]. Normal urothelium is a transitional epithelium comprised of three layers: (1) superficial layer of umbrella cells, which establish an impermeable barrier to urine; (2) the intermediate layer; (3) and the basal layer, which is a single-cell layer in contact with the basement membrane [42]. An agreed upon, well-demarcated stem cell that can recapitulate all tissues of the bladder has yet to be identified [43]. The basal cell layer is generally considered the source of urothelial progenitor cells and is capable of rapid proliferation in the setting of injury [44–46]. More recent studies have identified a subpopulation of basal cells that are cytokeratin-5 and P63 positive and use the hedgehog/wnt pathway to recapitulate urothelial tissues [43, 44, 47]. The cytokeratin-5 population has not been evaluated for TEUD applications. Typically, UCs are obtained by tissue biopsy in humans and bladder digestion in animals [48]. Autologous UCs can be used for noncancer-related TEUDs.

Smooth Muscle Cells

Whereas the urothelium provides a barrier from urine, SMCs provide structural integrity and the ability for the bladder to contract and relax. They are not frequently used as a sole cell population in TEUDs and are often co-seeded with UCs. They are commonly harvested by bladder biopsy in humans and by bladder digestion in animal studies [24, 49–52]. In order to avoid a urinary source, SMCs have also been isolated from other tissues including adipose and peripheral blood [53]. Additionally, as mentioned earlier, smooth cells have been derived from other cells, notably MSCs [17, 54–56]. SMCs from native bladder have been shown to migrate into implanted acellular grafts; however, it incompletely repopulates the grafts and takes 4 weeks [11].

Stem Cells

Given their proliferative nature and plasticity, stem cells have been under intense investigation for use in TEUDs [57]. They are broadly characterized as embryonic stem cells (ESCs), adult stem cells, or induced pluripotent stem cells (iPSCs). ESCs are derived from the inner cell mass of blastocysts less than a week after ovum fertilization [58, 59]. They are pluripotent allowing them to form tissues from all three germ layers – ectoderm, mesoderm, and endoderm. Classic teaching dictates that the bladder trigone develops from the mesoderm and the remainder of the bladder develops from the endodermal urogenital sinus, with the innervating neurons of ectodermal origin [60, 61]. Therefore, ESCs are inherently capable to regenerate all tissues important to urothelial tract. Several studies have shown their ability to do so using both animal and human ESCs [62–64]. A recent report demonstrated high efficiency differentiation of human ESCs into urothelium without the need of culturing the cells in the presence of other cells or on urothelial inducing matrices [62]. These cells hold promise for TEUDs; however, they have not been sufficiently evaluated for this purpose. In addition to the well-known ethical controversies surrounding human ESCs, they have been shown to form teratomas in vivo [65–67]. Additionally, as with any allogenic stem cell, once differentiated they begin expressing their allogenic MHCs and can induce a rejection response, although studies suggest ESCs generate less of a response [68–70].

Circumventing the issues of ethics and rejection, iPSCs use cellular reprogramming to dedifferentiate an individual's adult cell into a pluripotent stem cell [71]. Urothelial differentiation from iPSCs has been demonstrated [62, 72, 73]. Similar to ESCs, these differentiated cells have not been evaluated for TEUD applications. iPSCs also harbor tumorigenicity, in part due to the genes, which are often manipulated to generate iPSCs (c-Myc, Oct4, and Sox2) and are shared with various malignancies [74]. Advancements in iPSC technology, such as no longer requiring DNA manipulation for their induction, have reduced their tumor-generating potential [74].

The majority of stem cell-based tissue engineering studies have used adult stem cell populations. They have the advantages over ESCs and iPSCs of being more easily obtained, avoid ethical concerns, do not elicit rejection (when used autologously), and do not form tumors. These benefits come at the cost of decreased proliferative and differentiation potential. MSCs have been the workhorse stem cell of tissue engineering applications including their use for TEUDs [36]. First discovered in the bone marrow over 40 years ago, analogous cell populations have since been isolated from many different sources including muscle, dermis, trabecular bone, adipose tissue, periosteum, pericyte, blood, synovial membrane, and amniotic fluid [75, 76]. Although similar to bone marrow-derived MSCs (BM-MSCs), these populations can have unique characteristics including CD markers, gene expression profiles, and differentiation propensities toward specific tissue types and are often given unique terminology. MSCs have been shown to have many characteristics; however, scientific consensus identifies them as adherent, fibroblast-like cells, which express CD105, CD73, and CD90 surface proteins and do not express hematopoietic surface markers CD45, CD14, CD11b, CD79α, and HLA-DR [77]. They can differentiate into myogenic, adipogenic, osteogenic, chondrogenic, neurogenic, and urothelial lineages in vitro when cultured under specific conditions [78, 79]. Allogenic human umbilical cord MSCs have been used in clinical trials for treatment of Sjogren's syndrome for their immune-modulating properties with promising results [80]. In TEUD applications where allogenic MSCs are expected to form differentiated tissues and persist, it is unclear if rejection to the MSCs will develop.

Adipose Stem Cell

Although initially believed to be equivocal to BM-MSCs, adipose stem cells (ASCs) have since been recognized as a unique stem cell population [79, 81, 82]. They have a similar differentiation profile as BM-MSCs and are easily expandable in culture [83]. ASCs are more easily obtained than BM-MSCs given the availability of adipose tissue and their relative abundance. They represent up to 3% of adherent cells in adipose tissue aspirates, whereas BM-MSCs represent less than 0.001% of adherent cells from bone marrow aspirates [17, 79, 81] (Fig. 7.3). Several studies have demonstrated ASCs ability to differentiate into UCs and SMCs with lineage-specific culturing conditions [17, 84, 85]. Human ASCs were differentiated into SMCs in vitro and seeded onto a poly-lactic-glycolic acid scaffold, which was used as a

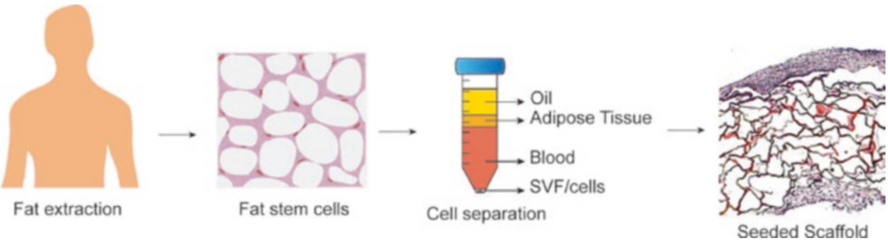


Fig. 7.3 Schematic demonstrating the steps involved in adipose-derived stem cell collection for scaffold seeding purposes. Subcutaneous fat is harvested by incisional biopsy or liposuction. The stromal vascular fraction (SVF) is isolated by gentle digestion, and cells are allowed to adhere to culture dishes where they are expanded and seeded onto scaffolds

bladder augment following removal of half of the bladder in nude rats [17]. The seeded grafts maintained pre-cystectomy capacity, and muscle strips isolated 12 weeks following implantation contracted during tissue bath stimulation.

Urine-Derived Stem Cells

Recently, stem cells with significant proliferative potential (60–70 population doublings) were identified in voided urine from 17 healthy volunteers aged 5–75 years [86]. A similar cell population was isolated from upper tract urine obtained from patients undergoing pyeloplasty [87]. In both studies, urine-derived stem cells (USCs) express MSC markers (CD44, CD73, CD105, CD133, STRO-1, and SSEA-4) as well as pericyte markers (CD146, NG2 proteoglycan, platelet-derived growth factor receptor beta) [86, 87]. Both cell populations were inducible to become differentiated UCs and SMCs and were able to be grown on collagen scaffolds and a urinary conduit [48, 87]. The ease of obtainment and autologous source makes them a good choice for tissue engineering applications; however, their urothelial source precludes their use for TEUDs in the setting of cancer.

Additional stem cell populations recently investigated for urinary tissue reconstruction include endometrial stem cells, amniotic fluid stem cells, and hair stem cells [23, 88–92]. Similar to prior studies using different cell types, scaffolds seeded with stem cells isolated from the follicular bulge (CD34, p63, and Ki-67 positive) demonstrated UC and SMC differentiation and improved tissue recellularization than acellular grafts alone [91]. Although promising, additional studies are needed to evaluate their use for TEUDs.

Growth Factors

Several growth factor stimuli serve as a source for the regenerative potential of an endogenous tissue-engineered organ. These stimuli include the microenvironment, endogenous production from cells seeded on the biomaterial, or ex vivo gene modification to secrete and overexpress growth factors that influence the milieu necessary for regeneration. An extracellular microenvironment is crucial for cell growth and development [57, 93]. Vascular endothelial growth factor (VEGF) has crucial roles in the formation of blood vessel networks [94]. Prior studies have examined the optimal VEGF concentration and found that those treated with 2 ng/g of tissue of VEGF have superior microvascular density and experience the most profound smooth muscle cell proliferation of the bladder in a porcine model [95].

Insulin-like growth factor-1 (IGF-1) is known to play a major role in development and cell proliferation. Lorentz et al. evaluated the effect of sustained IGF-1 delivery to a bladder lesion with recombinant IGF-1 [96]. The IGF-1 treatment group had twofold increased proliferation of SMCs compared to the control group. Accordingly, IGF-1 can potentiate SMC proliferation in tissue engineering with adult somatic cells.

Growth factors are also required to induce differentiation of stem cells. Transforming growth factor-β1 (TGF-β1) and platelet-derived growth factor (PDGF) can be used to differentiate stem cells into SMCs. Epidermal growth factor (EGF) is used for urothelial differentiation [87, 97, 98]. Subsequent studies that have analyzed candidate growth factor effects on bladder SMCs have identified several other targets for future cell proliferation. PDGF-BB, PDGF-CC, basic fibroblast growth factor (bFGF), VEGF, IGF-1, and hepatocyte growth factor enhanced proliferation, migration, and wound healing of the cells, while TGF-β1 inhibited these activities.

TEUD Vascularization

Nutrient supply is one of the largest obstacles to successful TEUD engraftment. Even in the setting of decellularized tissues where microvasculature structure may be preserved, inosculation of the implanted material must occur [99, 100]. Nutrient penetration by passive diffusion from surrounding tissue is less than 1 cm [101]. The omentum has been used surgically as a vascularized pedicle flap for wound repair for nearly 100 years [102]. Similarly, it has been used to wrap TEUDs to promote neovascularization. The benefit was clearly demonstrated in a small feasibility trial of pediatric patients undergoing bladder augmentation with cell-seeded scaffolds [49]. Grafts without the omental wrapped did not improve bladder capacity. Neovascularization of TEUDs from surrounding host tissue takes time, during which seeded cells must survive with passive diffusion alone. To facilitate this process, angiogenic growth factors (VEGF, bFGF, HGF) and cell types (endothelial progenitor cells) can be incorporated into TEUDs [103–105].

Clinical Experience

Several small clinical trials have evaluated the use of various TEUDs. Although they have shown promise and provided invaluable understanding, none have resulted in a clinically usable TEUD. The earliest trial by Atala et al. published in 2006 evaluated scaffolds of collagen or PGA and collagen seeded with autologous UCs and SMCs for augmentation cystoplasty in seven pediatric patients with myelomeningocele [49]. This study demonstrated the importance of omental wrapping and bladder cycling. Patients with the omental-wrapped scaffolds had a 56% decrease in leak point pressure at capacity, 1.58-fold increase in bladder volume, and 2.79-fold increase in compliance. Patients were followed for up to 61 months. A subsequent phase II multicenter prospective trial evaluated a biodegradable scaffold produced by Tengion® seeded with autologous UCs and SMCs in pediatric patients (mean age 8.2 years) with neurogenic bladder due to spina bifida [106]. Ten patients underwent augmentation cystoplasty. There was a trend of improvement in compliance at 36 months; however, it was not statistically significant. Additionally, four patients experienced serious adverse events including bowel obstruction and/or bladder rupture, which surpassed the acceptable safety standard for the trial.

Caione et al. published in 2012 a pilot trial of using commercially available unseeded decellularized porcine small intestinal submucosa (SIS) for bladder augmentation in pediatric exstrophy patients [107]. By 18-month post-engraftment, patients had clinically insignificant increases in bladder capacity and compliance. Histological analysis demonstrated no presence of the SIS graft by 18 months. The urothelium was indistinguishable from the adjacent native bladder; however, there was decreased smooth muscle tissue and increased collagen in the grafts. A phase I open-label clinical trial was recently performed evaluating an incontinent PGA neourinary conduit (NUC, Tengion®) seeded with autologous adipose-derived smooth muscle cells in patients who underwent cystectomy for bladder cancer [23, 108]. The phase I trial enrolled eight patients and was successful in that urinary tissue was found in the NUC. Specifically, engraftment of urothelium, smooth muscle, and neuronal tissue was identified which shows for the first time complete regeneration of urinary tissue in adult patients with bladder cancer [108]. While there was variability in how the NUC stored and preserved upper tract function with some patients having stable renal function for over a year, the long-term functional results of the NUC phase I trial in bladder cancer patients are forthcoming.

What Does the Future Hold for TEUD in Clinical Practice?

Thus far, all preclinical and clinical experiences in regenerating the lower urinary tract have shown histological evidence of complete urinary tissue recapitulation. This represents a major advance in the field of regenerative medicine; however, functional outcomes in particular urinary storage, contractile capacity, and neuronal innervation have not been demonstrated to date in human clinical trials. Therefore, all research efforts must focus on this aspect of TEUDs before patients with benign pathology or bladder cancer can be expected to benefit from this form of regenerative medicine. We and others continue to pursue these endeavors.

Conclusion

Successfully implementation of TEUDs will require harmonization of scaffolds and cells alone or in combination with growth factors/stem cells. No clear superior scaffold material or cell population has been identified. Continued advances in material science and cell biology increase our knowledge of the complex process of cell engraftment and engineered tissue incorporation into the human body. Despite the exciting preclinical reports, much remains to be understood before TEUDs become a bedside reality.

References

1. Jain D, Raghunath SK, Khanna S, Kumar P, Rawal S. Urinary diversion after cystectomy: An Indian perspective. Indian J Urol [Internet]. 2008 [cited 2015 Jul 25];24(1):99–103. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2684238&tool=pmcentrez&rendertype=abstract.
2. Atala A. Autologous cell transplantation for urologic reconstruction. J Urol [Internet]. 1998 [cited 2015 Jul 25];159(1):2–3. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9400425.
3. Monsour MJ, Mohammed R, Gorham SD, French DA, Scott R. An assessment of a collagen/vicryl composite membrane to repair defects of the urinary bladder in rabbits. Urol Res [Internet]. 1987 [cited 2015 Jul 25];15(4):235–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/3672670.
4. Imamura T, Ogawa T, Minagawa T, Yokoyama H, Nakazawa M, Nishizawa O, et al. Engineered bone marrow-derived cell sheets restore structure and function of radiation-injured rat urinary bladders. Tissue Eng Part A [Internet]. 2015 [cited 2015 Jul 29];21(9–10):1600–10. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25669695.
5. Talab SS, Kajbafzadeh A-M, Elmi A, Tourchi A, Sabetkish S, Sabetkish N, et al. Bladder reconstruction using scaffold-less autologous smooth muscle cell sheet engineering: early histological outcomes for autoaugmentation cystoplasty. BJU Int [Internet]. 2014 [cited 2015 Jul 29];114(6):937–45. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25230395.
6. Farhat W a. Tissue Engineering of the bladder—when will we get there? J Urol [Internet]. Am Urol Assoc Edu Res. 2014;192(4):1021–2. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0022534714040282.
7. Zhang, Yuanyuan, Atala A. Wound regeneration and repair. Methods Mol Biol [Internet]. 2013;1037:45–58. Available from: http://link.springer.com/10.1007/978-1-62703-505-7.
8. Song L, Murphy S, Yang B. Bladder acellular matrix and its application in bladder augmentation. Eng Part B [Internet]. 2013;0(0):1–10. Available from: http://online.liebertpub.com/doi/abs/10.1089/ten.teb.2013.0103.
9. Vardar E, Engelhardt E-M, Larsson HM, Mouloungui E, Pinnagoda K, Hubbell JA, et al. Tubular compressed collagen scaffolds for ureteral tissue engineering in a flow bioreactor system. Tissue Eng Part A [Internet]. 2015 [cited 2015 Jul 29]; Available from: http://www.ncbi.nlm.nih.gov/pubmed/26065873.
10. Chun SY, Lim GJ, Kwon TG, Kwak EK, Kim BW, Atala A, et al. Identification and characterization of bioactive factors in bladder submucosa matrix. Biomaterials [Internet]. 2007 [cited 2015 Jul 29];28(29):4251–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17617449.
11. Sutherland RS, Baskin LS, Hayward SW, Cunha GR. Regeneration of bladder urothelium, smooth muscle, blood vessels and nerves into an acellular tissue matrix. J Urol [Internet]. 1996 [cited 2015 Jul 27];156(2 Pt 2):571–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8683736.
12. Yang B, Zhang Y, Zhou L, Sun Z, Zheng J, Chen Y, et al. Development of a porcine bladder acellular matrix with well-preserved extracellular bioactive factors for tissue engineering. Tissue Eng Part C Methods [Internet]. 2010 [cited 2015 Jul 29];16(5):1201–11. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20170425.

13. Orabi H, AbouShwareb T, Zhang Y, Yoo JJ, Atala A. Cell-seeded tubularized scaffolds for reconstruction of long urethral defects: a preclinical study. Eur Urol [Internet]. European Association of Urology; 2013 [cited 2014 Nov 4];63(3):531–8. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3554849&tool=pmcentrez&rendertype=abstract.
14. Badylak SF, Gilbert TW. Immune response to biologic scaffold materials. Semin Immunol [Internet]. 2008 [cited 2015 Jul 29];20(2):109–16. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2605275&tool=pmcentrez&rendertype=abstract.
15. Melchels FPW, Tonnarelli B, Olivares AL, Martin I, Lacroix D, Feijen J, et al. The influence of the scaffold design on the distribution of adhering cells after perfusion cell seeding. Biomaterials [Internet]. Elsevier Ltd. 2011;32(11):2878–2884. Available from: http://dx.doi.org/10.1016/j.biomaterials.2011.01.023.
16. Ajalloueian F, Zeiai S, Fossum M, Hilborn JG. Constructs of electrospun PLGA, compressed collagen and minced urothelium for minimally manipulated autologous bladder tissue expansion. Biomaterials [Internet]. Elsevier Ltd. 2014;35(22):5741–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24768046.
17. Jack GS, Zhang R, Lee M, Xu Y, Wu BM, Rodríguez LV. Urinary bladder smooth muscle engineered from adipose stem cells and a three dimensional synthetic composite. Biomaterials [Internet]. 2009 [cited 2015 Jul 27];30(19):3259–70. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2744495&tool=pmcentrez&rendertype=abstract.
18. Atala A. Tissue engineering for the replacement of organ function in the genitourinary system. Am J Transplant. 2004;4(Suppl 6):58–73.
19. Mehr NG, Li X, Chen G, Favis BD, Hoemann CD. Pore size and LbL chitosan coating influence mesenchymal stem cell in vitro fibrosis and biomineralization in 3D porous poly(epsilon-caprolactone) scaffolds. J Biomed Mater Res Part A [Internet]. 2014;n/a-n/a. Available from: http://doi.wiley.com/10.1002/jbm.a.35381.
20. Chen W, Shi C, Hou X, Zhang W, Li L. Bladder acellular matrix conjugated with basic fibroblast growth factor for bladder regeneration. Tissue Eng Part A [Internet]. 2014 [cited 2015 Jul 29];20(15–16):2234–42. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24483233.
21. Pattison MA, Wurster S, Webster TJ, Haberstroh KM. Three-dimensional, nano-structured PLGA scaffolds for bladder tissue replacement applications. Biomaterials [Internet]. 2005 [cited 2015 Jul 29];26(15):2491–500. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15585251.
22. Horst M, Madduri S, Gobet R, Sulser T, Milleret V, Hall H, et al. Engineering functional bladder tissues [Internet]. J Tissue Eng Regen Med. 2013 [cited 2015 Jul 20]. 515–22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22438261.
23. Kates M, Singh A, Matsui H, Steinberg GD, Smith ND, Schoenberg MP, et al. Tissue-engineered urinary conduits. Curr Urol Rep [Internet]. 2015 [cited 2015 Jul 27];16(3):8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25677229.
24. De Filippo RE, Yoo JJ AA. Urethral replacement using cell seeded tubularized collagen matrices. J Urol [Internet]. 2002 [cited 2015 Jul 25];4(2):1789–92. Available from: http://www-ncbi-nlm-nih-gov.ezp.welch.jhmi.edu/pubmed?holding=jhumlib_fft_ndi&otool=jhumlib&term=12352360.
25. Drewa T, Sir J, Czajkowski R, Wozniak A. Scaffold seeded with cells is essential in urothelium regeneration and tissue remodeling in vivo after bladder augmentation using in vitro engineered graft. Transplant Proc [Internet]. [cited 2015 Jul 25];38(1):133–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16504684.
26. Atala A. Experimental and clinical experience with tissue engineering techniques for urethral reconstruction. Urol Clin North Am. 2002;29(2):485–92. ix
27. Palatinus JA, Rhett JM, Gourdie RG. Translational lessons from scarless healing of cutaneous wounds and regenerative repair of the myocardium. J Mol Cell Cardiol. 2010;48(3):550–7.
28. Sopko NA, Turturice BA, Becker ME, Brown CR, Dong F, Popović ZB, et al. Bone marrow support of the heart in pressure overload is lost with aging. PLoS One [Internet]. United States; 2010 [cited 2014 Sep 29];5(12):e15187. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3006343&tool=pmcentrez&rendertype=abstract.

29. Schipper BM, Marra KG, Zhang W, Donnenberg AD, Rubin JP. Regional anatomic and age effects on cell function of human adipose-derived stem cells. Ann Plast Surg [Internet]. 2008 [cited 2015 Apr 27];60(5):538–44. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4160894&tool=pmcentrez&rendertype=abstract.
30. Khan M, Ali F, Mohsin S, Akhtar S, Mehmood A, Choudhery MS, et al. Preconditioning diabetic mesenchymal stem cells with myogenic medium increases their ability to repair diabetic heart. Stem Cell Res Ther [Internet]. 2013 [cited 2015 Jul 25];4(3):58. Available from: http://stemcellres.com/content/4/3/58.
31. Li X, Liu L, Meng D, Wang D, Zhang J, Shi D, et al. Enhanced apoptosis and senescence of bone-marrow-derived mesenchymal stem cells in patients with systemic lupus erythematosus. Stem Cells Dev [Internet]. Mary Ann Liebert, Inc. 140 Huguenot Street, 3rd Floor New Rochelle, NY 10801 USA; 2012 [cited 2015 Jul 25];21(13):2387–94. Available from: http://online.liebertpub.com/doi/abs/10.1089/scd.2011.0447.
32. Kondo T, Hayashi M, Takeshita K, Numaguchi Y, Kobayashi K, Iino S, et al. Smoking cessation rapidly increases circulating progenitor cells in peripheral blood in chronic smokers. Arterioscler Thromb Vasc Biol [Internet]. 2004 [cited 2015 Jul 25];24(8):1442–7. Available from: http://atvb.ahajournals.org/content/24/8/1442.short.
33. Scriven SD, Booth C, Thomas DF, Trejdosiewicz LK, Southgate J. Reconstitution of human urothelium from monolayer cultures. J Urol [Internet]. 1997 [cited 2015 Jul 25];158(3 Pt 2):1147–52. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9258159.
34. Puthenveettil JA, Burger MS, Reznikoff CA. Replicative senescence in human uroepithelial cells. Adv Exp Med Biol [Internet]. 1999 [cited 2015 Jul 25];462:83–91. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10599415.
35. Cilento BG, Freeman MR, Schneck FX, Retik AB, Atala A. Phenotypic and cytogenetic characterization of human bladder urothelia expanded in vitro. J Urol [Internet]. 1994 [cited 2015 Jul 25];152(2 Pt 2):665–70. Available from: http://www.ncbi.nlm.nih.gov/pubmed/7517459.
36. Aboushwareb T, Atala A. Stem cells in urology. Nat Clin Pract Urol [Internet]. 2008 [cited 2015 Jul 25];5(11):621–31. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18852709.
37. Ankrum JA, Ong JF, Karp JM. Mesenchymal stem cells: immune evasive, not immune privileged. Nat Biotechnol [Internet]. 2014;32(3):252–60. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24561556.
38. Ma S, Xie N, Li W, Yuan B, Shi Y, Wang Y. Immunobiology of mesenchymal stem cells. Cell Death Differ [Internet]. 2014;21(2):216–25. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3890955&tool=pmcentrez&rendertype=abstract
39. Li P, Li S-H, Wu J, Zang W-F, Dhingra S, Sun L, et al. Interleukin-6 downregulation with mesenchymal stem cell differentiation results in loss of immunoprivilege. J Cell Mol Med [Internet]. 2013 [cited 2015 Jul 25];17(9):1136–45. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4118173&tool=pmcentrez&rendertype=abstract.
40. Huang XP, Sun Z, Miyagi Y, Kinkaid HM, Zhang L, Weisel RD, et al. Differentiation of allogeneic mesenchymal stem cells induces immunogenicity and limits their long-term benefits for myocardial repair. Circulation. 2010;122(23):2419–29.
41. Sutherland GR, Bain AD. Culture of cells from the urine of newborn children. Nature. 1972;239(5369):231.
42. Jost SP. Gosling J a, Dixon JS. The morphology of normal human bladder urothelium. J Anat. 1989;167:103–15.
43. Haiyang Zhang, Guiting Lin, Xuefeng Qiu, Hongxiu Ning, Lia Banie TFL, Lin and C-S. Label retaining and stem cell marker expression in the developing rat urinary bladder. Urology. 2012;29(3):997–1003.
44. Shin K, Lee J, Guo N, Kim J, Lim A, Qu L, et al. Hedgehog/Wnt feedback supports regenerative proliferation of epithelial stem cells in bladder. Nature [Internet]. Nature Publishing Group; 2011;472(7341):110–4. Available from: http://dx.doi.org/10.1038/nature09851.
45. Yamany T, Van Batavia J, Mendelsohn C. Formation and regeneration of the urothelium. Curr Opin Organ Transplant [Internet]. 2014;19(3):323–30. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24752063.

46. Kurzrock EA, Lieu DK, Degraffenried LA, Chan CW, Isseroff RR. Label-retaining cells of the bladder: candidate urothelial stem cells. Am J Physiol Renal Physiol. 2008;294(6):F1415–F1421.
47. Gandhi D, Molotkov A, Batourina E, Schneider K, Dan H, Reiley M, et al. Retinoid signaling in progenitors controls specification and regeneration of the urothelium. Dev Cell [Internet]. Elsevier Inc. 2013;26(5):469–82. Available from: http://dx.doi.org/10.1016/j.devcel.2013.07.017.
48. Bodin A, Bharadwaj S, Wu S, Gatenholm P, Atala A, Zhang Y. Tissue-engineered conduit using urine-derived stem cells seeded bacterial cellulose polymer in urinary reconstruction and diversion. Biomaterials [Internet]. Elsevier Ltd. 2010;31(34):8889–901. Available from: http://dx.doi.org/10.1016/j.biomaterials.2010.07.108.
49. Atala A, Bauer SB, Soker S, Yoo JJ, Retik AB. Tissue-engineered autologous bladders for patients needing cystoplasty. Lancet [Internet]. 2006 [cited 2015 May 9];367(9518):1241–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16631879.
50. Atala A. Future trends in bladder reconstructive surgery. Semin Pediatr Surg [Internet]. 2002 [cited 2015 Jul 27];11(2):134–42. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11973766.
51. Lai J-Y, Chang P-Y, Lin J-N. Bladder autoaugmentation using various biodegradable scaffolds seeded with autologous smooth muscle cells in a rabbit model. J Pediatr Surg [Internet]. 2005 [cited 2015 Jul 27];40(12):1869–73. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16338308.
52. Yoo JJ, Meng J, Oberpenning F, Atala A. Bladder augmentation using allogenic bladder submucosa seeded with cells. Urology. 1998;51(2):221–5.
53. Basu J, Jayo MJ, Ilagan RM, Guthrie KI, Sangha N, Genheimer CW, et al. Regeneration of native-like neo-urinary tissue from nonbladder cell sources. Tissue Eng Part A [Internet]. 2012 [cited 2015 Jul 27];18(9–10):1025–34. Available from: http://www-ncbi-nlm-nih-gov.ezp.welch.jhmi.edu/pubmed?holding=jhumlib_fft_ndi&otool=jhumlib&term=Regeneration+of+native-like+neo-+urinary+tissue+from+nonbladder+cell+sources.
54. Qin D, Long T, Deng J, Zhang Y. Urine-derived stem cells for potential use in bladder repair. Stem Cell Res Ther [Internet]. 2014 [cited 2015 Jul 27];5(3):69. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4055102&tool=pmcentrez&rendertype=abstract.
55. Becker C, Laeufer T, Arikkat J, Jakse G. TGFbeta-1 and epithelial-mesenchymal interactions promote smooth muscle gene expression in bone marrow stromal cells: possible application in therapies for urological defects. Int J Artif Organs [Internet]. 2008 [cited 2015 Jul 27];31(11):951–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19089797.
56. Sharma AK, Hota P V, Matoka DJ, Fuller NJ, Jandali D, Thaker H, et al. Urinary bladder smooth muscle regeneration utilizing bone marrow derived mesenchymal stem cell seeded elastomeric poly(1,8-octanediol-co-citrate) based thin films. Biomaterials [Internet]. 2010 [cited 2015 Jul 27];31(24):6207–17. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20488535.
57. Drewa T, Adamowicz J, Sharma A. Tissue engineering for the oncologic urinary bladder. Nat Rev Urol [Internet]. Nature Publishing Group; 2012 [cited 2014 Oct 31];9(10):561–72. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22907387.
58. Evans MJ, Kaufman MH. Establishment in culture of pluripotential cells from mouse embryos. Nature [Internet]. 1981 [cited 2014 Dec 18];292(5819):154–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/7242681.
59. Thomson JA, Itskovitz-Eldor J, Shapiro SS, Waknitz MA, Swiergiel JJ, Marshall VS, et al. Embryonic stem cell lines derived from human blastocysts. Science [Internet]. 1998 [cited 2014 Oct 17];282(5391):1145–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9804556.
60. Viana R, Batourina E, Huang H, Dressler GR, Kobayashi A, Behringer RR, et al. The development of the bladder trigone, the center of the anti-reflux mechanism. Development. 2007;134(20):3763–9.

61. Tanaka ST, Ishii K, Demarco RT, Pope JC, Brock JW, Hayward SW. Endodermal origin of bladder trigone inferred from mesenchymal-epithelial interaction. J Urol [Internet]. 2010 [cited 2015 Jul 27];183(1):386–91. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2794964&tool=pmcentrez&rendertype=abstract.
62. Osborn SL, Thangappan R, Luria A, Lee JH, Nolta J, Kurzrock EA. Induction of human embryonic and induced pluripotent stem cells into urothelium. Stem Cells Transl Med [Internet]. 2014;3(5):610–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24657961.
63. Frimberger D, Morales N, Shamblott M, Gearhart JD, Gearhart JP, Lakshmanan Y. Human embryoid body-derived stem cells in bladder regeneration using rodent model. Urology [Internet]. 2005 [cited 2015 Jul 27];65(4):827–32. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15833555.
64. Oottamasathien S, Wang Y, Williams K, Franco OE, Wills ML, Thomas JC, et al. Directed differentiation of embryonic stem cells into bladder tissue. Dev Biol. 2007;304(2):556–66.
65. Blum B, Bar-Nur O, Golan-Lev T, Benvenisty N. The anti-apoptotic gene survivin contributes to teratoma formation by human embryonic stem cells. Nat Biotechnol [Internet]. 2009 [cited 2015 Jul 27];27(3):281–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19252483.
66. Hentze H, Soong PL, Wang ST, Phillips BW, Putti TC, Dunn NR. Teratoma formation by human embryonic stem cells: evaluation of essential parameters for future safety studies. Stem Cell Res [Internet]. 2009 [cited 2015 Jul 15];2(3):198–210. Available from: http://www.sciencedirect.com/science/article/pii/S187350610900018X.
67. Nussbaum J, Minami E, Laflamme MA, Virag JAI, Ware CB, Masino A, et al. Transplantation of undifferentiated murine embryonic stem cells in the heart: teratoma formation and immune response. FASEB J [Internet]. 2007 [cited 2015 Jun 9];21(7):1345–57. Available from: http://www.fasebj.org/content/21/7/1345.short.
68. Drukker M, Katchman H, Katz G, Even-Tov Friedman S, Shezen E, Hornstein E, et al. Human embryonic stem cells and their differentiated derivatives are less susceptible to immune rejection than adult cells. Stem Cells [Internet]. 2006 [cited 2015 Jul 27];24(2):221–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16109762.
69. Accepting stem cells. Nat Immunol. 2001;2(12):1085.
70. Swijnenburg R-J, Tanaka M, Vogel H, Baker J, Kofidis T, Gunawan F, et al. Embryonic stem cell immunogenicity increases upon differentiation after transplantation into ischemic myocardium. Circulation [Internet]. 2005 [cited 2015 Jul 27];112(9 Suppl):I166–72. Available from: http://circ.ahajournals.org/content/112/9_suppl/I-166.short.
71. Takahashi K, Yamanaka S. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. Cell [Internet]. 2006 [cited 2014 Jul 9];126(4):663–76. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16904174.
72. Moad M, Pal D, Hepburn AC, Williamson SC, Wilson L, Lako M, et al. A novel model of urinary tract differentiation, tissue regeneration, and disease: reprogramming human prostate and bladder cells into induced pluripotent stem cells. Eur Urol [Internet]. 2013 [cited 2014 Nov 5];64(5):753–61. Available from: http://www.sciencedirect.com/science/article/pii/S0302283813003412.
73. Kang M, Kim HH, Han YM. Generation of bladder urothelium from human pluripotent stem cells under chemically defined serum- and feeder-free system. Int J Mol Sci. 2014;15(5):7139–57.
74. Lu X, Zhao T. Clinical therapy using iPSCs: hopes and challenges. Genomics, Proteomics Bioinforma [Internet]. Beijing Institute of Genomics, Chinese Academy of Sciences and Genetics Society of China. 2013;11(5):294–8. Available from: http://dx.doi.org/10.1016/j.gpb.2013.09.002.
75. Mafi R, Hindocha S, Mafi P, Griffin M, Khan WS. Sources of adult mesenchymal stem cells applicable for musculoskeletal applications – a systematic review of the literature. Open Orthop J [Internet]. 2011 [cited 2015 Jul 27];5 Suppl 2:242–8. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3149887&tool=pmcentrez&rendertype=abstract.

76. Friedenstein AJ, Chailakhjan RK, Lalykina KS. The development of fibroblast colonies in monolayer cultures of guinea-pig bone marrow and spleen cells. Cell Tissue Kinet [Internet]. 1970 [cited 2015 May 22];3(4):393–403. Available from: http://www.ncbi.nlm.nih.gov/pubmed/5523063.
77. Dominici M, Le Blanc K, Mueller I, Slaper-Cortenbach I, Marini F, Krause D, et al. Minimal criteria for defining multipotent mesenchymal stromal cells. The International Society for Cellular Therapy position statement. Cytotherapy [Internet]. 2006 [cited 2014 Jul 9];8(4):315–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16923606.
78. Tian H, Bharadwaj S, Liu Y, Ma PX, Atala A, Zhang Y. Differentiation of human bone marrow mesenchymal stem cells into bladder cells: potential for urological tissue engineering. Tissue Eng Part A [Internet]. 16(5):1769–79. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2952115&tool=pmcentrez&rendertype=abstract
79. De Ugarte DA, Morizono K, Elbarbary A, Alfonso Z, Zuk PA, Zhu M, et al. Comparison of multi-lineage cells from human adipose tissue and bone marrow. Cells Tissues Organs [Internet]. 2003 [cited 2015 Jul 27];174(3):101–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12835573.
80. Xu J, Wang D, Liu D, Fan Z, Zhang H, Liu O, et al. Allogeneic mesenchymal stem cell treatment alleviates experimental and clinical Sjögren syndrome. Blood [Internet]. 2012 [cited 2015 Jul 27];120(15):3142–51. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3471521&tool=pmcentrez&rendertype=abstract.
81. Zuk PA, Zhu M, Ashjian P, De Ugarte DA, Huang JI, Mizuno H, et al. Human adipose tissue is a source of multipotent stem cells. Mol Biol Cell [Internet]. 2002 [cited 2015 Jan 12];13(12):4279–95. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=138633&tool=pmcentrez&rendertype=abstract.
82. Busser H, Najar M, Raicevic G, Pieters K, Velez Pombo R, Philippart P, et al. Isolation and characterization of human mesenchymal stromal cells subpopulations: comparison of bone marrow and adipose tissue. Stem Cells Dev [Internet]. 2015 [cited 2015 Jun 20]; Available from: http://www.ncbi.nlm.nih.gov/pubmed/26086188.
83. Tsuji W, Rubin JP, Marra KG. Adipose-derived stem cells: Implications in tissue regeneration. World J Stem Cells [Internet]. 2014 [cited 2015 Mar 9];6(3):312–21. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4131273&tool=pmcentrez&rendertype=abstract.
84. Zhang M, Xu M-X, Zhou Z, Zhang K, Zhou J, Zhao Y, et al. The differentiation of human adipose-derived stem cells towards a urothelium-like phenotype in vitro and the dynamic temporal changes of related cytokines by both paracrine and autocrine signal regulation. PLoS One [Internet]. 2014 [cited 2015 Jul 27];9(4):e95583. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3994076&tool=pmcentrez&rendertype=abstract.
85. Shi J-G, Fu W-J, Wang X-X, Xu Y-D, Li G, Hong B-F, et al. Transdifferentiation of human adipose-derived stem cells into urothelial cells: potential for urinary tract tissue engineering. Cell Tissue Res [Internet]. 2012 [cited 2015 Jul 27]; Available from: http://www.ncbi.nlm.nih.gov/pubmed/22290635.
86. Bharadwaj S, Liu G, Shi Y, Wu R, Yang B, He T, et al. Multipotential differentiation of human urine-derived stem cells: potential for therapeutic applications in urology. Stem Cells [Internet]. 2013 [cited 2014 Nov 4];31(9):1840–56. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23666768.
87. Bharadwaj S, Liu G, Shi Y, Markert C, Andersson K-E, Atala A, et al. Characterization of urine-derived stem cells obtained from upper urinary tract for use in cell-based urological tissue engineering. Tissue Eng Part A [Internet]. 2011 [cited 2014 Nov 4];17(15–16):2123–32. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21513463.
88. Shoae-Hassani A, Sharif S, Seifalian AM, Mortazavi-Tabatabaei SA, Rezaie S, Verdi J. Endometrial stem cell differentiation into smooth muscle cell: a novel approach for bladder tissue engineering in women. BJU Int [Internet]. 2013 [cited 2015 Jul 27];112(6):854–63. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24028767.

89. De Coppi P, Callegari A, Chiavegato A, Gasparotto L, Piccoli M, Taiani J, et al. Amniotic fluid and bone marrow derived mesenchymal stem cells can be converted to smooth muscle cells in the cryo-injured rat bladder and prevent compensatory hypertrophy of surviving smooth muscle cells. J Urol [Internet]. 2007 [cited 2015 Jul 9];177(1):369–76. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17162093.
90. Kang HH, Kang JJ, Kang H-G, Chung SS. Urothelial differentiation of human amniotic fluid stem cells by urothelium specific conditioned medium. Cell Biol Int [Internet]. 2014 [cited 2015 Jul 27];38(4):531–7. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3959875&tool=pmcentrez&rendertype=abstract.
91. Drewa T, Joachimiak R, Kaznica A, Sarafian V, Pokrywczynska M. Hair stem cells for bladder regeneration in rats: preliminary results. Transplant Proc [Internet]. Elsevier Inc. 2009;41(10):4345–51. Available from: http://dx.doi.org/10.1016/j.transproceed.2009.08.059.
92. Drewa T, Joachimiak R, Bajek A, Gagat M, Grzanka A, Bodnar M, et al. Hair follicle stem cells can be driven into a urothelial-like phenotype: An experimental study. Int J Urol. 2013;20(5):537–42.
93. Hyndman ME, Kaye D, Field NC, Lawson KA, Smith ND, Steinberg GD, et al. The use of regenerative medicine in the management of invasive bladder cancer. Adv Urol. Southern Alberta Institute of Urology, University of Calgary, Alberta, Canada T2 V 1P9. 2012;2012:653652.
94. Zachary I, Gliki G. Signaling transduction mechanisms mediating biological actions of the vascular endothelial growth factor family. Cardiovasc Res. Centre for Cardiovascular Biology and Medicine, Department of Medicine, University College London, 5 University Street, WC1E 6JJ, London, UK. i.zachary@ucl.ac.uk; 2001;49(3):568–81.
95. Loai Y, Yeger H, Coz C, Antoon R, Islam SS, Moore K, et al. Bladder tissue engineering: tissue regeneration and neovascularization of HA-VEGF-incorporated bladder acellular constructs in mouse and porcine animal models. J Biomed Mater Res Part A. Wiley Online Library; 2010;94(4):1205–15.
96. Lorentz KM, Yang L, Frey P, Hubbell JA. Engineered insulin-like growth factor-1 for improved smooth muscle regeneration. Biomaterials. Institute of Bioengineering, Ecole Polytechnique Federale de Lausanne, CH-1015 Lausanne, Switzerland.: Elsevier Ltd. 2012;33(2):494–503.
97. Wu R, Liu G, Bharadwaj S, Zhang Y. Isolation and myogenic differentiation of mesenchymal stem cells for urologic tissue engineering. In: Organ regeneration. New York, Philadelphia: Springer Healthcare LLC. 2013. p. 65–80.
98. Sangha N. Isolation of urothelial cells from bladder tissue. In: Organ regeneration. New York, Philadelphia: Springer Healthcare LLC. 2013. p. 21–33.
99. Osborn SL, So M, Hambro S, Nolta JA, Kurzrock EA. Inosculation of blood vessels allows early perfusion and vitality of bladder grafts—implications for bioengineered bladder wall. Tissue Eng Part A [Internet]. 2015 [cited 2015 Jul 25];21(11–12):150422120242000. Available from: http://online.liebertpub.com/doi/10.1089/ten.tea.2014.0630.
100. Novosel EC, Kleinhans C, Kluger PJ. Vascularization is the key challenge in tissue engineering. Adv Drug Deliv Rev [Internet]. 2011 [cited 2014 Aug 14];63(4–5):300–11. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21396416.
101. Dorin RP, Pohl HG, De Filippo RE, Yoo JJ, Atala A. Tubularized urethral replacement with unseeded matrices: what is the maximum distance for normal tissue regeneration? World J Urol. 2008;26(4):323–6.
102. Liebermann-Meffert D. The greater omentum. Anatomy, embryology, and surgical applications. Surg Clin North Am [Internet]. 2000 [cited 2015 Jul 30];80(1):275–93, xii. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10685153.
103. Schultheiss D, Gabouev AI, Cebotari S, Tudorache I, Walles T, Schlote N, et al. Biological vascularized matrix for bladder tissue engineering: matrix preparation, reseeding technique and short-term implantation in a porcine model. J Urol [Internet]. 2005 [cited 2015 Jul 30];173(1):276–80. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15592096.

104. Cartwright L, Farhat WA, Sherman C, Chen J, Babyn P, Yeger H, et al. Dynamic contrast-enhanced MRI to quantify VEGF-enhanced tissue-engineered bladder graft neovascularization: pilot study. J Biomed Mater Res A [Internet]. 2006 [cited 2015 Jul 30];77(2):390–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16429423.
105. Nomi M, Miyake H, Sugita Y, Fujisawa M, Soker S. Role of growth factors and endothelial cells in therapeutic angiogenesis and tissue engineering. Curr Stem Cell Res Ther [Internet]. 2006 [cited 2015 Jul 30];1(3):333–43. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18220878.
106. Joseph DB, Borer JG, De Filippo RE, Hodges SJ, McLorie GA. Autologous cell seeded biodegradable scaffold for augmentation cystoplasty: Phase II study in children and adolescents with spina bifida. J Urol [Internet]. Elsevier Ltd; 2014 [cited 2015 Jul 27];191(5):1389–94. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24184366.
107. Caione P, Boldrini R, Salerno A, Nappo SG. Bladder augmentation using acellular collagen biomatrix: a pilot experience in exstrophic patients. Pediatr Surg Int [Internet]. 2012 [cited 2015 Jul 30];28(4):421–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22350082.
108. Bivalacqua T, Steinberg G, Smith N, et al. Pre-clinical and clinical translation of a tissue engineered neo-urinary conduit using adipose derived smooth muscle cells for urinary reconstruction. Eur Urol Suppl. 2014; 13. Abstract 178.

Long-Term Complications of Urinary Diversion

8

Erfan Amini and Hooman Djaladat

Introduction

Radical cystectomy and urinary diversion serve as the gold standard treatment for muscle-invasive and high-risk non-muscle-invasive bladder cancer. This approach has been associated with significant improvement in survival. These patients might live for years after surgery and present with long-term complications mostly related to urinary diversion. Complication rate in patients with urinary diversion has been reported to be as high as 60%. These complications could have detrimental effects on health and quality of life and may even be life-threatening. Long-term follow-up of patients with urinary diversion is of utmost importance as many of diversion-related complications may occur years after surgery. This chapter aims to describe and classify various long-term complications associated with urinary diversion as well as prevention and management strategies.

Cystectomy and urinary diversion may be required in patients with bladder cancer, those who undergo pelvic exenteration, as well as some benign pelvic conditions. Bladder urothelial cancer is the eighth leading cause of cancer death in men with 16,390 deaths anticipated in the United States in 2016 [1]. Surgery for muscle-invasive bladder cancer consists of radical cystectomy, pelvic lymph node dissection, and urinary diversion. Advances in surgical technique and postoperative care have significantly reduced mortality, and large series have shown 10-year cancer-specific survival of 65–78% in pathologically organ-confined bladder cancer patients. An increasing number of diversion-related complications are being observed in these patients as a consequence of improved survival that requires

E. Amini
Department of Urology, Uro-oncology Research Center, Tehran University of Medical Sciences, Tehran, Iran

H. Djaladat (✉)
The Institute of Urology, Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA, USA
e-mail: djaladat@med.usc.edu

S. Daneshmand (ed.), *Urinary Diversion*, DOI 10.1007/978-3-319-52186-2_8

prompt diagnosis and treatment. The nature and frequency of complications vary widely depending on the type and length of the bowel segment used for diversion, surgical technique used in the creation of diversion, and ureterointestinal anastomosis as well as continence status. Ureterosigmoidostomy was among the first types of continent urinary diversion, and despite initial enthusiasm, high complication rates including increased risk of developing secondary cancers, deterioration of renal function, and serious metabolic imbalances limited its usefulness. Subsequent surgical advances in diversion and reconstruction of lower urinary tract have led to decreased complication rate and improved quality of life. However, long-term complication rate associated with urinary diversion is still significant and has been reported to be as high as 60% in patients who survived beyond 5 years [2]. Choice of urinary diversion including ileal conduit, orthotopic neobladder, and continent cutaneous urinary diversion depends on patient characteristics and surgeon preferences. There might be biases associated with reporting long-term complications of urinary diversion. Patients who receive a continent urinary diversion are more likely to be younger and have less comorbid conditions. Furthermore, continent diversions are utilized more frequently in high-volume centers.

In this chapter, long-term complications associated with different types of urinary diversion have been reviewed and classified as voiding dysfunction in orthotopic neobladder diversion, bowel- and stoma-related complications, ureteroenteric anastomosis stricture, infection, renal function deterioration, as well as complications attributable to metabolic imbalances.

Voiding Dysfunction in Orthotopic Neobladder Urinary Diversion

Construction of orthotopic neobladder has the potential to restore normal body image in patients who undergo cystectomy and is usually the preferred type of diversion for most patients following cystectomy. However, some patients with orthotopic neobladder may suffer from voiding dysfunction. Definition of voiding dysfunction and whether it is reported by the patient or assessed by physician as well as time frame of evaluations relative to surgery vary significantly between different studies. This lack of uniformity in the literature limits our ability to compare the results and explains for observed variations. Voiding dysfunction in patients with orthotopic neobladder may be a consequence of problems in storage (filling) and/or voiding (emptying) phase.

Failure to Store

Continent diversions including orthotopic neobladder rely upon a low-pressure reservoir constructed from detubularized bowel segments. The aim is reconfiguring the bowel into as near a sphere as possible. Spherical geometry provides the most volume for the least surface area. Over time, the volume capacity of the reservoir increases. This accommodation in reservoir volume enhances compliance and storage performance. It has also been postulated that detubularization of the bowel segment discoordinates motor activity leading to ineffective contractions and decreased intraluminal pressure. Patients with low-compliant, high-pressure reservoirs have problem with urine storage and suffer from urine leakage as well as possible upper tract damage.

Continence mechanism in orthotopic neobladders is mainly dependent on the function of external striated sphincter. Damage to the innervation of the external sphincter during the cystectomy may lead to sphincter incompetence and storage failure. Urinary incontinence after orthotopic neobladder urinary diversion occurs more frequently in elderly as compared to younger patients which may be a consequence of decreased tone of urethral sphincter with advanced age [3]. In several large series addressing functional outcomes of orthotopic urinary diversion, continence rate has been reported between 57% and 100% [4–15] (Table 8.1). Storage function improves gradually as the reservoir volume increases after surgery, and improvement of continence may be observed up to years after surgery. It has also

Table 8.1 Long-term voiding function in patients undergoing radical cystectomy and orthotopic neobladder reconstruction

Study	Design	Number of patients	Follow-up duration	Continence rate		Intermittent catheterization rate
				Daytime	Nighttime	
Elmajian et al. (1996) [4]	Retrospective	250	Median: 42 months	87%	86%	8%
Hautmann et al. (1999) [5]	Retrospective	363	Median: 57 months	96%	95%	6%
Steven et al. (2000) [6]	Prospective	166	5 years	100% after 5 years	97% after 5 years	44% after 5 years
Abol-Enin et al. (2001) [7]	Prospective	450	Median: 38 months	93%	80%	NR
Stein et al. (2004) [8]	Retrospective	209	Median: 33 months	87%	72%	20% of men and 43% of women
Carrion et al. (2004) [9]	Retrospective	138	Median: 41 months	91%	70%	NR
Sevin et al. (2004) [10]	Retrospective	124	NR	92%	90%	NR
Studer et al. (2006) [11]	Prospective	482	Median: 42 months	92% after 1 year	79% after 1 year	7%

(continued)

Table 8.1 (continued)

Study	Design	Number of patients	Follow-up duration	Continence rate		Intermittent catheterization rate
				Daytime	Nighttime	
Novara et al. (2010) [12]	Retrospective	113	44 months	17.7% fully continent 31.9% mild incontinence		13%
Anderson et al. (2012) [13]	Retrospective	51 (female)	Mean: 3.1 years	57%	45%	31%
Ahmadi et al. (2013) [14]	Prospective	179	Mean: 4.5 years Range: 1–8 years	60.3%	45.3%	9.5%
Dellis et al. (2014) [15]	Prospective	181	Up to 20 years	88%, 98.4%, and 99.2% after 6 months, 5 years, and 20 years, respectively	70.2%, 94%, and 95.8% after 6 months, 5 years, and 20 years, respectively	1.7%, 8.7%, and 16% after 6 months, 5 years, and 20 years, respectively
Clifford et al. (2016) [16]	Prospective	188 (male)	3 months to > 3 years	92%	51%	10%

NR not reported

been observed that daytime continence returns more rapidly compared to nighttime continence [8]. In a series of 166 patients, Copenhagen group reported nighttime continence rate of 75% and 94% at 1 and 3 years after surgery, respectively [6]. Similarly in a series of 935 patients with orthotopic neobladder reconstruction after cystectomy, continence rate was found to be 59% and 92% at 3 months and 1 year, respectively [16].

Failure to Empty

Problems pertinent to the voiding phase present as failure in emptying of the neobladder and usually occur months after surgery; however, some patients after a number of years of spontaneous voiding present with urinary retention and require self-intermittent catheterization (rates of approximately 10% in men and 30–50% in women). The underlying causes of incomplete emptying and retention have not been clearly defined. Mechanical obstruction, posterior displacement of the neobladder and kinking of the urethra, as well as inability to maintain abdominal straining may be attributable to emptying failure.

Risk Factors

Construction of orthotopic neobladder was initially limited to men as it was thought to be associated with higher rate of voiding dysfunction and compromised oncologic outcome in women. Although the technique is feasible in women and is not associated with unfavorable oncologic outcome, voiding dysfunction occurs more frequently. Anderson et al. evaluated 49 women with orthotopic neobladder urinary diversion for a mean follow-up period of 3.1 years. They reported nighttime incontinence, daytime incontinence, and emptying failure in 55%, 43%, and 31% of patients, respectively [13]. Furthermore history of concurrent or previous hysterectomy was associated with higher rate of incontinence in their series. In contrast, several other studies have reported daytime and nighttime continence rates of 75–93% and 72–84% in women, respectively. These values are quite high and parallel to those reported from series of men [17–20]. Despite controversies on continence rate, most series have reported higher frequency of emptying failure and need to intermittent catheterization in women compared to men [13, 21]. Posterior prolapse of the neobladder during Valsalva maneuver and subsequent angulation of the urethra have been suggested as the cause of impaired neobladder emptying in women. Lengthening of the urethra in an attempt to improve continence may also increase the likelihood of emptying failure, whereas superior and anterior fixation of the neobladder and using omental or peritoneal flaps to fill the posterior pelvis may secure proper orientation of the neobladder and prevent prolapse. Furthermore, meticulous dissection and preservation of pelvic floor fascia and levator muscles in women may prevent neobladder prolapse. Emptying failure rarely occurs in men. In a series of 655 men, Simon et al. observed incomplete emptying (defined as a residual urine volume >100 mL) in 75 (11.5%) patients. Mechanical obstruction secondary to either benign strictures or local tumor recurrence was the major cause of incomplete emptying in their series [22].

Some investigators have also reported older age and diabetes mellitus as predicting factors for voiding dysfunction in patients with orthotopic neobladder [14]. The use of colonic segments in pouch reconstruction is associated with increased voiding pressures and higher likelihood of incontinence. In addition, non-nerve sparing technique during cystectomy results in compromised sphincter function and higher probability of incontinence [11].

Management

A combination of lifestyle modification, behavioral therapy, pharmacological intervention, catheterization, and surgery might be necessary in the management of voiding dysfunction in patients with orthotopic neobladder urinary diversion. Daytime and nighttime incontinence usually improve with time; however, persistent incontinence requires evaluation and appropriate management. Incontinence may be related to intrinsic contractions of the neobladder. Anticholinergics may be useful in controlling uninhibited pouch contractions in patients with high-pressure reservoirs; however, refractory cases require surgical intervention to increase the capacity of reservoir. Nighttime incontinence can be managed by limiting fluid intake before bedtime and evaluation for other medical issues such as peripheral edema and congestive heart failure. In patients with persistent stress urinary continence refractory to the aforesaid therapeutic strategies, artificial urinary sphincter is an effective treatment with acceptable complication rate and outcome [23].

Management of incomplete emptying in patients with orthotopic neobladder consists of timed voiding, double voiding, and physical therapy to promote pelvic floor muscle relaxation during voiding as well as self-intermittent catheterization. Long-term and regular urologic follow-up in terms of voiding function is of utmost importance and may improve quality of life and functional outcomes.

Stoma-Related Complications

Complications related to stoma are quite common among patients with ileal conduit or continent cutaneous urinary diversion, and the incidence has been reported to be as high as 60% [24]. Problems associated with stoma consist of stomal stenosis, difficulties with catheterization, parastomal hernia, and bleeding. Patients with continent cutaneous diversion need to empty the reservoir by self-catheterization through stoma. Complication rates related to stoma in these patients including difficulties with catheterization and incontinence can be significant. Some of these complications have been covered in detail in previous chapters but will be elaborated here for completeness.

Stomal Stenosis

Stomal stenosis may be a consequence of long-term ischemia, skin irritation, and/or facial constriction. Although earlier series have reported a stricture rate of 20–25% and 10–25% in ileal and colon conduits, respectively [25], more recent studies have reported lower rates of conduit stricture. In a study from Mayo Clinic, conduit stricture was reported in less than 3% of 1057 patients after a median follow-up of 9.4 years [26]. However, stomal stenosis and catheterization difficulties occur in a significant proportion of patients with catheterizable stomas [27]. Reported rate of stomal stenosis and difficult catheterization in patients with continent cutaneous diversion varies between 4 and 15% in the literature. Continence mechanism applied in the diversion may also affect the stenosis rate [28]. Stomal stenosis impedes proper urinary drainage and may require open surgical revision. Proper surgical technique and careful attention to the vascularity of the bowel segment as well as proper alignment of the conduit minimize the risk of stenosis. Furthermore, parastomal skin care and the use of a properly fitting external appliance may also reduce the risk of stomal stenosis.

Elongation of the Bowel Segment

Elongation of the bowel segment used in the creation of conduit or reservoir is another complication associated with urinary diversion and indicates a distal obstruction or failure to adequately catheterize the reservoir (Fig. 8.1). Sometimes it is associated with massive enlargement and may rarely result in a volvulus of the segment. Improper drainage and increased pressure of the segment may lead to deterioration of the renal function; therefore, prompt attention and revision are warranted.

Fig. 8.1 Elongated and dilated ileal conduit with right kidney stone due to distal obstruction

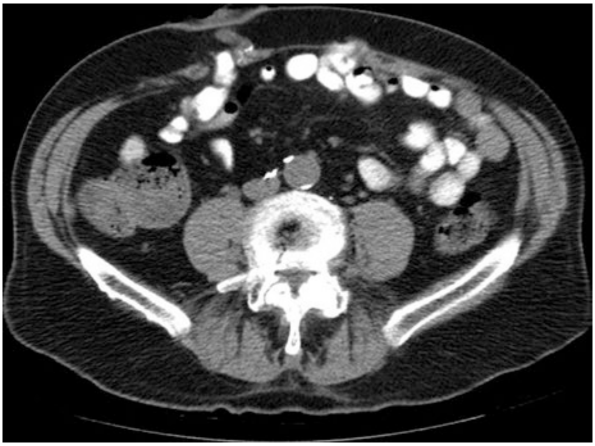


Fig. 8.2 CT scan of the abdomen with oral contrast showing parastomal hernia containing a segment of the ileum

Parastomal Hernia

Parastomal hernia is defined as protrusion of peritoneal content through the abdominal wall defect adjacent to the stoma (Fig. 8.2). Parastomal hernia may be associated with discomfort and inappropriate fitting of external appliance and has negative impacts on quality of life. It might also lead to urinary obstruction and/or bowel obstruction, incarceration, strangulation, and perforation.

This is a common complication in patients with conduit diversions, and the incidence varies from 2.3 to more than 60% in different series [29–32]. This variation may be related to different criteria used to define the condition, duration of follow-up, and whether the diagnosis is made clinically or based on radiological evaluations. The diagnosis is usually made clinically; however, radiologic evaluation increases the accuracy of diagnosis. Parastomal hernias are categorized into three different subtypes based on a clinico-radiological classification system proposed by Moreno-Matias et al. [33]. In type 1, the bowel loop forming the stoma is herniated through the wall defect. In type 2, hernia sac contains omentum or abdominal fat, and type 3 refers to herniated bowel loops other than stoma. Using this classification system, Donahue et al. noted that 5(4%), 90 (66%), and 41(30%) patients develop type 1, 2, and 3 parastomal hernia, 2 years after cystectomy and ileal conduit diversion, respectively. In a series from the University of Southern California, with a median follow-up of 57 months, the rate of parastomal hernia was found to be 23% [34]. In a study from Mayo Clinic addressing complications associated with conduit diversion in 1045 patients, parastomal hernia was the most common stoma-related complication occurring in 14% at a median of 2 years [26]. Similarly in a retrospective review of Indiana University cystectomy database, risk of parastomal hernia was 12% and 22% at 1 and 2 years after cystectomy [35].

Risk Factors

Factors that increase the risk of parastomal hernia can be categorized as patient- or technique specific. Patient-specific factors including female gender, obesity, weight gain after surgery, malnutrition, and lower preoperative serum albumin level may significantly increase the risk of parastomal hernia [32]. In addition, some investigators have proposed prior laparotomy, older age, malnutrition, and immunosuppression as predisposing factors for developing parastomal hernia [35–37]. Improper surgical technique (i.e., placement of stoma lateral to the rectus sheath) may increase the likelihood of parastomal hernia as well. Also, there is no high level of evidence that Turnbull stoma would increase the chance of parastomal hernia in comparison to end stoma.

Management

Some patients with parastomal hernia do not have significant symptom or sign to warrant repair. Parastomal hernia may be detected during radiological evaluations in these patients. Surgical repair of parastomal hernia is associated with a relatively high recurrence rate and is not recommended in asymptomatic or mildly symptomatic patients; however, these patients should be educated about signs and symptoms pertinent to acute complications of parastomal hernia including bowel obstruction and strangulation [38]. Stoma belts (ostomy binder) can also be applied in patients without absolute indication for surgical repair. These binders lessen the bulging of the skin and help to stabilize the external appliance [39].

Surgical repair is indicated in patients with bothersome symptoms that impair quality of life as well as those who develop intestinal complications [38]. Primary repair of the parastomal hernia involves dissection of the fascia and re-approximation of the edges with nonabsorbable sutures. This can be performed through a laparotomy incision, extra-abdominally or laparoscopically; however, laparoscopic repair has not been standardized, and long-term follow-up results are lacking [40].

Another approach is prosthetic mesh repair. Mesh can be placed either anterior to the rectus (onlay technique) or preperitoneally below the muscularis layer (sublay technique). Mesh repair is the most common technique used for parastomal hernia repair and is associated with higher success rates compared to repair not using mesh [41]. There is a randomized clinical trial open that aims to evaluate the use of prophylactic biologic mesh (FlexHD) to prevent parastomal hernia (NCT02439060, ClinicalTrials.gov)

Ureteral Stricture

Ureteral strictures in patients with urinary diversion are frequently seen at the site of ureteroenteric anastomosis. Occasionally strictures occur away from the anastomosis. This type of stricture usually involves the left ureter where it crosses between the aorta and inferior mesenteric artery. Extensive mobilization of the ureter and aggressive stripping of ureteral periadventitial tissue as well as angulation of the ureter at the inferior mesenteric artery are predisposing factors. Furthermore, ureteroenteric anastomoses that are designed to prevent reflux are associated with higher risk of stricture. In a randomized clinical trial comparing refluxing and non-refluxing ureteroenteric anastomosis, Shaban et al. showed that non-refluxing anastomoses are associated with significantly higher rate of ureteral obstruction and subsequent renal function deterioration [42].

Stricture usually occurs within few months of the procedure; however, late-onset occurrence of up to 13 years following surgery has also been reported [43]. Therefore, lifelong observation for ureteral stricture is imperative in patients with urinary diversion.

Risk of ureteroenteric strictures varies in different series. In a large series of 1964 patients from the University of Southern California with a median follow-up of 12.4 years, 49 patients and 51 (2.6%) renal units were reported to develop benign ureteral stricture with median time of 10 months from surgery to diagnosis [44]. In a single institutional study of 112 patients receiving Indiana pouch, ureteroenteric anastomosis stricture was reported to be 7% over a 14-year period [27]. Risk of ureteral stricture seems to be higher at the left side. In a study of 436 patients, Richard et al. reported ureteral stricture rate of 5.9% and 10.0% on the right and left sides after a median follow-up of 459 days, respectively [45]. Previous history of abdominal/pelvic irradiation has been postulated to increase the risk of ureteroenteric anastomosis; however, in a recent large series from University of Southern California, multivariate logistic regression analysis did not show any correlation between ureteroenteric anastomosis stricture and history of perioperative radiation therapy [44]. Surgical technique seems to be the most important determining factor, and by applying a meticulous surgical technique, ureteroenteric anastomosis stricture rarely occurs. Advances in surgical technology may also improve the surgical outcome. In a study comparing 375 and 103 patients who underwent open and robot-assisted laparoscopic radical cystectomy, respectively, Anderson et al. reported higher stricture rates in the former group (12% vs. 8.5%); however, the difference was not statistically significant.

Ureteral stricture after urinary diversion presents with flank pain and/or urinary tract infection; however, it may be asymptomatic in 30% of patients [44]. Once the diagnosis of ureteral stricture is made, various techniques including endoscopic and open approaches can be used for repair. Poulakis et al. evaluated the efficacy of cold-knife endoureterotomy and reported a durable success rate of 60% in 40 patients with 43 ureteroenteric anastomosis stricture; nevertheless, patients with favorable predictive factors, including occurrence of stricture after 12 months from the primary surgery and stricture length of 1.5 cm or less as well as the absence of severe hydronephrosis, revealed 100% success rate [46]. Some studies have compared endourologic versus open surgical correction of the ureteroenteric anastomosis stricture. Dimarco et al. compared 27 open repairs with 52 balloon dilations and revealed that open repair offers excellent long-term patency in patients with ureteroenteric stricture (76% after 3 years), whereas balloon dilation had a success rate of 5% at 3 years. Although in selected cases endourologic methods may be effective, overall success rate is lower compared to open surgical repair, and retreatment rate exceeds 50% [47]. Occasionally stricture is a consequence of cancer recurrence at the site of ureteroenteric anastomosis, and these patients should be considered for systemic chemotherapy [48].

Bowel-Related Complications

Bowel complications are among the most common complications in patients with urinary diversion and are associated with significant morbidity and high reoperation rates.

Bowel Obstruction

Intestinal obstruction is one of the most common bowel complications after urinary diversion, and the incidence varies based on the type of segment used for the creation of diversion. There is a 10% risk of bowel obstruction in patients with ileoileal anastomosis, and when a segment of colon is utilized for the diversion, the incidence of obstruction is 5% [49, 50]. Reported incidence of bowel obstruction varies significantly in different series. In a large series of 1057 patients from Mayo Clinic, bowel obstruction was reported to occur in 16% of patients at a median follow-up period of 1.7 years. In another study of 923 patients with follow-up duration of 20 years, bowel obstruction was reported in 3.6% of patients [51]. Bowel obstruction may be a consequence of intestinal stenosis, adhesion bands, internal hernia, or volvulus. Stricture of the intestinal anastomosis may occur either in early postoperative period or during the long-term evaluation. Early-onset strictures usually occur as a consequence of improper technique, whereas late-onset strictures develop due to ischemia (i.e., using irradiated bowel). In addition to the aforesaid benign causes of bowel obstruction, recurrence of cancer and peritoneal carcinomatosis should be considered in patients presenting with bowel obstruction.

Fistulas

Another complication related to the bowel segment is fistula formation. Fistula can develop between the conduit or neobladder/pouch and intestine as well as between the neobladder and vagina or rectum. Some patients may also develop cutaneous urinary or fecal fistulas. These complications generally occur within the first weeks after the surgery and are associated with significant morbidity and mortality. These patients frequently develop sepsis with an associated mortality rate of 2% [52].

In most series incidence of fistula formation after cystectomy and urinary diversion has been reported to be less than 5%, although some series with long-term evaluation have reported that up to 10% of patients with urinary diversion may develop fistulas [26, 53, 54].

Total parenteral nutrition and urinary drainage using large-bore catheters are initial considerations in the management of patients; however, conservative management is not effective in the majority of patients, and they require surgical repair [13, 26, 53]. The probability of cancer recurrence should also be considered at the site of fistula.

Pouch Perforation

Pouch/neobladder perforation is an extremely rare and potentially life-threatening complication in patients with continent diversion. Patients usually present with acute abdominal pain and distention. Rupture may occur as a consequence of traumatic catheterization or blunt trauma to a full urinary reservoir. The rupture usually occurs intraperitoneally [51]; therefore, immediate laparotomy and repair of the reservoir are necessary. Few reports of conservative management also exist in the literature [55, 56].

Cancer

The development of neoplasia following ureterosigmoidostomy is a well-known complication that occurs in more than 10% of patients with this form of urinary diversion [57, 58]. Tumors with different histologic features including adenomatous polyps, adenocarcinoma, sarcomas, as well as urothelial cell carcinoma may develop. The pathogenesis has not been described thoroughly; however, mixing of fecal and urinary streams and a combination of carcinogenic action may cause progressive changes in mucosa and subsequent dysplasia and carcinoma. Risk of cancer increases significantly when the urothelium is juxtaposed to the colonic epithelium and both are bathed by feces and urine [59]. Malignant transformation is not limited solely to diversions with mixing fecal and urinary streams, and more recent series have shown higher risk of intestinal tumor development in all types of urinary diversion using bowel even with separation of urine and feces [60]. Therefore, all patients with urinary diversion require lifelong follow-up and evaluation for the development of cancer; particularly patients with ureterosigmoidostomy may require colonoscopic screening with regular intervals beginning 5 years after surgery. Other primary tumors of the urinary diversion (usually adenocarcinomas) are extremely rare but may occur after long latent periods. Any unexplained bleeding from the diversion should prompt endoscopic evaluation.

Nutritional and Metabolic Complications

Urinary diversion may be associated with serious metabolic complications, and its severity may be influenced by several factors including the type and length of bowel segment used in diversion. Short bowel syndrome, electrolyte and acid-base disturbances, altered sensorium, metabolic bone disorders, urolithiasis, and abnormal drug absorption are the main metabolic consequences associated with urinary diversion.

Short Bowel Syndrome

Resection of bowel segment may be associated with significant loss of intestinal absorptive surface and subsequent nutritional problems. Resection of a segment of the ileum or colon can lead to malabsorption of bile salts and vitamin B12. Clinical consequences of vitamin B12 deficiency, including anemia and neurologic abnormalities, may not manifest for several years after surgery as the liver stores enough vitamin B12 to supply the body requirements for an extended period of time. The incidence of B12 deficiency after urinary reconstruction ranges from zero to as high as 33% [5, 6, 26]. This variability may be related to applying different screening methods as well as variations in length of the ileum used in diversion. Bile salts are also mainly absorbed in terminal ileum, and extensive ileal resection results in significant impairment of the enterohepatic circulation of bile salts and diminished liver ability to upregulate bile acid synthesis that is necessary for enhancing fat solubility. Lack of bile salt absorption in the ileum allows bile salt entry into the colon and subsequent mucosal irritation and diarrhea. Another mechanism that can be impaired in patients with urinary diversion is called “ileal brake.” Ileal brake enhances absorption by decreasing gut motility when lipids come in contact with ileal mucosa. Resection of the ileum can impair ileal brake mechanism and results in fatty diarrhea and nutritional deficiencies. The use of ileocecal segment in patients undergoing urinary diversion is associated with loss of ileocecal valve that also serves as a brake, prolongs transit time, and enhances absorption.

Electrolyte and Acid-Base Disturbances

A variety of electrolyte and acid-base disturbances can occur in patients with urinary diversion. The type of electrolyte abnormality depends on the bowel segment that has been used for urinary diversion, surface area of the intestinal segment, and the amount of time that urine is exposed to the bowel mucosa. In patients who undergo ureterosigmoidostomy, urine is exposed to a significant surface of colonic mucosa for a long period of time with metabolic disturbances develop in up to 80% of these patients [61]. When the ileum or colon is used, a hypokalemic hyperchloremic metabolic acidosis may ensue. The ileum absorbs chloride and excretes bicarbonate leading to metabolic acidosis. Clinical manifestations include fatigue, weakness, lethargy, anorexia, and weight loss. Furthermore, metabolic acidosis has been reported to be the main cause of readmission following radical cystectomy [62]. Metabolic acidosis may occur less frequently in patients with ileal conduit as the contact time between urine and bowel mucosa is limited. Occurrence of metabolic acidosis in patients with ileal conduit should raise suspicion of loop malfunction, i.e., stomal stenosis. An ileal loopogram can confirm the diagnosis in these patients [61, 63, 64]. In patients with orthotopic neobladder, alkalinizing treatment to overcome metabolic acidosis is necessary in approximately half of patients [5]. Sodium bicarbonate and other alkalinizing agents including sodium citrate or potassium citrate can be used to correct the metabolic acidosis. Blockers of the chloride transport, i.e., nicotinic acid and chlorpromazine, are also of value in treating patients with persistent hyperchloremic metabolic acidosis especially when excessive sodium load is harmful [65].

Hypokalemia is another electrolyte disturbance in patients with urinary diversion. Metabolic acidosis is commonly associated with decreased sodium and bicarbonate reabsorption and subsequent activation of renin angiotensin aldosterone system. Aldosterone increases potassium secretion and results in hypokalemia [66]. The ileum is capable of potassium reabsorption, whereas sigmoid secretes potassium; therefore, hypokalemia is more common in sigmoid diversions as compared with ileal diversion. It also should be considered that correction of metabolic acidosis may be associated with further decline in serum potassium to a critical level; therefore potassium replacement is of utmost importance before the initiation of any alkalinizing agent.

Altered Sensorium

Patients with urinary diversion may develop altered sensorium also known as clouded sensorium. Alteration of the mental status usually occurs as a consequence of micronutrient deficiencies, i.e., hypomagnesemia, drug intoxication, or altered ammonia metabolism. Hyperammonemic encephalopathy is a rare complication in patients with urinary diversion and usually occurs in patients who also suffer from liver insufficiency. Urinary obstruction and urinary tract infection are other predisposing factors. Urinary obstruction increases exposure time of urine with the bowel mucosa and exacerbates hyperammonemia. Infection with urease-positive organisms such as

Proteus or *Klebsiella* also produces excessive amount of ammonia as the urea is hydrolyzed to ammonium [67]. Treatment of hyperammonemic encephalopathy consists of appropriate drainage of the urinary intestinal diversion, restriction of protein consumption, and administration of neomycin to reduce the ammonia load from the enteric tract. These patients should also be evaluated and, if indicated, treated for urinary tract infections, urinary tract obstruction, and hepatic dysfunction.

Bone Metabolic Complications

A population-based study has recently shown that cystectomy is associated with significant increase in the risk of fracture. Using SEER-Medicare database, authors evaluated 50,520 patients including 4878 patients who underwent cystectomy and revealed 21% greater risk of fracture in cystectomy population [68]. Osteomalacia and osteoporosis in patients with urinary diversion are multifactorial but are mainly pertinent to metabolic acidosis. Chronic metabolic acidosis accentuates osteoclast bone resorption and decreases osteoblastic activity. In addition, the bone buffers excess proton that induces calcium efflux from the bone. It has been shown that correction of metabolic acidosis results in remineralization of the bone [69]. However, bone remineralization does not occur in some patients despite correction of metabolic acidosis. These patients may suffer from vitamin D resistance and require administration of 1-alpha-hydroxycholecalciferol for bone remineralization [70]. The mainstay in the management of osteomalacia in patients with urinary diversion is correction of metabolic acidosis and supplementation of calcium. Sometimes, the disease is not amenable to the aforesaid treatments, and administration of active forms of vitamin D becomes necessary.

Urolithiasis

Patients with urinary diversion are at higher risk of developing urinary stones (Fig. 8.3). Resection of a bowel segment results in short bowel syndrome and subsequent hyperoxaluria. Furthermore, hypocitraturia develops as a consequence of chronic metabolic acidosis [71]. Struvite stones may also arise as these patients are more likely to develop urinary tract infection and bacterial colonization of the urinary reservoir [72]. A major cause of stone formation in patients with urinary diversion is a foreign body such as a nonabsorbable suture or an exposed staple that acts as a nidus and facilitates stone formation. In a cohort of 445 consecutive patients with stapled orthotopic neobladder, the authors reported the incidence of stone formation to be about 10% after a median follow-up of 41 months. However, the incidence of stone formation increased over time up to 25%, 7 years after surgery [73]. Stone incidence rate seems to be slightly higher in series applying staples [6, 73] compared to hand-sewn diversions [5, 8]; however, no randomized study has evaluated the role of staples in stone formation within reservoirs. Appropriate hydration and treating metabolic and electrolyte disturbances as well as adequate reservoir emptying are the main preventive measures.

Fig. 8.3 Large stones in continent cutaneous diversion 25 years following surgery

Infection

Patients with urinary diversion are susceptible to infectious complications. Infectious complications are among the most common causes of admission in patients with urinary diversion [62]. In a cohort of 66 patients with orthotopic neobladder, Wood et al. reported bacteriuria in 78% of patients, and symptomatic urinary tract infection developed in half of these patients [74]. Despite high incidence of bacteriuria, urosepsis is rare and occurs in the context of recurrent symptomatic infections [74]. Using bowel segments that are normally colonized with bacteria is one of the contributing factors [75]. Bowel mucosa in contrast to urothelium is not capable of inhibiting bacterial proliferation. Incomplete neobladder/pouch emptying occurs in some patients with continent urinary diversion, and residual urine may induce urinary tract infection in these patients. On the other hand, intermittent catheterization is required in some cases to empty the urinary reservoir and can introduce bacteria into the pouch, increasing the risk of infectious complications. Although incomplete emptying and intermittent catheterization are limited to continent diversions, incidence of urinary tract infection is comparable between conduit and continent diversions [76]. Acute pyelonephritis has been reported to occur in up to 17% of patients with conduit diversion [77], and about 4% of patients with ileal conduit die of sepsis [78].

Many patients with chronic bacteriuria do not show any untoward effects and not require any treatment. However, patients with symptomatic infection and those with positive cultures for *Proteus* or *Pseudomonas* require treatment as infection with the aforementioned organisms has been postulated to be associated with renal function deterioration [77].

Renal Function Deterioration

Renal function compromise may occur in patients with urinary diversion. Aging, underlying disorders, urinary tract obstruction, reflux nephropathy, infection, and stone formation have been considered as contributory factors [79]. Incidence of renal function deterioration varies significantly and ranges from 20% to more than

80% in different studies [26, 76, 80–83]. Renal function assessment, definition of renal function deterioration, and duration of follow-up vary in different series that account for the wide range of observed results.

Different measurement tools have been utilized in different series. Chronic Kidney Disease Epidemiology Collaboration equation has been used to calculate eGFR in recent series and seems to be more precise compared to serum creatinine measurement [76, 83]. In a recent large series containing 1383 patients who underwent radical cystectomy and urinary diversion, Gershman et al. applied Chronic Kidney Disease Epidemiology Collaboration equation to estimate eGFR 10 years after surgery and reported renal function compromise (>10% decline in eGFR) in 81% and 78% of patients with incontinent and continent diversions, respectively [83]. In another study assessing 169 patients, renal function deterioration, defined as >25% decline in eGFR, was reported in 57%, 50%, and 39% of patients with cutaneous ureterostomy, ileal conduit, and orthotopic neobladder, respectively [82]. Age, chronic hypertension, ureteroenteric anastomosis stricture, and pyelonephritis have been reported as independent risk factors for renal function deterioration in different series. Type of urinary diversion does not seem to be a predisposing factor for renal dysfunction. Although larger surface area of continent diversion is in contact with urine, these types of diversion have not been associated with greater risk of decline in renal function [76]. Renal dysfunction has been hypothesized to be associated with higher risk of cardiovascular disorders and subsequent mortality [84]; therefore, all patients with urinary diversion should be regularly monitored for renal function compromise and receive appropriate preventive and therapeutic care.

Conclusion

Radical cystectomy with urinary diversion is the treatment of choice for patients with muscle-invasive and high-risk non-muscle-invasive bladder cancer. Postoperative morbidity is significant, and in the long term, at least 60% of patients will develop complications associated with the urinary diversion. Voiding dysfunction, bowel- and stoma-related complications, metabolic disturbances, infection, ureteral stricture, and renal function deterioration are among chronic complications following urinary diversion that may occur up to several years after surgery, emphasizing the need for a long-term, regular follow-up. Optimal long-term care is best achieved through a multidisciplinary approach incorporating urologists, enterostomal therapy nurses, and physical therapists preferably in high-volume experienced centers.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin. 2016;66:7.
2. Madersbacher S, Schmidt J, Eberle JM, et al. Long-term outcome of ileal conduit diversion. J Urol. 2003;169:985.
3. Kassouf W, Hautmann RE, Bochner BH, et al. A critical analysis of orthotopic bladder substitutes in adult patients with bladder cancer: is there a perfect solution? Eur Urol. 2010;58:374.

4. Elmajian DA, Stein JP, Esrig D, et al. The Kock ileal neobladder: updated experience in 295 male patients. J Urol. 1996;156:920.
5. Hautmann RE, de Petriconi R, Gottfried HW, et al. The ileal neobladder: complications and functional results in 363 patients after 11 years of followup. J Urol. 1999;161:422.
6. Steven K, Poulsen AL. The orthotopic Kock ileal neobladder: functional results, urodynamic features, complications and survival in 166 men. J Urol. 2000;164:288.
7. Abol-Enein H, Ghoneim MA. Functional results of orthotopic ileal neobladder with serous-lined extramural ureteral reimplantation: experience with 450 patients. J Urol. 2001;165:1427.
8. Stein JP, Dunn MD, Quek ML, et al. The orthotopic T pouch ileal neobladder: experience with 209 patients. J Urol. 2004;172:584.
9. Carrion R, Arap S, Corcione G, et al. A multi-institutional study of orthotopic neobladders: functional results in men and women. BJU Int. 2004;93:803.
10. Sevin G, Soyupek S, Armagan A, et al. Ileal orthotopic neobladder (modified Hautmann) via a shorter detubularized ileal segment: experience and results. BJU Int. 2004;94:355.
11. Studer UE, Burkhard FC, Schumacher M, et al. Twenty years experience with an ileal orthotopic low pressure bladder substitute--lessons to be learned. J Urol. 2006;176:161.
12. Novara G, Ficarra V, Minja A, et al. Functional results following vescica ileale Padovana (VIP) neobladder: midterm follow-up analysis with validated questionnaires. Eur Urol. 2010;57:1045.
13. Anderson CB, Cookson MS, Chang SS, et al. Voiding function in women with orthotopic neobladder urinary diversion. J Urol. 2012;188:200.
14. Ahmadi H, Skinner EC, Simma-Chiang V, et al. Urinary functional outcome following radical cystoprostatectomy and ileal neobladder reconstruction in male patients. J Urol. 2013;189:1782.
15. Dellis AE, Papatsoris AG, Skolarikos AA, et al. Modified S-ileal neobladder for continent urinary diversion: functional and urodynamic results after 20 years of follow-up. Urol Int. 2014;93:43.
16. Clifford TG, Shah SH, Bazargani ST, et al. Prospective evaluation of continence following radical cystectomy and orthotopic urinary diversion using a validated questionnaire. J Urol. 2016;196:1685.
17. Ali-el-Dein B, el-Sobky E, Hohenfellner M, et al. Orthotopic bladder substitution in women: functional evaluation. J Urol. 1999;161:1875.
18. Stenzl A, Jarolim L, Coloby P, et al. Urethra-sparing cystectomy and orthotopic urinary diversion in women with malignant pelvic tumors. Cancer. 2001;92:1864.
19. Hautmann RE, de Petriconi R, Kleinschmidt K, et al. Orthotopic ileal neobladder in females: impact of the urethral resection line on functional results. Int Urogynecol J Pelvic Floor Dysfunct. 2000;11:224.
20. Arai Y, Okubo K, Konami T, et al. Voiding function of orthotopic ileal neobladder in women. Urology. 1999;54:44.
21. Finley DS, Lee U, McDonough D, et al. Urinary retention after orthotopic neobladder substitution in females. J Urol. 2011;186:1364.
22. Simon J, Bartsch Jr G, Kufer R, et al. Neobladder emptying failure in males: incidence, etiology and therapeutic options. J Urol. 2006;176:1468.
23. Simma-Chiang V, Ginsberg DA, Teruya KK, et al. Outcomes of artificial urinary sphincter placement in men after radical cystectomy and orthotopic urinary diversions for the treatment of stress urinary incontinence: the University of Southern California experience. Urology. 2012;79:1397.
24. Farnham SB, Cookson MS. Surgical complications of urinary diversion. World J Urol. 2004;22:157.
25. McDougal WS. Urinary tract reconstruction. J Urol. 1994;152:343.
26. Shimko MS, Tollefson MK, Umbreit EC, et al. Long-term complications of conduit urinary diversion. J Urol. 2011;185:562.
27. Holmes DG, Thrasher JB, Park GY, et al. Long-term complications related to the modified Indiana pouch. Urology. 2002;60:603.
28. Vergho D, Kocot A, Bauer C, et al. Insufficiency of the efferent segment in continent cutaneous diversion. Urologe A. 2012;51:485.

29. Kouba E, Sands M, Lentz A, et al. Incidence and risk factors of stomal complications in patients undergoing cystectomy with ileal conduit urinary diversion for bladder cancer. J Urol. 2007;178:950.
30. Nastro P, Knowles CH, McGrath A, et al. Complications of intestinal stomas. Br J Surg. 2010;97:1885.
31. Pilgrim CH, McIntyre R, Bailey M. Prospective audit of parastomal hernia: prevalence and associated comorbidities. Dis Colon Rectum. 2010;53:71.
32. Donahue TF, Bochner BH, Sfakianos JP, et al. Risk factors for the development of parastomal hernia after radical cystectomy. J Urol. 2014;191:1708.
33. Moreno-Matias J, Serra-Aracil X, Darnell-Martin A, et al. The prevalence of parastomal hernia after formation of an end colostomy. A new clinico-radiological classification. Colorectal Dis. 2009;11:173.
34. Movassaghi K, Shah SH, Cai J, et al. Incisional and parastomal hernia following radical cystectomy and urinary diversion: The University of Southern California Experience. J Urol. 2016;196:777.
35. Liu NW, Hackney JT, Gellhaus PT, et al. Incidence and risk factors of parastomal hernia in patients undergoing radical cystectomy and ileal conduit diversion. J Urol. 2014;191:1313.
36. Ripoche J, Basurko C, Fabbro-Perray P, et al. Parastomal hernia. A study of the French federation of ostomy patients. J Visc Surg. 2011;148:e435.
37. Jansen PL, Mertens Pr P, Klinge U, et al. The biology of hernia formation. Surgery. 2004;136:1.
38. Hotouras A, Murphy J, Thaha M, et al. The persistent challenge of parastomal herniation: a review of the literature and future developments. Color Dis. 2013;15:e202.
39. Carne PW, Robertson GM, Frizelle FA. Parastomal hernia. Br J Surg. 2003;90:784.
40. Mancini GJ, McClusky 3rd DA, Khaitan L, et al. Laparoscopic parastomal hernia repair using a nonslit mesh technique. Surg Endosc. 2007;21:1487.
41. Hansson BM, Slater NJ, van der Velden AS, et al. Surgical techniques for parastomal hernia repair: a systematic review of the literature. Ann Surg. 2012;255:685.
42. Shaaban AA, Abdel-Latif M, Mosbah A, et al. A randomized study comparing an antireflux system with a direct ureteric anastomosis in patients with orthotopic ileal neobladders. BJU Int. 2006;97:1057.
43. Shapiro SR, Lebowitz R, Colodny AH. Fate of 90 children with ileal conduit urinary diversion a decade later: analysis of complications, pyelography, renal function and bacteriology. J Urol. 1975;114:289.
44. Shah SH, Movassaghi K, Skinner D, et al. Ureteroenteric strictures after open radical cystectomy and urinary diversion: The University of Southern California Experience. Urology. 2015;86:87.
45. Richards KA, Cohn JA, Large MC, et al. The effect of length of ureteral resection on benign ureterointestinal stricture rate in ileal conduit or ileal neobladder urinary diversion following radical cystectomy. Urol Oncol. 2015;33:65.e1.
46. Poulakis V, Witzsch U, De Vries R, et al. Cold-knife endoureterotomy for nonmalignant ureterointestinal anastomotic strictures. Urology. 2003;61:512.
47. Schondorf D, Meierhans-Ruf S, Kiss B, et al. Ureteroileal strictures after urinary diversion with an ileal segment-is there a place for endourological treatment at all? J Urol. 2013;190:585.
48. Westerman ME, Parker WP, Viers BR, et al. Malignant ureteroenteric anastomotic stricture following radical cystectomy with urinary diversion: patterns, risk factors, and outcomes. Urol Oncol. 2016;34:485.e1.
49. Varkarakis IM, Chrisofos M, Antoniou N, et al. Evaluation of findings during re-exploration for obstructive ileus after radical cystectomy and ileal-loop urinary diversion: insight into potential technical improvements. BJU Int. 2007;99:893.
50. Richie JP. Nonrefluxing sigmoid conduit for urinary diversion. Urol Clin North Am. 1979;6:469.
51. Hautmann RE, de Petriconi RC, Volkmer BG. 25 years of experience with 1,000 neobladders: long-term complications. J Urol. 2011;185:2207.

52. Hill JT, Ransley PG. The colonic conduit: a better method of urinary diversion? Br J Urol. 1983;55:629.
53. Msezane L, Reynolds WS, Mhapsekar R, et al. Open surgical repair of ureteral strictures and fistulas following radical cystectomy and urinary diversion. J Urol. 2008;179:1428.
54. Gilbert SM, Lai J, Saigal CS, et al. Downstream complications following urinary diversion. J Urol. 2013;190:916.
55. Mansson W, Bakke A, Bergman B, et al. Perforation of continent urinary reservoirs. Scandinavian experience. Scand J Urol Nephrol. 1997;31:529.
56. Singh S, Choong S. Rupture and perforation of urinary reservoirs made from bowel. World J Urol. 2004;22:222.
57. Zabbo A, Kay R. Ureterosigmoidostomy and bladder exstrophy: a long-term followup. J Urol. 1986;136:396.
58. Stewart M, Macrae FA, Williams CB. Neoplasia and ureterosigmoidostomy: a colonoscopy survey. Br J Surg. 1982;69:414.
59. Shands 3rd C, McDougal WS, Wright EP. Prevention of cancer at the urothelial enteric anastomotic site. J Urol. 1989;141:178.
60. North AC, Lakshmanan Y. Malignancy associated with the use of intestinal segments in the urinary tract. Urol Oncol. 2007;25:165.
61. Mundy AR. Metabolic complications of urinary diversion. Lancet. 1999;353:1813.
62. Harraz AM, Osman Y, El-Halwagy S, et al. Risk factors of hospital readmission after radical cystectomy and urinary diversion: analysis of a large contemporary series. BJU Int. 2015;115:94.
63. Tanrikut C, McDougal WS. Acid-base and electrolyte disorders after urinary diversion. World J Urol. 2004;22:168.
64. Koch MO, McDougal WS. The pathophysiology of hyperchloremic metabolic acidosis after urinary diversion through intestinal segments. Surgery. 1985;98:561.
65. Koch MO, McDougal WS. Nicotinic acid: treatment for the hyperchloremic acidosis following urinary diversion through intestinal segments. J Urol. 1985;134:162.
66. Aronson PS, Giebisch G. Effects of pH on potassium: new explanations for old observations. J Am Soc Nephrol. 2011;22:1981.
67. Samtoy B, DeBeukelaer MM. Ammonia encephalopathy secondary to urinary tract infection with Proteus mirabilis. Pediatrics. 1980;65:294.
68. Gupta A, Atoria CL, Ehdaie B, et al. Risk of fracture after radical cystectomy and urinary diversion for bladder cancer. J Clin Oncol. 2014;32:3291.
69. Richards P, Chamberlain MJ, Wrong OM. Treatment of osteomalacia of renal tubular acidosis by sodium bicarbonate alone. Lancet. 1972;2:994.
70. Perry W, Allen LN, Stamp TC, et al. Vitamin D resistance in osteomalacia after ureterosigmoidostomy. N Engl J Med. 1977;297:1110.
71. Okhunov Z, Duty B, Smith AD, et al. Management of urolithiasis in patients after urinary diversions. BJU Int. 2011;108:330.
72. Dretler SP. The pathogenesis of urinary tract calculi occurring after ileal conduit diversion. I. Clinical study. II. Conduit study. 3. Prevention. J Urol. 1973;109:204.
73. Ferriero M, Guaglianone S, Papalia R, et al. Risk assessment of stone formation in stapled orthotopic ileal neobladder. J Urol. 2015;193:891.
74. Wood Jr DP, Bianco Jr FJ, Pontes JE, et al. Incidence and significance of positive urine cultures in patients with an orthotopic neobladder. J Urol. 2003;169:2196.
75. Wullt B, Holst E, Steven K, et al. Microbial flora in ileal and colonic neobladders. Eur Urol. 2004;45:233.
76. Al Hussein Al Awamlh B, Wang LC, Nguyen DP, et al. Is continent cutaneous urinary diversion a suitable alternative to orthotopic bladder substitute and ileal conduit after cystectomy? BJU Int. 2015;116:805.
77. McDougal WS. Bladder reconstruction following cystectomy by uretero-ileo-colourethrostomy. J Urol. 1986;135:698.

78. Schmidt JD, Hawtrey CE, Flocks RH, et al. Complications, results and problems of ileal conduit diversions. J Urol. 1973;109:210.
79. Amini E, Djaladat H. Long-term complications of urinary diversion. Curr Opin Urol. 2015;25:570.
80. Jin XD, Roethlisberger S, Burkhard FC, et al. Long-term renal function after urinary diversion by ileal conduit or orthotopic ileal bladder substitution. Eur Urol. 2012;61:491.
81. Eisenberg MS, Thompson RH, Frank I, et al. Long-term renal function outcomes after radical cystectomy. J Urol. 2014;191:619.
82. Nishikawa M, Miyake H, Yamashita M, et al. Long-term changes in renal function outcomes following radical cystectomy and urinary diversion. Int J Clin Oncol. 2014;19:1105.
83. Gershman B, Eisenberg MS, Thompson RH, et al. Comparative impact of continent and incontinent urinary diversion on long-term renal function after radical cystectomy in patients with preoperative chronic kidney disease 2 and chronic kidney disease 3a. Int J Urol. 2015;22:651.
84. Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med. 2004;351:1296.

Stomal Complications

9

Sumeet Syan-Bhanvadia and Siamak Daneshmand

Radical cystectomy remains a morbid procedure with a 90-day complication rate of greater than 60% and readmission rate between 25% and 35% [1–3]. A recent randomized controlled trial comparing open versus laparoscopic-/robotic-assisted RC with extracorporeal diversion showed no difference in complication rates. The urinary diversion accounts for a significant portion of the morbidity associated with the operation and includes that associated with bowel resection, the ureteroileal anastomosis, urinary leak, infection, and the stoma, the latter of which will be the scope of this chapter.

Between the incontinent and continent diversion options, statistically the majority of patients undergoing urinary diversion will end up with some type of cutaneous stoma. While the majority of stomal complications can be managed conservatively, stomal issues are still the most common reason for reoperation after cystectomy [4–6]. In addition, even commonplace complications have significant quality of life impacts on patients [7]. Given this, an understanding of the complications associated with the various types of stoma is imperative for preoperative planning and discussion with the patient, as well as for selection of diversion type.

Stomal Complications in the Incontinent Stoma

Historically, it has been reported that up to 60% of conduit patients will experience stomal complications of some type in the postoperative period; a modern series of 137 of patients undergoing cystectomy with IC showed a stomal complication rate of 16% at a median follow-up of 2 years [4]. Some of the complications are covered in the chapter on ileal conduits; however, this is a comprehensive review and reflects our institutional practices.

S. Syan-Bhanvadia, MD (✉) • S. Daneshmand, MD
Institute of Urology, Norris Comprehensive Cancer Center,
University of Southern California, Los Angelos, CA, USA
e-mail: ssyan@med.usc.edu; daneshma@med.usc.edu

S. Daneshmand (ed.), *Urinary Diversion*, DOI 10.1007/978-3-319-52186-2_9

Ileal conduit comprises over 80% of diversions performed after radical cystectomy worldwide and is by far the most commonly employed type of incontinent stoma performed, for both its ease of construction and that its use of a small, easily accessible bowel segment that is well tolerated [8]. Early complications encompass appliance issues, skin irritation, bowel obstruction, necrosis of the conduit, leak from the bowel or ureteroenteric anastomoses, wound infection, or stomal dehiscence, and have been reported to occur in 20–56% of patients [4]. Late complications include skin and appliance issues and bowel obstruction, as well as stomal retraction, stomal stenosis, parastomal hernia, and ureteroileal stricture, and have been reported to occur in 28–81% of patients [9]. While colonic conduits are occasionally employed for urinary diversion (for example, when a patient has an existing colostomy that is no longer required) the vast majority of urinary conduits are ileal. Stomal complication rates have also been found to be higher with colonic conduits [8].

Complications involving the incontinent stoma are extremely common, the vast majority of which are temporary and can be avoided with a combination of good surgical technique and good stomal care as described in the previous chapter on ileal conduits. In regard to the latter, consultation with a stomal therapist preoperatively and postoperatively should be an integral part of the treatment plan. Stomal site must be determined and marked preoperatively with the patient standing, sitting up, and supine. The key principles involved are that the stoma should be placed through the rectus muscle and should sit such that it does not fall in the belt line, within a skinfold or other area that would complicate good placement of the appliance. Ideal placement is typically just below the level of the umbilicus; in a particularly protuberant abdomen, a slightly supraumbilical placement may be necessary in order for the patient to easily visualize the stoma and perform stomal care. The combination of consultation with a stomal therapist and a properly selected stomal site has been shown to decrease the incidence of early stomal complications from 44% to 32% [10, 11].

Unlike continent stomas, the incontinent stoma should be a protruding type. This in combination with an appropriately fitting appliance and collection bag can reduce the incidence of stomal stenosis and minimize peristomal problems such as skin irritation or superficial mucosal denuding (see Fig. 9.1) [4].

Perioperatively the main considerations with ileal conduit stoma are bleeding and the risk of bowel necrosis. Massive bleeding is rare but if it occurs is usually associated with stomal varices that form through branches of the superior mesenteric vein and usually form within 2–3 years of surgery. While it is possible for these to form as a result of aberrant scarring, these are typically associated with portal hypertension secondary to hepatic dysfunction. In these patients this bleeding is typically refractory to local control with compression or suture ligation, and even “mucocutaneous disconnection” will fail in the long run due to the inevitable recanalization that will occur with ongoing high portal pressures [12]. In these cases transjugular intrahepatic portosystemic shunt (TIPS) has been successfully performed [13]. However, TIPS carries a 30% risk of hepatic encephalopathy and a high mortality rate in Child-Pugh B and C patients. In these cases, embolization and angiographic sclerosis have been described [14].

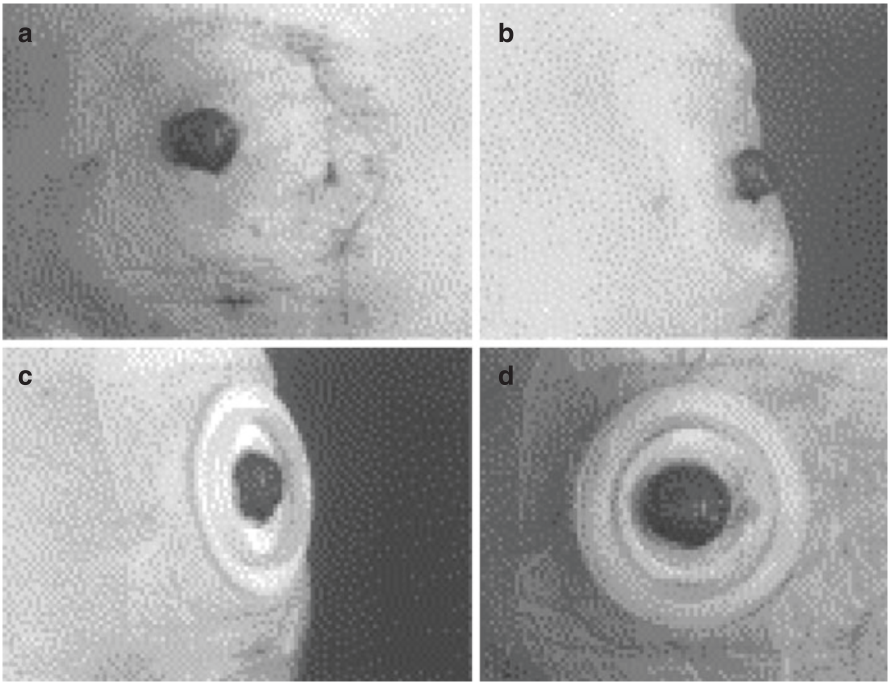


Fig. 9.1 (**a**) An ileal conduit should have a protruding stoma and be sited through the rectus sheath. (**b**) The stoma should not be sited in a crease line or belt line. (**c**) The stoma protrudes nicely above the ring of the appliance, allowing for improved drainage into the stomal bag. (**d**) The wafer should be cut such that there is no pressure on the delicate mucosa while ensuring that minimal peristomal skin is exposed

Ischemia and even necrosis of the bowel segment used is another serious complication that can be encountered. It is crucial during the harvesting of the distal ileal segment that the blood supply is identified and carefully maintained. It is our practice to take the distal end at the avascular line of Treves, thereby preserving an arcade to what will be the distal end of the bowel anastomosis as well as to the stomal end of the conduit. Ischemia can occur as a result of strangulation of the bowel at the level of the fascia, so it is important to pay attention to this. The stoma will be edematous and may appear dusky due to congestion for the first 2–3 days, but the mucosa should still blanch or pink up with touch and should become progressively pinker. Necrosis of the mucosa can also occur due to poor stomal care such as an appliance that compresses the mucosa instead of the surrounding skin only [15]. Patients who have undergone pelvic irradiation are especially susceptible to this, as the distal ileum may have experienced some treatment effects. It should be noted that while several relatively small case series have noted higher complication rates in IC patients with prior radiation, the actual stomal complications are negligible, at only two patients in one study. All of these were managed conservatively and not associated with full-thickness necrosis below the level of the fascia [16]. A transparent appliance is always recommended for ease of examination of the stoma. When mucosal level necrosis does occur, the superficial tissues will slough within a few weeks of improved stomal care. However, there is a risk of stomal retraction or stenosis in the long term. If full-thickness necrosis is suspected, this can be investigated at the bedside by gentle placement of a test tube into the stoma and illumination to assess the mucosa below the fascia. If this is indeterminate, flexible cystoscopy is an excellent way to visualize the entire luminal surface of the conduit. In the extremely rare situation that true bowel necrosis has occurred, emergent laparotomy must be pursued.

Long-term complications of the ileal conduit stoma include parastomal hernia, stomal stenosis, and retraction. The impact of the type of stoma constructed on these complications is debated. Historically, the Turnbull loop stoma has been reported to have a lower incidence of stomal stenosis but a higher incidence of parastomal hernia [17]. However, several large series comparing loop and end stomas specifically within ileal conduits found comparable rates of parastomal hernia in end and loop stomas [18–20].

Robotic-assisted radical cystectomy (RARC) is becoming more commonplace, although only 18% of diversions are being performed completely intracorporally [21]. In the case of ileal conduit, the bowel segment is harvested and prepared robotically, and typically the robot is undocked, and then the conduit is brought up and the stoma created in the typical fashion. Necrosis of the conduit due to inappropriate orientation has been cited in the literature; establishing and maintaining orientation during the robotic portion is key since the conduit itself is not examinable during stomal construction.

The International Robotic Cystectomy Consortium (IRCC) offers the largest series to date of RARC, comprised of over 900 patients from tertiary and community centers undergoing RARC from 2003 to 2011; 72% of these were ileal conduit. A 2014 analysis of intracorporeal versus extracorporeal diversion outcomes in this group by Ahmed et al. found lower complication, readmission, and transfusion rates for the intracorporeal group, although they had a higher 30-day reoperation rate at 8% [22]. The overall 30-day reoperation rate was 7%; cause of reoperation was not included in the database. While the intracorporeal group complications were lower than the extracorporeal group, it may be explained by the fact that more experienced robotic surgeons are more likely to perform the former. In addition, the 90-day mortality rates of both groups (1.6% and 4.9%, respectively) are higher than seen in other RARC or open RC series [21]. The IRCC data suggests that in the hands of experienced robotic surgeons, intracorporeal diversion has reasonable outcomes.

Differences between open and robotic conduit stomal rates of hernia or stenosis have not been reported, but are unlikely to be different since stomal construction is performed by open technique in both.

Parastomal Hernia in the Incontinent Stoma

Parastomal hernia is defined as a fascial defect allowing for protrusion of peritoneum or bowel segment. Although it may be diagnosed clinically with Valsalva maneuver and digital exam, more often the diagnosis is made using cross-axial imaging. The majority of patients are asymptomatic but occasionally may present with parastomal pain, symptoms of intermittent obstruction and, rarely, of bowel strangulation.

Widely accepted risk factors for development of a parastomal hernia are the same as those for development of an incisional hernia: obesity, poor nutrition, prolonged ileus, steroid use, wound infection, previous surgery, or radiation. However, this is largely anecdotal, and the published data is mixed. In a 2007 paper examining 137 radical cystectomy ileal conduit patients, an overall stomal complication rate of 15.7% was found of which the most common complication was parastomal hernia (91% of complications and 14% incidence overall); one went on to develop stomal prolapse [17]. The only predictor found was BMI, where obese patients had a complication rate of 27.3% compared to 4.1% in those with a normal BMI. Gender, age, and smoking status, prior radiation, did not predict stomal complications or parastomal hernia. However, this was just a univariable analysis. Similar outcomes were found in another series of 97 patients where BMI, diabetes, and emergent surgery predicted complications such as poor siting and skin excoriation, but no hernia or stenosis [23]. One third of parastomal hernia patients in this series went on to surgical repair for symptoms, of which 50% had a recurrence. This is similar to other reported rates of recurrence and highlights the difficulty in management of those patients who are symptomatic.

Given this, prevention of parastomal hernia is very important. Placement of the stoma through the rectus muscle and not lateral to it showed a reduction in incidence of hernia from 22% to 2% in a study of 130 patients [24], although other series did not find a difference [25, 26]. Nevertheless, given the absence of any randomized studies, we feel that surgeons should adhere to the principle of placement through the rectus muscle and rectus sheath. In addition, it is important not to make the fascial opening too large. Our practice is to create a defect that just barely allows two fingers for a loop conduit, which is just enough to accommodate the typical ileal diameter snugly. Similarly, the posterior fascial opening should be opened only enough to accommodate the bowel snugly, as enlargement of this has also been postulated to contribute to hernia formation.

A study of 782 ostomy patients from a large French database in 2011 found a parastomal hernia rate of 25.6% in urostomies (loop type, $n = 180$), which was lower than that seen in colostomy (28%) and higher that seen in ileostomy (16%), with a median time to diagnosis of 18 months.

Overall, the incidence of parastomal hernia in ileal conduit varies widely, with some reporting rates as low as 4.5 [27]; the variability in how it is defined, and the fact that two thirds of patients are asymptomatic and so may never present, may explain this. In a 1975 review, Leadbetter points out that while its incidence in the ileal conduit may be less than in colostomy, its propensity to cause symptoms due to urine leakage and resultant difficulty with appliance placement and skin irritation is higher [28]. While, as is true for ileostomy patients, the vast majority of ileal conduit patients with a parastomal hernia are asymptomatic, this may explain a higher rate of reoperation of around 30% compared to 10–20% in large series of all parastomal hernias [17, 29]. Additionally, the presence of a hernia adds to the psychological impact of a new stoma on the patient and has been associated with lower QOL after cystectomy [7].

In the largest series to date of parastomal hernia in ileal conduit after radical cystectomy patients specifically, Donahue et al. reviewed records of 433 patients who underwent surgery between 2006 and 2010. In order to establish a true incidence rate, all CT scans performed for oncologic follow-up were reviewed for PH. PH was found in 137 of 386 patients, an incidence of 27% at 1 year and 48% at 2 years [19]. Interestingly, of the 93 patients that had clinically appreciable PH, nearly half had recurrent or metastatic disease. Half of these patients had no symptom data available, so it is hard to comment on whether larger, more clinically significant PH tend to be more symptomatic. On multivariable analysis, the authors found that female gender (HR 2.2), BMI (HR 1.1), and preoperative albumin (HR 0.4) were associated with the development of PH, similar to other series [30, 31]. They did not, unfortunately, comment on the symptomatic rate overall.

The repair of parastomal hernia is challenging and morbid, with a disappointing success rate. Given this, surgical repair should be avoided unless a patient is symptomatic and has failed conservative measures. These include belts and appliances that keep the hernia reduced. Surgical options include repairing the fascial defect versus relocating the stoma either primarily or with a biologic or synthetic mesh.

Primary repair has quite uniformly been shown to have a high failure rate. In a series of 94 patients with parastomal hernia, Rubin et al. found that recurrence rates were 76% for fascial repair, 33% with stomal relocation, and 50% with synthetic mesh, although this latter group was comprised of only seven patients [32]. Median time to recurrence was 29 months in the stoma relocation group, compared to only 13.5 and 11 in the other two, but there was no difference in reoperation rate, which was exceedingly high at 40%. Additionally, postoperative complication rates overall were over 60%. The authors concluded that even when primary fascial repair is abandoned for its dismal results, a durable surgical repair is rare, morbidity is high, and thus repair should be avoided if possible.

Mesh repair has shown better results regardless of approach. There are four possible techniques: onlay, in which the mesh is placed on top of the anterior fascia; inlay, in which mesh is sutured only to the sides of the fascial defect; sublay, in which mesh is placed between the rectus and posterior sheath; and an intraperitoneal onlay, in which mesh is affixed to the peritoneum. The latter can be done in an open or minimally invasive approach and often employs a biologic or two-layer mesh where the nonabsorbable side is affixed to the abdominal wall and an absorbable side is in contact with the abdominal contents in order to minimize mesh complications. Whereas the onlay and inlay techniques have not gained wide use due to the need for extensive dissection and high failure rate, respectively, the sublay technique has performed well [33].

Prophylactic placement of mesh at time of stomal creation is an option. To date, seven randomized trials have been performed in the general surgery arena examining this. Two used partially absorbable synthetic mesh in the setting of end colostomy. In one, at 1-year follow-up, parastomal hernia was present in 1 of 27 in the treatment arm compared to 13 in the control arm [34]. In the other, again with 27 patients in each arm but with a longer follow-up of 29 months, 14.8% in the treatment arm versus 40.7% in the control arm developed a hernia clinically and 22.2% versus 44.4% radiographically, respectively [34]. Another trial used biologic mesh for a loop stoma; at a short follow-up of 6 months, there were no hernias in the treatment group and 33.3% in the control group [35]. Although detailed complication data was not included in most of these, no mesh infections were noted in any trial.

Several studies have examined laparoscopic placement of parastomal mesh in an onlay (intraperitoneal) approach at time of ostomy creation. Lopez-Cano et al. randomized 36 patients at time of laparoscopic abdominoperineal resection and colostomy using synthetic mesh and at 1 year found parastomal hernia in 50% of the mesh group and 93.8% of patients in the control group [36]. Vierimaa et al. found, in a similar trial, no difference in the rate of radiographic PH at 1 year, but a decrease in clinically appreciable PH in the mesh (14.3%) versus control (32.3%) groups [37].

A recent meta-analysis of prophylactic mesh placement trials at time of end colostomy concluded that from six trials (156 mesh patients, 153 control patients) using either sublay or intraperitoneal, open or lap approaches, placement of mesh decreased the incidence of parastomal hernia by almost half (24.4% vs. 50.3%, respectively), (RR 0.65, 95% CI 0.33–1.30), with no difference seen between approach and no improvement in "overall stomal morbidity," although reoperation rate was lower [34]. The shortcomings of this meta-analysis include the wide heterogeneity among these trials as well as a lack of detail regarding their criteria for stomal morbidity. From an economic perspective, once patients with a life expectancy of less than 1 year were excluded, prophylactic mesh was cost-effective.

To date there are no published randomized trials of prophylactic mesh placement at time of ileal conduit. In the only series published, Styrke et al. describe their experience with 114 consecutive patients undergoing synthetic mesh placement with a sublay approach at time of IC, with follow-up data for 58 patients [38]. They found a clinical parastomal hernia rate of 14% at 32 months and no mesh complications. Randomized controlled trials are needed in this area to confirm what the general surgery data for colostomy suggests, which is that mesh placement at time of IC creation reduces the rate of PH formation and is well tolerated.

Stomal Stenosis in the Incontinent Stoma

The incidence of stomal stenosis ranges from 2.8% to 19% in patients with ileal conduits and 10–20% in patients with colon conduits, with lower rates seen in two large contemporary series (8.5% and 2.8%, respectively) [4, 18]. While this incidence rate is lower than that seen in continent stomas, it still represents a significant problem and one that can be challenging to manage. By impairing drainage, stenosis can lead to hydronephrosis and stasis, increasing the risk for stones, renal compromise, and infection. An easily avoidable cause of stomal stenosis is stomal retraction, which can lead to difficulty with appliance placement and subsequent skin irritation, hyperkeratosis, and, eventually, stenosis.

A too small fascial opening can also lead to stenosis, both distally where ischemia may lead to stenosis in this distal segment, as well as ongoing pressure at the level of the fascia with resultant stenosis over time.

Loop stomas have a lower incidence of stenosis than end stomas. Care should be taken at time of stoma creation to bring the mucosa at least 2 inches above the skin. Again, we advocate for a fascial opening that just barely allows two fingers, which should be sufficient to avoid ischemia while minimizing the risk of hernia. In obese patients, a thick and short mesentery is often present. Although an end stoma is often advocated in the literature in this situation, we favor a loop stoma in these patients for easier management of a bulky mesentery. While ligation of the distal mesentery has been shown to be safe in animals, this does risk devascularization. Defatting the creeping fat off of the bowel itself can be helpful.

Another way to prevent retraction is to place anchoring sutures to the anterior rectus sheath, but care must be taken that there is no tension from the intraperitoneal side and account for postoperative distention in order to avoid bowel ischemia, which will be a setup for stomal retraction. We prefer placement of four circumferentially placed absorbable sutures. Proper eversion of the distal mucosa to form a nice, conical "rosebud"-type orientation is also important to avoid retraction and promote appliance fit. The placement of everting sutures can accomplish this.

Stenosis of the conduit has a higher incidence among obese patients; obesity likely contributes in several ways such as a thick abdominal wall and a shorter and thickened mesentery. These then contribute to poorly fitting devices as well as stomal retraction. The incidence of stomal retraction in ileal conduit is reported to range from 9Stomal Complications to 15% [14]. Panniculectomy at time of revision has been reported in this scenario. In a case series of four female patients, Katkoori et al. describe the procedure, which does not involve any intraperitoneal dissection, with good short-term outcomes: operative time of 2 h, LOS of 3 days, and no recurrences at 2-year follow-up [39].

Taneja et al. advocate maturing the stoma prior to transposing it to the skin to minimize stomal retraction [40]. This is done using an end stoma, defatting the distal mesentery and circumferentially everting the mucosa prior to bringing it up into the skin.

Another cause of stenosis is hyperkeratosis. This is a consequence of ongoing irritation to the surrounding peristomal skin, typically caused by a poorly fitting appliance, and is characterized by progressive hardening and proliferation of the skin and eventual stenosis of the stoma (see Fig. 9.2). Bacterial or fungal infections can also compound the problem. Hyperkeratosis can be managed by placing a catheter into the stoma to avoid urinary contact along with light therapy or topical vitamin C or 0.25% acetic acid washes [27]. Overall, early management with a combination of minimizing urine contact and skin treatments can reverse the problem, although if stenosis is significant, excision of the hyperkeratotic skin is an option. Again, perioperative consultation with an enterostomal therapist has been shown to decrease the development of stomal complications including chronic skin disorders [10].

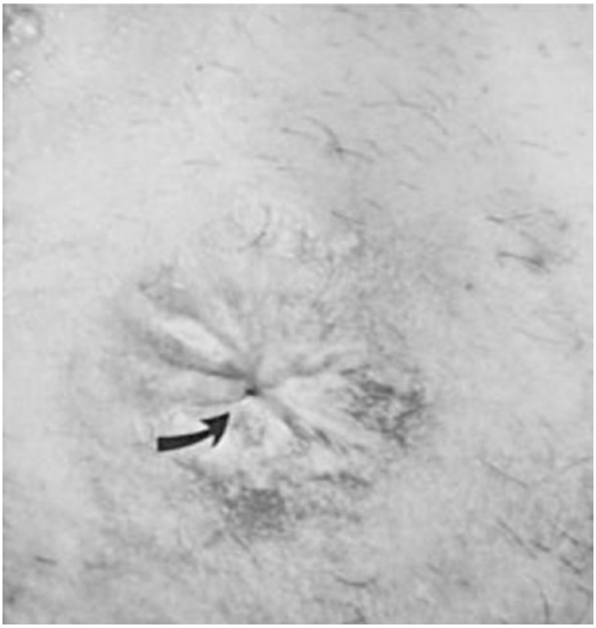


Fig. 9.2 A severe stomal stenosis with surrounding hyperkeratotic skin

In a series of over 300 patients where stenosis was seen in 8.5%, 5% of patients required surgical management [18]. Surgical management can be divided into two groups, that at the skin level and that involving intraperitoneal mobilization, depending on the severity and location of stenosis. As such, a loopogram can aid in preoperative planning. At the skin level, the simplest option involves making a circumferential incision around the stoma and mobilizing the conduit to the level of the fascia, excising the stenotic ring and hyperkeratotic skin, and reanastomosing to the skin. A local V flap can alternatively be rotated into the defect. However, these repairs do not address stomal retraction and may even lead to it [27]. Another option, again using a circumscribing incision at the stoma, is to continue mobilization intraperitoneally from this approach, to allow sufficient conduit length to be advanced. If intraperitoneal mobilization cannot be achieved through the existing fascial opening, it can be extended, although this may increase the risk of parastomal hernia development. Rarely, full laparotomy is required to gain sufficient mobilization of the conduit. Of note, one must be careful not to compromise the mesentery during the superficial mobilization regardless of approach.

Stomal Complications in Continent Cutaneous Diversion

While much less commonly performed than the conduit, the continent cutaneous diversion is an important option for patients desiring continent diversion in whom an orthotopic substitution is contraindicated or in whom the potential risks of an orthotopic diversion such as incontinence, retention, or fistula are high. Although up to 80% of men and 65% of women have been shown to be suitable candidates for continent diversion after cystectomy [41], it is well established that the rates of continent diversion performed in this setting are far less. A review of over 5,000 cystectomies in the United States found a continent diversion rate of 14.3% [42]. A subsequent review of the same database found only an 8.3% incidence of continent diversions [43]. Of these only a small fraction was CCD. The most likely explanation of why CCD is employed relatively infrequently even at large volume centers is that it is more complex to construct and is perceived to carry a higher rate of complications than other diversions. In fact, a meta-analysis of several series using a host of different types of CCD has shown continence rates overall to be excellent, ranging from 83% to 100% [44]. Several papers in addition to this have shown acceptable complication rates, similar to those seen with a conduit. However, multiple quality of life studies have not shown a significant difference between diversion types overall, thus weighing against the benefit of CCD [45]. One study comparing IC and CCD found that 41% versus 71%, respectively, reported being satisfied with their diversion [46].

Overall the CCD is an important option for a certain subset of patients with reasonable overall complication rates, and as such, it is an important part of the urologist's armamentarium. It does carry a unique set of complications, namely, those involving the efferent channel, that is, the stoma and the catheterizable channel, which will be the focus of discussion here. There are a multitude of different forms of CCD; we will focus on complications as they arise in the most commonly performed types.

Preventing Complications

Appropriate patient selection is extremely important prior to undertaking a CCD. The indications for CCD are any patient who desires a continent diversion but for whom an orthotopic diversion is contraindicated or not suitable. This includes patients with a positive urethral margin, prior pelvic radiation, locally extensive disease, extensive urethral stricture, renal insufficiency (defined at Cr > 1.8 mg/dl or GFR < 40 ml/min/1.73 m^2), hepatic insufficiency, chronic inflammatory bowel disease, and neurologic impairment of dexterity [47]. In addition to these, for some patients, the functional outcomes of an orthotopic diversion may not be desirous; this usually pertains to continence outcomes. In females, where up to 40% will be in retention requiring intermittent catheterization and up to 30% will be significantly incontinent, a CCD may be more attractive than an orthotopic diversion [48]. Men with existing stress incontinence may similarly fare better with a CCD if they desire a continent diversion.

An in-depth preoperative consultation is important to evaluate a patient's suitability for CCD. Foremost, the ability and willingness to perform catheterization four to six times per day is critical, requiring motivation and manual dexterity. As in the case of the conduit, preoperative counseling with an enterostomal therapist can be helpful in familiarizing the patient and their family with the process of catheterization and irrigation, the latter which will often need to be done regularly in the first few months. In general, patients with neurologic diseases such as Parkinson's, multiple sclerosis, quadriplegia, and those with mental impairment are thus considered to be poor candidates for CCD [49]. The exception to this may be young, cervical spinal cord injury patients with good support systems, in whom high levels of satisfaction with CCD have been reported [45].

Patients should also be aware that they may leak mucus or urine and may need to wear a pad or gauze over the stoma. Postoperatively, once drains have been removed, another consultation with the stomal therapist is very helpful to not only review catheterization and irrigation but also to go over commonly encountered issues in this initial period to facilitate some troubleshooting at home. It must be stressed to patients that inability to catheterize is an emergency with a CCD. Given the rarity of these reconstructions, a patient living in a more remote region with little or no access to a urologist or center that is familiar with these may not be a great candidate for this diversion.

Surgical Technique

An array of techniques of CCD construction has been described, with different types of reservoirs as well as continence mechanisms. Ideally, a technique should be as simple as possible and reproducible, have a low complication rate, and of course offer excellent continence. The most common type of CCD is the Indiana pouch, in which a buttressed ileocecal valve serves as the primary continence mechanism. In this, a 20 cm segment of the right colon serves as the reservoir and the terminal ileum as the catheterizable channel. The ileum is tapered in order to facilitate ease of catheterization by removing redundant tissue, but this does not contribute to the continence of the diversion. Retrospective series have reported complication rates from 12% to 45% and continence rates as high as 97%. However, newer series with longer follow-up and diligent complication reporting reveal less favorable although still acceptable results. Holmes et al. found a incontinence rate of 28% and stomal stenosis rate of 19% [50]. Extracorporeal Indiana pouch with robotic-assisted radical cystectomy has been shown to be feasible and comparable to outcomes after open cystectomy [51]. Overall the Indiana pouch offers a relatively simple and reproducible form of CCD.

Flap-valve mechanism efferent channels such as the appendicovesicostomy or Yang-Monti are also popular. These employ a submucosally imbedded channel such that as the reservoir fills, there is greater pressure on the efferent channel and, presumably, better continence. Based on the Mitrofanoff procedure, the use of appendix as a continent stoma for CCD was first described in 1990 [52], offering an easily available structure with an appropriate diameter for catheterization. Whereas the Indiana pouch carries a long-term risk of worsening continence, the appendiceal stoma is prone to stomal stenosis, occurring from 16% to 55% of the time [53, 54]. It is accepted that the natural history of the appendix is for it to progressively narrow without regular catheterization. Intraoperative evaluation of the appendix is important. Ideally the appendix should be 5–6 cm long, should accommodate a 12F catheter easily, and should be able to soft dilate up to 16F. If these criteria are not met, or if the appendix is absent, another channel should be considered.

A Yang-Monti tube can be constructed in these situations. A 3 cm segment of distal ileum is harvested and detubularized along its antimesenteric border, then retubularized transversely, thereby creating a channel of adequate length and diameter. It can then be secured to the base of the cecum and embedded in a subserosal tunnel as described for the appendix. Although the Yang-Monti offers the benefit of requiring a small and easily accessible segment of bowel and simple construction, it has been reported in some series to have up to a 40% rate of difficulty catheterizing, likely due to mucosal buckling or eccentric dilatation of the channel over time [55]. Stomal stenosis has been reported at 15% and incontinence up to 30%. At our institution, however, we have had good results with the Yang-Monti, although patients are counseled to have an even lower threshold for returning if problems with catheterization are encountered. If initial attempt to pass a catheter fails, we perform endoscopic evaluation and catheter placement. This avoids creating a false passage in this delicate channel. In our experience leaving a catheter in place will allow reestablishment of the stomal channel and good long-term results. Overall, Ardelt et al.'s meta-analysis found rates of incontinence, catheterization difficulty, and stomal stenosis to be 13.3%, 20.3% and 19.5%, respectively, in flap-valve channels.

Another category of CCD stomal channel is the nipple valve, originally popularized by Kock in 1982. Although it has largely been abandoned today, it was a common form of CCD in the past, and therefore an understanding of its long-term complications and their management remains relevant. The Kock pouch stoma was initially described as a free-floating channel within the reservoir in which the increasing pressure on the channel was circumferentially applied as the pouch filled, but this also allowed compression of the base of the channel that theoretically compromised continence and was later modified to include fixation to the reservoir, usually with staples. The largest series of Kock pouches reported a continence rate of 86% in over 500 patients. [56]. Although overall stomal stenosis and incontinence rates with nipple valves are good, the technical complexity of the Kock pouch along with other complications such as stones and extussusception of the valve has made the procedure essentially obsolete.

Urinary Incontinence

Continence after CCD is the biggest determinant of patient satisfaction and QOL outcomes, and any degree of leak will be regarded as a failure to the surgeon [46]. As a rule the reservoir must be created such that it is low pressure, requiring that it be of adequate volume, completely detubularized, and spherical in shape as per Laplace's law. If this principle has been followed, the cause of incontinence is the efferent channel, and the cause varies by channel type. Unlike stomal stenosis, which can often be managed outside of the operating room, incontinence almost always requires a surgical repair of some type [49].

Urodynamic studies of Mitrofanoff tubes in children have demonstrated that the appendix has superior resting and dynamic closure pressures than utereral and tapered ileal channels. A minimum tunneled length of 2 cm was also correlated to continence in these appendiceal channels [57]. Another study performed reservoir leak point pressures intraoperatively and made adjustments to the appendiceal or ileal channel (by tunneling or placing more buttressing sutures) when a leak point pressure of less than 80 cm H_2O was seen, with an overall continence rate of 100% [58]. The lack of a control group makes it difficult to assess the usefulness of this intraoperative assessment. Some advocate performing a formal urodynamic study of the pouch prior to attempting an open revision; if reservoir pressures are high, an ileal patch can be added with or without revision of the efferent channel [49].

In the Indiana pouch, incontinence typically reflects incompetence of the ileocecal valve. At the time of initial construction, the valve is buttressed with permanent suture to avoid this, but incontinence may still develop, typically progressively, with a reported rate as high as 28% [50]. Management of this in general involves surgical reinforcement of the valve with additional Lembert buttressing sutures at its base. A more involved but definitive option is to convert the efferent channel (distal ileum) into a Monti channel by burying it in a subserosal tunnel. Or a part of the pouch itself can be tubularized in a Boari flap fashion and buried. Injection of a bulking agent in this area is also reasonable, although this is unlikely to provide a long-term solution [59].

Incontinence in a CCD with an appendiceal channel is less commonly encountered but is seen in up to 8% of patients [60]. Buttressing of the base of the channel is an option when this is encountered. A small midline incision is made at the level of the stoma, and the efferent channel and distal pouch are freed. This part of the pouch is then plicated around the base of the channel in a Nissen fundoplication manner. However, endoscopic injection of a bulking agent offers good results and should be attempted first. We use Coaptite for this, as, unlike collagen, it does not dissipate. Several injections may be required to achieve good results [59]. The Yang-Monti channel has higher rates of incontinence than the appendix but can be managed in the same fashion. If these attempts fail, a complete revision of the efferent channel can restore continence.

Stomal Stenosis

This is seen most commonly in the appendiceal channel and least frequently in the intussuscepted ileal nipple valve. Fortunately, the majority of these can be managed with soft dilation or endoscopically guided catheter placement in the clinic setting. Of those that do require a revision, many can be managed as a relatively simple outpatient repair. However, a stenosis will often present with the patient being unable to catheterize at all, and this is an emergency and one that the patient should be well counseled on perioperatively. Overdistention of the pouch may cause kinking of the channel thereby making catheterization even more difficult. When a patient presents in this scenario, percutaneous drainage of the pouch will provide relief to the patient and may facilitate placement of a stomal catheter. The safest

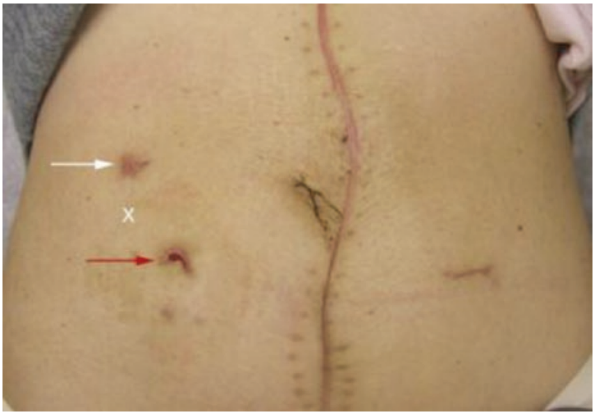


Fig. 9.3 Photograph of the abdominal wall of a patient 6 months following cystectomy and nephroureterectomy with a right colon pouch and appendiconeovesicostomy, with a right lower quadrant stomal site marked by the *red arrow*. The *white arrow* points to the site of the perioperative cecostomy tube. This scar, or just inferior to it, is a safe place for percutaneous placement of a catheter in the event of retention and inability to pass a stomal catheter

place to do this is through the suprapubic tube scar or just below it, as there should be no intervening bowel in this region (see Fig. 9.3).

When office management fails, a trip to the operating room is required and must be undertaken expediently so as to avoid further obliteration of the stoma. The distal stoma is examined first, as stenosis is commonly encountered at the skin level. This is especially true in appendiceal stomas. The fibrotic skin at the stomal opening is excised, the surrounding healthier skin is mobilized, and the stomal edges are anastomosed. Alternatively, a Y-V plasty of the stoma can be performed using a new flap of skin. When the stenosis is located more proximally in the channel, endoscopic incision can be attempted although recurrence rates are high; a study of pediatric patients with CCD for management of neurogenic bladder found a recurrence rate of 59% [61]. When endoscopy reveals a lengthy segment of fibrosis or an obliterated channel, complete revision is needed.

As in the case of an stomal incontinence, open revision should be attempted with the simplest procedures first, since the potential for further complications, such as bowel injury, injury to the pouch, urine leak, further disruption of the efferent channel, and fistula, is high. This is especially risky in the first several months postoperatively when inflammation and adhesions are at their peak. The stoma is completely taken down, and the pouch is carefully identified and mobilized through the previous incision. Any redundancy, as is often seen in ileal channels, is resected. Use of a flap off of the reservoir itself can be used to bridge the gap if the stenosis is proximal and only segmental, (see Fig. 9.4) [62]. If the channel is truly stenotic beyond salvage, a new segment of bowel must be harvested and used to construct a new channel. The complexity of such types of operations is significant, and great care must be taken not to disrupt the continence mechanism or the ureteroenteric anastomoses during the repair, in addition to avoiding the aforementioned risks.

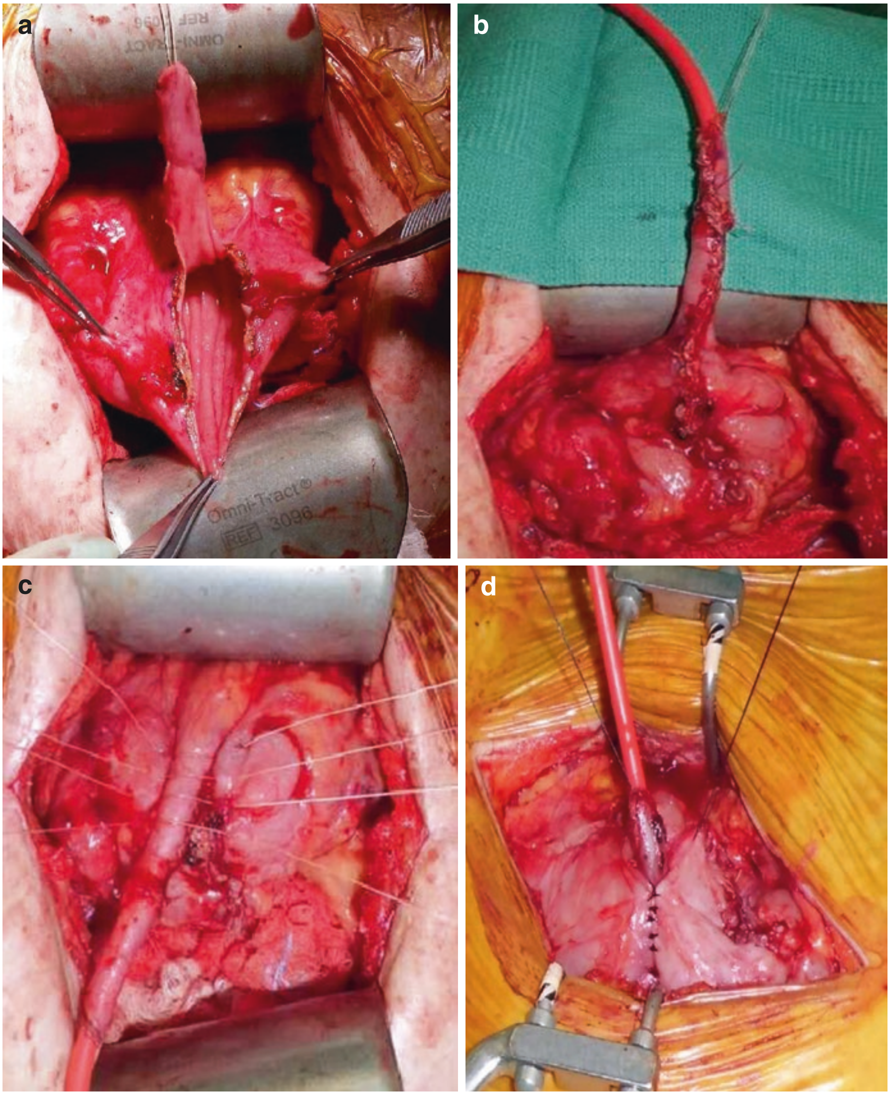


Fig. 9.4 (**a**) A U-shaped vascularized flap is created off of the pouch. (**b**) The flap is tapered over a 16F catheter. (**c**) The pouch is then imbricated over the base of efferent channel. (**d**) The flap-valve mechanism is thereby reestablished

In patients with a history of pelvic radiation, stomal stenosis is of even greater concern. Typically orthotopic diversion is contraindicated in this subset because of the high rates of fistula and significant incontinence, making CCD the only option for continence. Although a small series found that stomal stenosis in these patients was equal to that seen in non-radiated patients [63], in our experience, stenosis rates are indeed higher in this group. Particularly in females with a history of gynecological tumors where radiation fields tend to be wider, the periumbilical tissues are compromised and more prone to stenosis. The radiation-induced fibrosis furthermore makes repair more difficult. Although there is not conclusive data on this subject, we approach CCD in these patients with caution.

Pouch Stones

With the exception of the Kock pouch, where stones can form along the staple line of the intussuscepted nipple, stones in a CCD occur in the pouch itself. However, great care must be taken of the stoma during the management of pouch stones and as such warrants a brief discussion here.

Stones occur with greater frequency in CCD as compared to orthotopic continent diversions, presumably due to the higher rate of bacteriuria and urinary stasis, with an incidence of approximately 12% [6, 64, 65]. Rates in the Kock pouch have been reported as high as 25%, although it approaches those of other types of CCD when metal staples are not used at the nipple valve [66].

Common presenting symptoms include abdominal pain, hematuria, difficulty catheterizing, new-onset incontinence, and recurrent infections. While these stones are almost always radiopaque, the radiologist's unfamiliarity with the diversion can easily lead to missed diagnosis, and it is advisable for the urologist to review the imaging carefully.

When stones do occur, the majority are small and can be managed endoscopically. There is little to no published data regarding the efficacy of this, but anecdotal reports suggest good outcomes. The goal of the procedure is complete removal of stones without damaging the efferent channel. Flexible ureteroscopy and lithotripsy with holmium laser, electrohydraulic, ultrasonic, or pneumatic technologies are all good initial options, and basketing can be done through these small caliber scopes safely. When a larger diameter scope is required for removal of larger stones, Skinner et al. advocate the use of an offset nephroscope and Amplatz sheath [49]. The soft dilation required to accommodate this may not be feasible with all efferent channels, especially appendiceal ones. Care must be taken to minimize torque on the stoma when a rigid scope of any caliber is used. The authors point out that postoperative edema of the stoma is typical, and 24 h of an indwelling catheter is advisable.

Percutaneous access directly into the pouch is also an option and avoids manipulation of the stoma. Again, the previous cecostomy tube site provides a safe location for access; an alternative is image-guided placement. Rarely, stones are so large as to warrant an open removal, which can be performed through a small incision. Patients who do develop stones should undergo formal metabolic evaluation as well as routinely irrigate the pouch with saline to minimize recurrence.

Parastomal Hernia

The incidence of parastomal hernia is much lower in the CCD as compared to the conduit at 4% [49]. Similar to the conduit, however, it is a difficult problem to manage when it does occur. Stomal location does not seem to impact the incidence. PH in a CCD may cause problems in catheterization or incontinence.

Of note, when an umbilical stoma is created, care must be taken at the time of initial midline incision to leave several centimeters between the umbilicus and the fascial opening in order to avoid a concurrent ventral hernia. High-risk patients are those who are at a higher risk for hernias in general: the obese, elderly, and smokers. Given the high risks of injury to the CCD, ureters, or surrounding structures, high rate of recurrence and low rates of long-term success surgical repair should in general be avoided. When the patient strongly desires a repair despite this, placement of mesh onlay around the stoma can be performed locally without requiring laparotomy. Biologic mesh is advisable to avoid the risk of erosion into the channel over time. The most invasive option is to relocate the stoma completely, requiring mobilization of the stoma and reservoir and potentially the need for a new efferent channel.

Necrosis of the Efferent Channel

In a study of 419 CCD with appendiceal stomas, Weisner et al. found a stomal necrosis rate of 2% [60]. Similarly, another series of 118 patients reported a 2.5% incidence. Patients presented with complete incontinence at time of perioperative catheter removal [53].

Regardless of efferent channel constructed, great care must be taken intraoperatively not to compromise mesenteric blood supply to the channel, especially at the distal end where this is most tenuous. As in the incontinent stoma, duskiness immediately postoperatively is typical and reflects mucosal edema. However, if this persists beyond the initial day or two, or true necrosis is seen, prompt evaluation should be performed, which involves removal of the stomal catheter and flexible cystoscopy. If the mucosa in the channel itself appears healthy, a catheter should be replaced, and no further intervention is indicated. If the efferent limb is indeed necrotic, reoperation and construction of a new channel is needed.

Difficult Catheterization

Difficulty in catheterization has a number of causes, several of which have been covered. A detailed history can help sort through these etiologies. Endoscopic evaluation of the channel and reservoir is the next step to elucidate the underlying issue. A common cause is stomal stenosis, which is most common in the appendiceal channel but is seen in other types as well. The patient will typically describe progressive difficulty in advancing the catheter beyond a certain point.

Ileal channels such as that seen in the Indiana pouch can become elongated and eccentrically dilated over time, also causing progressive difficulty in passing a catheter. In this situation an open revision is required involving mobilization of the entire channel and likely the pouch as well and then shortening the channel. Stomal length does not impact continence, although great care must be taken not to disrupt the ileocolic valve during this revision.

Mucus plugging of catheters is another common cause of catheterization problems. While all continent diversions will produce mucus, the amount produced is very variable between patients although in most it tends to decrease over time. Regular irrigation with a saline solution is typically all that is required in these cases.

Conclusions

The majority of urinary diversions will involve either an incontinent or continent stoma, and while the former is much easier to construct, it is not without a complication burden that patients must be counseled on in advance. In the case of the ileal conduit, the most common complications can be prevented by appropriate placement and good stomal care; however, parastomal hernia and stomal stenosis are not insignificant, and their management is complex.

CCD represents a small minority of urinary diversions and carries a unique set of complications, many of which are linked to the stoma and catheterizable channel. The vast majority of these can be managed with in-office or minor outpatient procedures by a surgeon with experience in these reconstructions. Given the potential excellent continence outcomes and high patient satisfaction, this diversion should be carefully considered for those patients for whom continence is desired, but an orthotopic substitution is not suitable.

References

1. Gore JL, Lai J, Gilbert SM. Project UDiA. Readmissions in the postoperative period following urinary diversion. World J Urol. 2011;29(1):79–84.
2. Bochner BH, Dalbagni G, Sjoberg DD, et al. Comparing open radical cystectomy and robot-assisted laparoscopic radical cystectomy: a randomized clinical trial. Eur Urol. 2015;67(6):1042–50.
3. Daneshmand S, Ahmadi H, Schuckman AK, et al. Enhanced recovery protocol after radical cystectomy for bladder cancer. J Urol. 2014.
4. Dahl D. Use of intestinal segments in urinary diversion. In: Wein A, Louis RK, Martin A, Peters C, editors. Campbell-Walsh urology. 11th ed. Philadelphia: Elsevier; 2016. p. 2281–316.
5. Bricker EM. Current status of urinary diversion. Cancer. 1980;45(12):2986–91.
6. Farnham SB, Cookson MS. Surgical complications of urinary diversion. World J Urol. 2004;22(3):157–67.
7. Gerharz EW, Månsson A, Hunt S, Skinner EC, Månsson W. Quality of life after cystectomy and urinary diversion: an evidence based analysis. J Urol. 2005;174(5):1729–36.
8. Cheung MT. Complications of an abdominal stoma: an analysis of 322 stomas. Aust N Z J Surg. 1995;65(11):808–11.
9. Killeen KP, Libertino JA. Management of bowel and urinary tract complications after urinary diversion. Urol Clin North Am. 1988;15(2):183–94.
10. Bass EM, Del Pino A, Tan A, Pearl RK, Orsay CP, Abcarian H. Does preoperative stoma marking and education by the enterostomal therapist affect outcome? Dis Colon Rectum. 1997;40(4):440–2.

11. Szymanski KM, St-Cyr D, Alam T, Kassouf W. External stoma and peristomal complications following radical cystectomy and ileal conduit diversion: a systematic review. Ostomy Wound Manage. 2010;56(1):28–35.
12. Beck DE, Fazio VW, Grundfest-Broniatowski S. Surgical management of bleeding stomal varices. Dis Colon Rectum. 1988;31(5):343–6.
13. Medina CA, Caridi JG, Wajsman Z. Massive bleeding from ileal conduit peristomal varices: successful treatment with the transjugular intrahepatic portosystemic shunt. J Urol. 1998;159(1):200–1.
14. Valaydon Z, Desmond P. Treatment of refractory stomal variceal haemorrhage with embolisation and sclerosis. Intern Med J. 2015;45(2):214–7.
15. Barr JE. Assessment and management of stomal complications: a framework for clinical decision making. Ostomy Wound Manage. 2004;50(9):50–2, 4, 6 passim.
16. Chang SS, Alberts GL, Smith JA, Cookson MS. Ileal conduit urinary diversion in patients with previous history of abdominal/pelvic irradiation. World J Urol. 2004;22(4):272–6.
17. Kouba E, Sands M, Lentz A, Wallen E, Pruthi RS. Incidence and risk factors of stomal complications in patients undergoing cystectomy with ileal conduit urinary diversion for bladder cancer. J Urol. 2007;178(3 Pt 1):950–4.
18. Klein EA, Montie JE, Montague DK, Novick AC, Straffon RA. Stomal complications of intestinal conduit urinary diversion. Cleve Clin J Med. 1989;56(1):48–52.
19. Donahue TF, Bochner BH, Sfakianos JP, et al. Risk factors for the development of parastomal hernia after radical cystectomy. J Urol. 2014;191(6):1708–13.
20. Chechile G, Klein EA, Bauer L, Novick AC, Montie JE. Functional equivalence of end and loop ileal conduit stomas. J Urol. 1992;147(3):582–6.
21. Guru K. Minimally invasive urinary diversion. In: Wein A, ed. Campbell-Walsh urology. 11th ed. Elsevier; 2016. p. 2369–78.
22. Ahmed K, Khan SA, Hayn MH, et al. Analysis of intracorporeal compared with extracorporeal urinary diversion after robot-assisted radical cystectomy: results from the International Robotic Cystectomy Consortium. Eur Urol. 2014;65(2):340–7.
23. Arumugam PJ, Bevan L, Macdonald L, et al. A prospective audit of stomas--analysis of risk factors and complications and their management. Color Dis. 2003;5(1):49–52.
24. McGrath A, Porrett T, Heyman B. Parastomal hernia: an exploration of the risk factors and the implications. Br J Nurs. 2006;15(6):317–21.
25. Ortiz H, Sara MJ, Armendariz P, de Miguel M, Marti J, Chocarro C. Does the frequency of paracolostomy hernias depend on the position of the colostomy in the abdominal wall? Int J Color Dis. 1994;9(2):65–7.
26. Londono-Schimmer EE, Leong AP, Phillips RK. Life table analysis of stomal complications following colostomy. Dis Colon Rectum. 1994;37(9):916–20.
27. Kanofsky J, Godoy G, Taneja S. Complications of conduit urinary diversion. In: Tanja SS, editor. Complications of urologic surgery: prevention and management. 4th ed. Elsevier; 2010. p. 533–46.
28. Marshall FF, Leadbetter WF, Dretler SP. Ileal conduit parastomal hernias. J Urol. 1975;114(1):40–2.
29. Martin L, Foster G. Parastomal hernia. Ann R Coll Surg Engl. 1996;78(2):81–4.
30. Hong SY, Oh SY, Lee JH, Kim DY, Suh KW. Risk factors for parastomal hernia: based on radiological definition. J Korean Surg Soc. 2013;84(1):43–7.
31. Song IH, Ha HK, Choi SG, Jeon BG, Kim MJ, Park KJ. Analysis of risk factors for the development of incisional and parastomal hernias in patients after colorectal surgery. J Korean Soc Coloproctol. 2012;28(6):299–303.
32. Rubin MS, Schoetz DJ, Matthews JB. Parastomal hernia. Is stoma relocation superior to fascial repair? Arch Surg 1994;129(4):413–8; discussion 418–9.
33. Donahue TF, Cha EK, Bochner BH. Rationale and early experience with prophylactic placement of mesh to prevent parastomal hernia formation after ileal conduit urinary diversion and cystectomy for bladder cancer. Curr Urol Rep. 2016;17(2):9.

34. Jänes A, Cengiz Y, Israelsson LA. Preventing parastomal hernia with a prosthetic mesh. Arch Surg. 2004;139(12):1356–8.
35. Hammond TM, Huang A, Prosser K, Frye JN, Williams NS. Parastomal hernia prevention using a novel collagen implant: a randomised controlled phase 1 study. Hernia. 2008;12(5):475–81.
36. López-Cano M, Lozoya-Trujillo R, Quiroga S, et al. Use of a prosthetic mesh to prevent parastomal hernia during laparoscopic abdominoperineal resection: a randomized controlled trial. Hernia. 2012;16(6):661–7.
37. Vierimaa M, Klintrup K, Biancari F, et al. Prospective, randomized study on the use of a prosthetic mesh for prevention of parastomal hernia of permanent colostomy. Dis Colon Rectum. 2015;58(10):943–9.
38. Styrke J, Johansson M, Granåsen G, Israelsson L. Parastomal hernia after ileal conduit with a prophylactic mesh: a 10 year consecutive case series. Scand J Urol. 2015;49(4):308–12.
39. Katkoori D, Samavedi S, Kava B, Soloway MS, Manoharan M. Synchronous panniculectomy with stomal revision for obese patients with stomal stenosis and retraction. BJU Int. 2010;105(11):1586–9.
40. Taneja SS, Godoy G. Creation of urinary stoma before abdominal wall transposition of ileal conduit improves stomal protrusion, eversion, and symmetry. Urology. 2009;73(4):893–5.
41. Hautmann RE, Abol-Enein H, Hafez K, et al. Urinary diversion. Urology. 2007;69(1 Suppl):17–49.
42. Ashley MS, Daneshmand S. Factors influencing the choice of urinary diversion in patients undergoing radical cystectomy. BJU Int. 2010;106(5):654–7.
43. Kim SP, Shah ND, Weight CJ, et al. Population-based trends in urinary diversion among patients undergoing radical cystectomy for bladder cancer. BJU Int. 2013;112(4):478–84.
44. Fisch M, Thüroff JW. Continent cutaneous diversion. BJU Int. 2008;102(9 Pt B):1314–9.
45. Ardelt PU, Woodhouse CR, Riedmiller H, Gerharz EW. The efferent segment in continent cutaneous urinary diversion: a comprehensive review of the literature. BJU Int. 2012;109(2):288–97.
46. Okada Y, Oishi K, Shichiri Y, et al. Quality of life survey of urinary diversion patients: comparison of continent urinary diversion versus ileal conduit. Int J Urol. 1997;4(1):26–31.
47. Daneshmand S, Bartsch G. Improving selection of appropriate urinary diversion following radical cystectomy for bladder cancer. Expert Rev Anticancer Ther. 2011;11(6):941–8.
48. James AC, Lin DW, Wright JL. Neobladders and continent catheterizable stomas for the bladder cancer survivor. Curr Opin Urol. 2014;24(4):407–14.
49. Skinner E, Dunn M. Complications of continent cutaneous diversion. In: Taneja S, editor. Complications of urologic surgery. 4th ed: Elsevier. 2010:547–7.
50. Holmes DG, Thrasher JB, Park GY, Kueker DC, Weigel JW. Long-term complications related to the modified Indiana pouch. Urology. 2002;60(4):603–6.
51. Josephson DY, Chen JA, Chan KG, Lau CS, Nelson RA, Wilson TG. Robotic-assisted laparoscopic radical cystoprostatectomy and extracorporeal continent urinary diversion: highlight of surgical techniques and outcomes. Int J Med Robot. 2010;6(3):315–23.
52. Riedmiller H, Bürger R, Müller S, Thüroff J, Hohenfellner R. Continent appendix stoma: a modification of the Mainz pouch technique. J Urol. 1990;143(6):1115–7.
53. Gerharz EW, Köhl UN, Melekos MD, Bonfig R, Weingärtner K, Riedmiller H. Ten years' experience with the submucosally embedded in situ appendix in continent cutaneous diversion. Eur Urol. 2001;40(6):625–31.
54. McAndrew HF, Malone PS. Continent catheterizable conduits: which stoma, which conduit and which reservoir? BJU Int 2002;89(1):86–9.
55. Narayanaswamy B, Wilcox DT, Cuckow PM, Duffy PG, Ransley PG. The Yang-Monti ileovesicostomy: a problematic channel? BJU Int. 2001;87(9):861–5.
56. Skinner DG, Boyd SD, Lieskovsky G. Clinical experience with the Kock continent ileal reservoir for urinary diversion. J Urol. 1984;132(6):1101–7.
57. Watson HS, Bauer SB, Peters CA, et al. Comparative urodynamics of appendiceal and ureteral Mitrofanoff conduits in children. J Urol. 1995;154(2 Pt 2):878–82.

58. Bissada NK, Marshall I. Leak point pressure use for intraoperative adjustment of the continence mechanism in patients undergoing continent cutaneous urinary diversion. Urology. 1998;52(5):790–2.
59. Roth CC, Donovan BO, Tonkin JB, Klein JC, Frimberger D, Kropp BP. Endoscopic injection of submucosal bulking agents for the management of incontinent catheterizable channels. J Pediatr Urol. 2009;5(4):265–8.
60. Wiesner C, Stein R, Pahernik S, Hähn K, Melchior SW, Thüroff JW. Long-term followup of the intussuscepted ileal nipple and the In Situ, submucosally embedded appendix as continence mechanisms of continent urinary diversion with the cutaneous ileocecal pouch (Mainz Pouch I). J Urol. 2006;176(1):155–60.
61. Deuker M, Roos FC, Großmann A, Faé P, Thüroff JW, Stein R. Long-term outcome after urinary diversion using the ileocecal segment in children and adolescents: Complications of the efferent segment. J Pediatr Urol. 2016.
62. Syan-Bhanvadia S, Daneshmand S. Management of the continent cutaneous stomal complications. Curr Bladder Dysfunct Rep. 2012;7(4):294–301.
63. Bochner BH, Karanikolas N, Barakat RR, Wong D, Chi DS. Ureteroileocecal appendicostomy based urinary reservoir in irradiated and nonirradiated patients. J Urol. 2009;182(5):2376–81.
64. Turk TM, Koleski FC, Albala DM. Incidence of urolithiasis in cystectomy patients after intestinal conduit or continent urinary diversion. World J Urol. 1999;17(5):305–7.
65. Terai A, Ueda T, Kakehi Y, et al. Urinary calculi as a late complication of the Indiana continent urinary diversion: comparison with the Kock pouch procedure. J Urol. 1996;155(1):66–8.
66. Rowland RG. The long-term study of continent cutaneous urinary reservoirs and neobladders. J Urol. 1996;155(4):1217.

Pelvic Floor Rehabilitation for Orthotopic Diversion

10

Eileen V. Johnson and Daniel J. Kirages

Overview of the Pelvic Floor Muscles

The pelvic floor muscles (PFM) are comprised of the superficial and deep layers of muscle, fascia, and ligaments. The structures span from the symphysis pubis anteriorly and travel to the coccyx and inferior lateral angles of the sacrum posteriorly. This complex architecture of muscles provides three important functions, including sphincter control of the bladder and bowel, sexual function, and support of the pelvic organs. The supportive nature of these muscles is depicted in its composition being approximately 70% type 1 slow-twitch fibers, which assist in muscle endurance through maintaining a sustained, less intense muscle contraction. The remaining 30% of muscle is comprised of type 2 fast-twitch fibers that allow for stronger and forceful contractions, but fatigue more easily than the type 1 fibers [1].

The deep layer of PFM, referred to as the levator ani, includes the puborectalis, pubococcygeus, and iliococcygeus muscles. The puborectalis (Fig. 10.1), also referred to as the pubovaginalis in the female, is a u-shaped muscle that travels from the pubic symphysis curving beneath the rectum, forming a supportive sling. The puborectalis also forms the anorectal angle and plays an important role in maintaining fecal continence and coordination of relaxation during defecation [2]. The "floor" of the pelvic bowl consists of the pubococcygeus and iliococcygeus muscles. As the image shows, the pubococcygeus originates at the dorsal surface of the pubis and inserts to the anococcygeal body (female shown in Fig. 10.2 and male shown in Fig. 10.3), whereas the iliococcygeus originates along the lateral wall of the arcus tendineus levator ani (ATLA) and ischial spine and inserts along the anococcygeal ligament and coccyx. During a pelvic floor muscle contraction, the coccyx moves in a cephalic direction to provide a shelflike support to the pelvic viscera.

E.V. Johnson, PT, DPT, WCS (✉) • D.J. Kirages, PT, DPT, OCS, FAAOMPT
Division of Biokinesiology and Physical Therapy, University of Southern California, Los Angeles, CA, USA
e-mail: Eileen.johnson@med.usc.edu

S. Daneshmand (ed.), *Urinary Diversion*, DOI 10.1007/978-3-319-52186-2_10

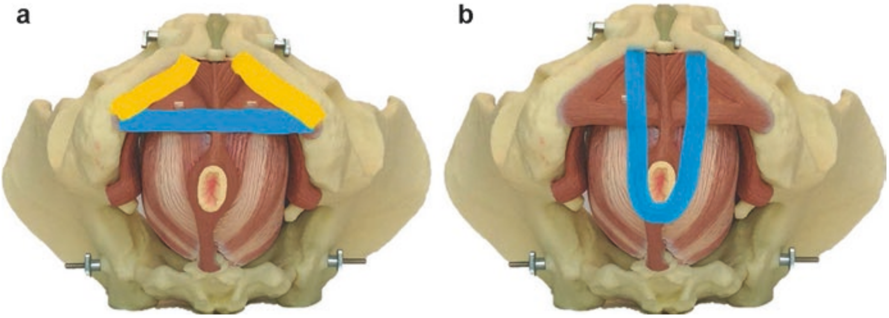


Fig. 10.1 The male pelvic floor (**a**) ischiocavernosus and superficial transverse perineal muscle, (**b**) puborectalis muscle

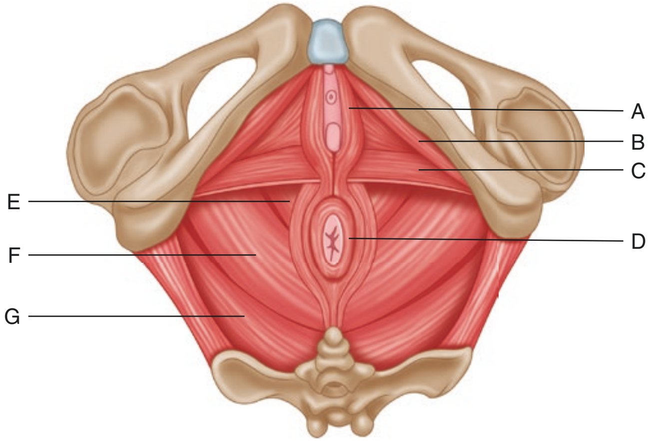


Fig. 10.2 The female pelvic floor (*A*) bulbospongiosus, (*B*) ischiocavernosus, (*C*) superficial and deep transverse perineal muscles, (*D*) puborectalis, (*E*) pubococcygeus, (*F)* iliococcygeus, (*G*) coccygeus (illustration by Leah Villanueva)

Controversy about the true innervation of the pelvic floor muscles still exists within the literature; however, the majority of experts concur that the pudendal nerve along with the S3 and S4 sacral motor nerve roots innervate the pelvic floor [3]. PFM dysfunction can be the result of surgical procedures or trauma. Oftentimes it is attributed to overstretching of the nerves (i.e., during vaginal delivery) or potential neural inhibition due to post-op swelling and tissue damage resulting in PFM weakness and lack of bowel and/or bladder control.

Neighboring the levator ani, there are several larger muscles that play an accessory role to providing PFM strength and power. These muscles include hip musculature, the obturator internus, piriformis, and the larger gluteus maximus and medius, which provide more global stabilization to the pelvic floor. Asavasopon

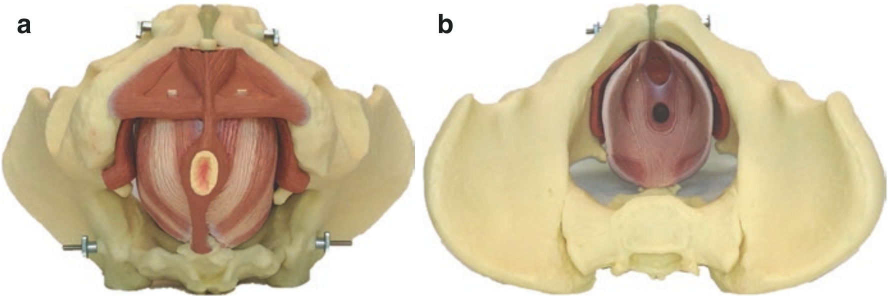


Fig. 10.3 The male pelvic floor (**a**) perineal view, (**b**) levator ani

et al. studied the cortical patterns that these global stabilizers played in pelvic floor muscle activation, noting a specific synergistic relationship between the gluteals and the pelvic floor muscles [4].

It was not until 1948 that Dr. Arnold Kegel, an obstetrician/gynecologist, published his study entitled, "A Nonsurgical Method of Increasing the Tone of Sphincters and their Supporting Structures," that the notion of conservative management in pelvic floor rehabilitation was brought to better awareness [5]. In turn, the term "Kegel" was coined for the exercise program he developed for postpartum women with stress urinary incontinence, involving the voluntary contraction and relaxation of the pelvic floor muscles to improve strength. Presently, these exercises have evolved and expanded to include many more interventions that specialized physical therapists treating pelvic floor dysfunctions can use to help patients improve their quality of life.

Urinary Incontinence

Throughout the lifespan, there are multiple variables that can place one at risk for experiencing urinary incontinence (UI), which is defined as the involuntary loss of urine. One of the key variables is gender, with women experiencing a higher rate of UI versus males [6]. Women may experience pregnancy, delivery, and postmenopausal changes that can influence the strength and muscle performance of the PFM, with epidemiological studies reporting up to 64% prevalence of UI during their life [3]. The excessive muscle lengthening, weakness, and ligamentous laxity postdelivery can also place women at further risk for pelvic organ prolapse (POP) later in life.

Additional factors that can influence risk for UI in both females and males include advanced age, obesity, race, and other neurological influences. Studies report 59% of people over 65 years old who are institutionalized experience some form of UI [7]. Additionally, the impact of UI in one's life can negatively impact one's health-related quality of life (HRQOL) from a psychological, social, work participation, sexual, and physical health position. The impact of these changes is also apparent in urogynecological cancer survivors.

White et al. explain how there are very few studies investigating the impact of UI on HRQOL among cancer survivors. In fact, UI and cancer are heavily associated with a decreased quality of life [8]. As postoperative UI symptoms have been associated with several forms of cancer, including prostate, breast, bladder, colorectal, uterine, and lung cancer, a multidisciplinary approach to care is most logical to improve the continuum of care for the patient. Stress urinary incontinence (SUI) is the most prevalent type of UI seen in those post-orthotopic neobladder surgeries, noting up to 23% prevalence in women post-surgery. Studies also demonstrate better return to daytime continence in the first 6–12 months versus nighttime continence. However, 20–50% of patients will experience persistent nocturnal enuresis.

Physical therapists specialized in treating pelvic floor dysfunction have an important role in helping cancer survivors regain their continence, as many of the principles of strengthening and neuromuscular reeducation can benefit this population. The initial process is through prehabilitation, or in other words, preoperative training of the pelvic floor along with patient education regarding pelvic health and the postoperative expectations.

The model of prehabilitation has shown to have merit in the areas of sports and orthopedic physical therapy. Although more studies are needed in the orthotopic neobladder population, there has been literature supporting the value of preoperative education and PFM training for men undergoing radical prostatectomy [9]. Centemero et al. compared two groups of men, one who received both pre- and postoperative PFM training and the other who received only postoperative training. His results showed improved early return to continence and quality of life in the preoperative training group, noting significant findings of 44.1% of patients reporting continence 1 month post-op versus 20.3% who only received postoperative PFM training. This trend continued at 3 months with 59.3% of men reporting continence versus 37.3% in the postoperative training group [10]. Further data and research continue to be needed in those post-orthotopic neobladder, but we can make an educated hypothesis that there will be a similar correlation between those results in the radical prostatectomy groups and neobladder population, given the similarities in the surgeries.

Pelvic Floor Training Program

The roles of the surgeon and medical team play can be quite different, although complimentary. The overall goal of the surgeon is to prolong the patient's life after a diagnosis of cancer, and the goal of the physical therapist is to help rehabilitate the patient post-medical treatment (surgery, chemotherapy), in order to help restore his or her function and quality of life. A collaborative approach is always the most beneficial to the patient's continuum of care, and fortunately many surgeons see the value that pelvic floor physical therapy, both pre- and post-op, can hold for their patients.

It is imperative that the postoperative PFM training program be initiated immediately after the catheter is removed because the external urethral sphincter, part of the pelvic floor, has been dormant for about 3 weeks while the indwelling catheter was in place. This time frame is to allow the postoperative anastomosis tissue healing. Therefore, the PFM are in desperate need of assistance to “wake up” again. Following the principles of exercise physiology, the physical therapist can devise a patient-specific program to help achieve the patient’s goals of returning to continence and his or her activities of daily living. The timeline for recovery can vary, depending on many variables, including the patient’s commitment with their rehabilitation program, level of fitness, general health, and any postoperative complications or existing comorbidities. Interestingly, in the post-prostatectomy group, patients who receive pelvic floor physical therapy (PFPT) demonstrated better retention of urinary continence, defined as no pads/day at 6 and 12 months versus those who do not receive one-on-one-guided PFPT [11].

Table 10.1 provides the recommended guideline for a PFPT protocol pre- and post-neobladder surgery based on the principles of exercise physiology and postoperative tissue healing

Biofeedback and PT Modalities

During the first 4–6 weeks of PFPT following catheter removal, the patient is going through the neuromuscular reeducation phase of rehabilitation. In other words, the focus is on improving the patient’s brain to muscle awareness, kinesthetic awareness, and coordination to improve the neuromuscular communication and in turn the muscle performance. This first month is a vital phase in the patient’s rehabilitation, as it sets the foundation of his or her prognosis with return to continence; thus, commitment and repetition are key. There can be several barriers during this initial phase, as it can often be quite challenging, as the patient is still recovering from the 6–8 h surgery along with side effects of fatigue/reduced cardiovascular endurance and general deconditioning. It is of paramount importance that the physical therapists find a balance between challenging the patient enough to improve those neural connections to the pelvic floor and core musculature while integrating cardiovascular endurance training at this stage, to improve overall endurance and energy levels.

Therapy is initiated with the patient in a supine position, to help eliminate the effects of gravity on the pelvic floor, and the patient is instructed on how to identify and isolate the PFM. The patient may still be experiencing neural inhibition secondary to tissue inflammation and swelling post-catheter removal, so patient education regarding the timeline to recovery is also important to keep realistic expectations post-op. Initially the main focus will be on improving the patient’s ability to isolate the PFM and improve sphincter coordination for both contraction and relaxation, as both will be essential in neobladder control. Visual biofeedback via mirror, video camera (Fig. 10.4) displaying the perineal muscle movement, or surface EMG biofeedback (Fig. 10.5) with more advanced graphic representation (Fig. 10.6) have proven to be a beneficial adjunct to

Table 10.1 Guideline for PFPT protocol

1. Preoperative pelvic floor training (*Initiate 4–6 weeks prior to surgery*)	Pelvic floor coordination training and awareness training
	Quick flicks 10 × 4 sets/day
	Endurance training 5–10 s holds 10 × 2 sets/day
2. Post-op	Early mobilization: modifying mobility strategies for getting out of bed (log roll), sit to stand with abdominal bracing, avoiding heavy lifting and straining
	Improving daily activity: short 10 min walks at least 3 times/day to improve endurance and assist in GI motility
	Adequate hydration with emphasis on water
3. Post-catheter removal (~3 weeks post-op)	Begin PFM awareness training: learning to isolate the pelvic floor muscles and decrease accessory use of the gluteals, abdominals, and hips to improve sphincter control
	Avoiding Valsalva training
	Neobladder retraining: timed voiding (improving interval between voids to at least every 1.5 h) with the use of alarms, fluid pacing, and PFM exercises
	Nighttime voiding alarms: every 2 h
4. Neuromuscular reeducation with PFPT (4–6 weeks)	Biofeedback training (either visual or via manual feedback) for PFM awareness training with isolating sphincter closure
	Quick flicks 10 × 4 sets, endurance holds (based on objective findings) 5 s holds 10 × 3 sets/day
	Anticipatory pelvic floor contraction reflex training with coughing to improve coordination
	Initiate gluteal/core strengthening in supine position
	Progress to functional strengthening with mobility (sit to stand) and use of PFM with transverse abdominous coactivation brace prior to movement
	Patient reeducation: fiber health and diet, toileting techniques, and PFM coordination for voiding/bowel evacuation
5. Hypertrophy phase (8–12 weeks)	Progress PFM strengthening to upright positions (seated on physioball, standing) with cocontraction of PFM with the transverse abdominous
	Progress endurance holds to 10 s, 15 s, 20 s as tolerated
	Progress motor control to combination quick flick and endurance PFM training in upright positions
	Biofeedback progression with motor control; pyramid, step-up, step-down PFM visual training
	Pelvic floor muscle exercises with cognitive distraction to influence involuntary motor plan development
	Functional mobility training; lifting, bending, gait, return to previous level of activity (sports, hiking, gym exercises)
	Achieve voiding interval of every 4 h during day and night with minimal leakage

Fig. 10.4 Example of one of the simplest forms of awareness training: video biofeedback or mirror feedback to visualize movement of the perineal region during PFM training

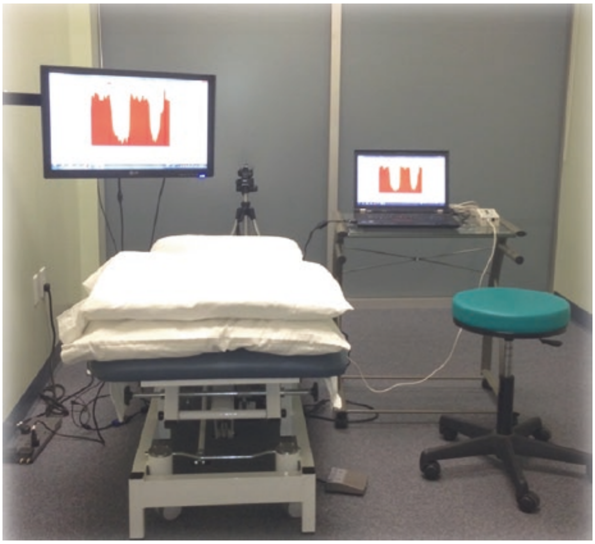


Fig. 10.5 Set up for surface electromyography (sEMG) biofeedback training or use with internal rectal sensor

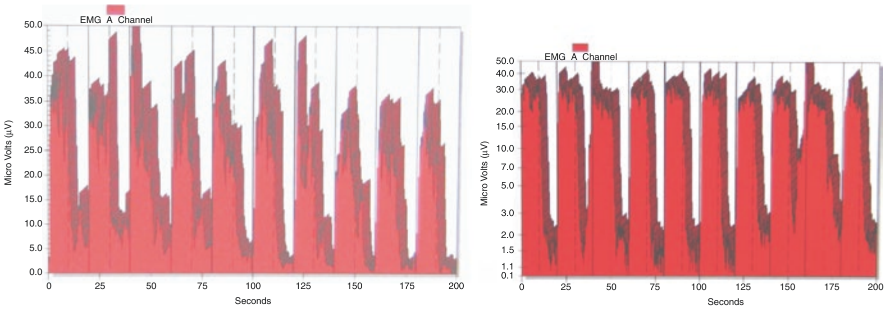


Fig. 10.6 Initial data for 10 s PFM endurance training, demonstrating poor PFM endurance and fatigue with progression of ten consecutive reps. Followed by post-training example, demonstrating improved PFM performance with endurance holds

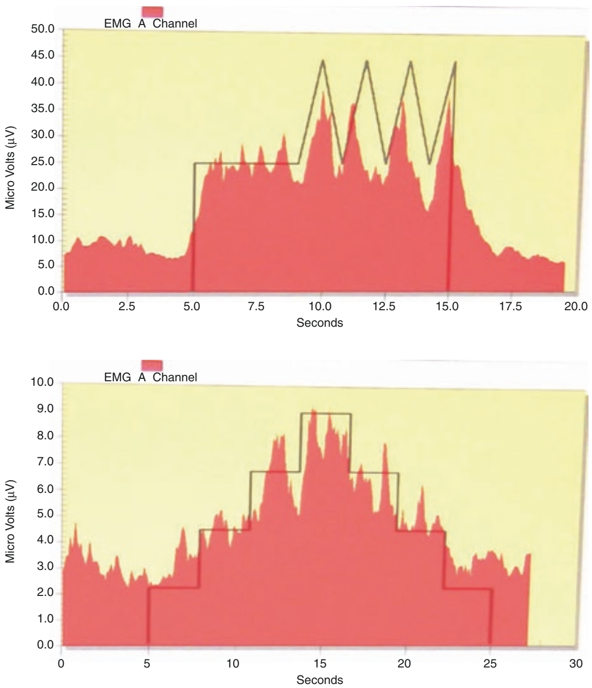


Fig. 10.7 Example of biofeedback progression training with focus on combination endurance holds and quick flicks: training both slow- and fast-twitch muscle fiber coordination and motor control

therapy for improving urinary incontinence [12]. Internal pelvic floor sensors are shown in Fig. 10.5.

Verbal cues to pull the pelvic floor muscles, "up and in," "stop the urine flow," "hold back gas," or "shorten the penis," can be effective in helping the patient visualize and correctly isolate the PFM [13, 14]. Once the patient is able to consistently demonstrate an isolated PFM contraction, further progression can be made in regard to improving PFM endurance holds (Fig. 10.7), coordination with coughing, sneezing, movements that provoke incontinence, and eventually progressions to train in more upright and dynamic postures.

Behavioral Modifications and Return to Sexual Function

To further enhance the patient's rehabilitation, behavioral modifications in regard to neobladder health, diet, and timed voiding can be beneficial. If we consider the neobladder as a form of weight or resistance on the pelvic floor muscles, the ability to maintain continence will be influenced by the time between voids and load/fullness of the neobladder on pelvic floor muscles. Considering time and fluid intake as the variables, the patient will be advised to pace fluid intake throughout the day. Voiding is recommended to be on a schedule of every 1–2 h intervals initially, but longer as improvement to the overall endurance and strength of the PFM occurs. Nighttime continence will also be better managed via timed voiding with the advice to set alarms every 2 h to void because the patient lacks the autonomic control of sphincter closure while asleep. In addition, advice to limit fluid intake 2–3 h prior to sleeping can also be valuable in reducing nighttime leakage, pending the recommended 64 oz of fluid intake has been already achieved.

Additional behavioral modifications PT can provide include education and training for correct toileting postures to help improve evacuation of bowel and bladder with minimal strain on the PFM. Instruction on toileting postures to reduce straining via an increased anorectal angle utilizing trunk and hip flexion can promote relaxation of the puborectalis muscle. Also enhancing PFM relaxation through PFM down training or relaxation training is implemented. This often incorporates biofeedback training to help reduce resting muscle activity through diaphragmatic breathing, PFM lengthening, and overall mindfulness with the use of increasing intra-abdominal pressure vs. straining the PFM. A healthy, balanced diet and exercise are also recommended to help promote bowel regularity and avoid constipation. While it is not uncommon for patients to experience some abdominal discomfort postoperatively, medical management through medications can provide relief and prevent further complications such as bowel obstruction. Lastly, a very common concern of the patient that is often discussed in the course of rehabilitation is the patient's ability to return to sexual function. This comes in the form of erectile dysfunction affecting males and dyspareunia affecting females post-surgery [15].

As returning to continence is often the primary goal for most patients, the idea of returning to sexual function may seem distant. There are multiple psychological factors that may prove challenging in the return to sexual function, but there is growing evidence to support the role of PFPT in returning to sexual health and function [16, 17, 18]. PT interventions to improve PFM relaxation and coordination training during intercourse can be applied to the female population, in addition to manual techniques to improve scar tissue mobility along the vaginal cuff which are utilized to improve tissue range of motion and reduce pain with penetration. Eventually, incorporation of PFM dilator training as a home program will be assigned with the patient's partner's involvement being key to the team approach with gradual return to sexual intercourse.

Overall, the role of the pelvic floor physical therapist both pre- and post-surgery is fundamental to the patient's rehabilitation and return to quality of life. PFPT can positively impact several facets of the patient's life from the psychosocial aspect of simply serving as a supportive educator postoperatively to providing skilled muscle training to return to their previous level of function and activities. The communication between the surgeon, medical team, and physical therapist is crucial in the plan of care with the ultimate goal being to provide the maximum quality care for the patient.

References

1. Marques A, Stothers L, Macnab A. The status of pelvic floor muscle training for women. Can Urol Assoc J. 2010;4(6):419–24.
2. Chaitow L, Jones R. Chronic pelvic pain and dysfunction: practical physical medicine. Edinburgh: Elsevier Health Sciences; 2012.
3. Davila GW, Ghoniem GM, Wexner SD. Pelvic floor dysfunction. London: Springer; 2006.
4. Asavasopon S, Rana M, Kirages DJ, Yani MS, Fisher BE, Hwang DH, Lohman EB, Berk LS, Kutch JJ. Cortical activation associated with muscle synergies of the human male pelvic floor. J Neurosci. 2014;34(41):13811–8.
5. Kegel AH. A nonsurgical method of increasing the tone of sphincters and their supporting structures. Ciba Clin Symp. 1952 Feb-Mar;4(2):35–51.
6. Bo K, Berghmans B, Morkved S, Van Kampen M. Evidence-based physical therapy for the pelvic floor: bridging science and clinical practice. Edinburgh: Elsevier Health Sciences; 2014.
7. Jerez-Roig J, Santos MM, Souza DL, Amaral FLJ, Lima KC. Prevalence of urinary incontinence and associated factors in nursing home residents. Neurourol Urodyn. 2016;35(1):102–7.
8. White AJ, Reeve BB, Chen RC, Stover AM, Irwin DE. Urinary incontinence and health-related quality of life among older Americans with and without cancer: a cross-sectional study. BMC Cancer. 2013;13(1):1.
9. Hirschhorn AD, Kolt GS, Brooks AJ. A multicomponent theory-based intervention improves uptake of pelvic floor muscle training before radical prostatectomy: a 'before and after' cohort study. BJU Int. 2014;113(3):383–92.
10. Centemero A, Rigatti L, Giraudo D, Lazzeri M, Lughezzani G, Zugna D, Montorsi F, Rigatti P, Guazzoni G. Preoperative pelvic floor muscle exercise for early continence after radical prostatectomy: a randomised controlled study. Eur Urol. 2010;57(6):1039–44.
11. Overgård M, Angelsen A, Lydersen S, Mørkved S. Does physiotherapist-guided pelvic floor muscle training reduce urinary incontinence after radical prostatectomy?: A randomised controlled trial. Eur Urol. 2008;54(2):438–48.
12. Hsu LF, Liao YM, Lai FC, Tsai PS. Beneficial effects of biofeedback-assisted pelvic floor muscle training in patients with urinary incontinence after radical prostatectomy: a systematic review and meta-analysis. Int J Nurs Stud. 2016;60:99–111.
13. Neumann P, Fuller A, Sutherland P. Verbal pelvic floor muscle instructions pre-prostate surgery assessed by transperineal ultrasound: do men get it? Australian New Zealand Continence J. 2015;21(3):84.
14. Biroli A. Post-prostatectomy incontinence and rehabilitation: timing, methods, and results. In: Male stress urinary incontinence. Cham: Springer International Publishing; 2015. p. 107–15.
15. Modh RA, Mulhall JP, Gilbert SM. Sexual dysfunction after cystectomy and urinary diversion. Nat Rev Urol. 2014;11(8):445–53.
16. Siegel AL. Pelvic floor muscle training in males: practical applications. Urology. 2014;84(1):1–7.
17. Pischedda A, Fusco F, Curreli A, Grimaldi G, Farina FP. Pelvic floor and sexual male dysfunction. Archivio Italiano di Urologia e Andrologia. 2013;85(1):1–7.
18. Tibaek S, Gard G, Dehlendorff C, Iversen HK, Erdal J, Biering-Sørensen F, Dorey G, Jensen R. The effect of pelvic floor muscle training on sexual function in men with lower urinary tract symptoms after stroke. Top Stroke Rehabil. 2015;22(3):185–93.

Urinary Diversion and Health-Related Quality of Life

11

Andrew Leone and Scott M. Gilbert

Introduction and Background

Urinary diversion is most commonly performed in conjunction with radical cystectomy, and as such, the majority of patients who undergo diversion do so as part of the management of muscle-invasive bladder cancer or for recurrent, noninvasive disease not controlled with endoscopic and/or intravesical treatments [1]. As a reconstructive surgery, however, urinary diversion also plays an important role in managing nonmalignant urologic conditions, such as severe bladder injury or dysfunction [2]. For example, diversion is often used to manage debilitating radiation cystitis, unrepairable bladder fistulae, end-stage interstitial cystitis, and severe neurogenic bladder injury.

The health and quality-of-life impact of urinary diversion can be profound. Among bladder cancer patients, cystectomy and urinary diversion is a complex and morbid surgery. Complications rates range between 40% and 60% [3, 4], and long-lasting functional changes and metabolic complications can be significant [5, 6]. Even with improvements in surgical and postoperative care [7, 8], the burdens associated with urinary diversion are substantial for many patients as detailed in the previous chapters. Many functional and metabolic complications are permanent, and consequently urinary diversion is life-altering. In contrast, diversion may alleviate suffering, restore function and quality of life, and move patients closer to a normal life when performed to palliate severe bladder dysfunction or deleterious symptoms such as debilitating pain [9]. Whether performed as an attendant part of an extirpative surgery or as a primary reconstructive procedure, urinary diversion may impact patients either positively or negatively.

Not surprisingly then, there has been long-staging interest in how urinary diversion affects quality of life, and more than two decades of research has focused on

A. Leone • S.M. Gilbert (✉)
Department of Genitourinary Oncology, H. Lee Moffitt Cancer Center, Tampa, FL, USA
e-mail: scott.gilbert@moffitt.org

S. Daneshmand (ed.), *Urinary Diversion*, DOI 10.1007/978-3-319-52186-2_11

this question [10, 11]. In fact, concerns surrounding the perceived negative quality-of-life effects of early forms of urinary diversions drove development of continent diversions (colon pouches in the early 1980s followed by orthotopic neobladders in the late 1980s) [12, 13], primarily to limit the life-altering physical changes associated with an external stoma and collection appliance (i.e., bag). These efforts were undoubtedly rooted in the belief that avoiding an altered body and restoring urinary function would preserve patient quality of life after diversion surgery. Many of the initial outcome studies comparing conduits to continent diversions, in fact, reported blunted changes and more limited deficits in physical and social functioning among patients managed with continent diversions compared to those who received ileal conduits [14, 15]. Nevertheless, debates regarding the *best* urinary diversion continue even today [16, 17]. Despite significant advances in and simplification of continent urinary diversions, approximately 80% of patients who undergo cystectomy currently receive an ileal conduit [18]. This is despite estimates that suggest upward of 80% of patients are candidates for a continent diversion and in the setting of increasing regionalization of cystectomy and urinary diversion to high-volume, academic centers [19, 20].

Readers may ask how this can be. Why has the uptake of continent diversion been so modest? Clues to the answer this questions will unfold later in the chapter, but as a point of entry, it is clear that quality of life is a key concern with and should be a focus of urinary diversion. Indeed, preserving and improving health-related quality of life are central tenets in defining successful treatment and disease management, and are particularly relevant to urinary diversion because of the tremendous impact it can have on patients' lives. Therefore, the objectives of this chapter are to provide the reader with a better understanding of how health-related quality of life is influenced by urinary diversion surgery, how it can be reliably assessed in research and clinical arenas, and how outcome information about quality of life can be used to guide patient decisions and care. To achieve these goals, we will review various definitions of health-related quality of life, consider a model of health-related quality of life to frame how potential causal and mediating factors influence it in the context of urinary diversion, examine available measures that can be used to assess health-related quality-of-life outcomes after diversion surgery, and briefly review existing research and the resultant knowledge base regarding health-related quality-of-life outcomes after urinary diversion.

A Definition and Framework for Health-Related Quality of Life

Though no standard, universally agreed-upon definition of health-related quality of life exists, most proposed descriptions point to similar meanings and constructs. The Center for Disease Control (CDC) defines health-related quality of life as "an individual's or group's perceived physical and mental health over time" [21]. The National Cancer Institute contextualized health-related quality of life as physical and psychosocial well-being that can be negatively affected by cancer and its treatment as perceived by individuals throughout the cancer care continuum [22], while the Healthy People 2020 definition explicitly focuses on multiple dimensions and domains that comprise health-related quality of life, including physical, emotional, and social functioning [23]. The World Health Organization defines health-related quality of life as "as individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" [24]. The International Society of Quality of Life, an organization committed to furthering the science supporting patient-reported outcomes research, lists several fundamental principles inherent in defining health-related quality of life, including that it is subjectively perceived by the individual and is multidimensional, "encompassing physical and occupation function, psychological state, social interaction and somatic sensation" [25, 26]. Others have defined it as "the extent to which one's usual or expected physical, emotional and social well-being are affected by a medical condition or its treatment" [27]. Across all of the above definitions, core concepts related to health-related quality-of-life center on patients' perspectives and perceptions and the impact of health, illness, and medical treatment in several areas of an individual's life, such as physical, functional, emotional well-being and the ability to maintain social interactions and connections.

Several frameworks have been proposed and outline theoretical underpinnings of health-related quality of life [28–30]. Although an extensive review of them is beyond the scope of this discussion, a focused consideration of how an exemplar model incorporates different health domains and connects them to contextual factors in a causal pathway may be instructive. For this purpose, we will examine an adapted version of an often cited conceptual model of health-related quality of life, the Wilson-Cleary framework [31, 32] (Fig. 11.1). As depicted in the figure, the framework proposes that both personal attributes and characteristics of an individual's environment interact with and influence causally interrelated domains of health. As such, the Wilson-Cleary model specifies causal links between biological and physiological factors, symptoms, functioning, perception of health, and overall quality of life within the context of mediating factors, such as how an individual experiences symptoms (amplified or blunted), a person's motivation level and preferences, as well as attributes of their surroundings (e.g., social and psychological

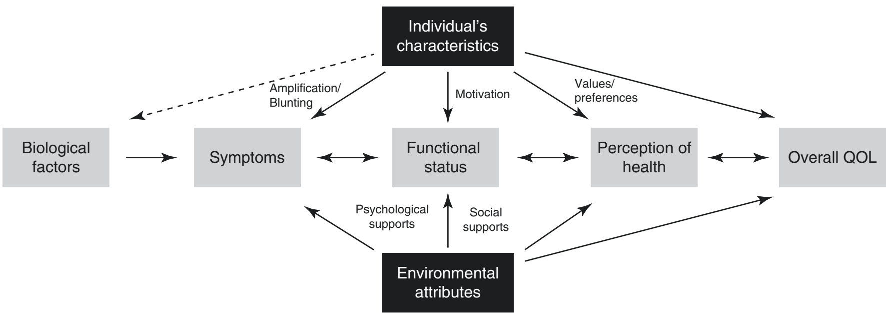


Fig. 11.1 Adapted Wilson-Cleary framework for HRQOL [31, 32]

support networks) [31]. Examples of biological and physiological factors include blood cholesterol levels and blood pressure, while symptoms refer to subjective perceptions experienced by patients that can be reported as complaints or concerns (e.g., chest pain). Functioning captures a person's ability to perform tasks and function physically, emotionally, or socially at home or in the workplace. Applied to the urinary diversion context, albeit as an outlier example, significant physiologic changes related to electrolyte abnormalities and low bicarbonate levels that underlie metabolic acidosis may precipitate subjective patient-reported symptoms, such as fatigue, lethargy, breathing problems, or confusion. These symptoms, in turn, may limit a person's ability to function normally, perhaps because they cannot maintain their energy level, walk normal distances, complete physical tasks, or engage in social routines, resulting in poor perception and appraisal of their health. Through this series of interconnected links, the mounting physical limitations and functional deficits experienced by the individual will likely impair health-related quality of life, but to differing degrees depending on the severity of the metabolic complication and associated symptoms, the individual's ability and motivation to manage their symptoms and combat negative effects on functioning, and their social support network and access to resources that may help them manage complications effectively.

The implication and application of such frameworks are important in that they can help researchers and clinicians more comprehensively measure a multitude of influencers that ultimately comprise good or poor health-related quality-of-life scores. In addition, they can help identify gaps or areas of concern along the proposed causal pathway, inform intervention development, and direct effective clinical interventions to alleviate poor patient outcomes.

Urinary Diversion Specific Domains Associated with HRQOL

Urinary diversion is associated with a multifaceted and distinct set of metabolic consequences, symptoms, and functional outcomes that interact and converge to form a spectrum of health-related quality-of-life experiences after diversion surgery. Concern and problem areas – or domains – that are specific to urinary diversion include changes in physical function, such as bowel, sexual and urinary function, altered physical appearance (i.e., body image) related to the presence of a stoma or urostomy and the change in how urine is eliminated, as well as resultant social concerns related to real or perceived strains in intimate relationships and casual social interactions. In high burden cases, these functional and social concerns can mount and spill into emotional and psychological domains, resulting in anxiety and depressive symptoms. In this section, we will consider each of these dominant domains in more detail.

General physical and psychological concerns may affect a large proportion of patients who undergo major extirpative or reconstructive surgery. Patients undergoing urinary diversion may suffer from several physical issues including pain, fatigue, and sleep disturbances. Additionally, they may experience distress related to disruption and limitations in physical function [33]. While a study by Henningsohn et al. suggests similar distress levels between orthotopic neobladder patients and matched control populations 1 year following surgery [34], Palapattu et al. showed that nearly half of cystectomy patients report general distress [35]. Benner et al. highlighted persistently elevated pain and fatigue scores up to 6 months after urinary diversion in their study of 33 patients treated with radical cystectomy and urinary diversion [36]. Another study suggested that patients' distress improves to baseline approximately 12 months after surgery [37]. The complex interplay between psychological distress and sleep disturbances may profoundly contribute to health-related quality-of-life deficits. Thulin et al. studied patterns of sleep disturbance following urinary diversion, reporting that negative sleep changes attributable among orthotopic neobladder, continent reservoir, and urostomy occurred in 37%, 14%, and 22% of patients, respectively [38]. The authors concluded that neobladder-specific urinary issues such as the need to set a voiding alarm may preclude adequate sleep.

Changes across several functional domains are also significant concerns after urinary diversion. For example, changes in urinary function are a predominant concern for patients before and after diversion surgery. Maintaining urinary continence after urinary diversion may have a tremendous impact on socialization and subsequently quality of life. Loss of volitional control over urinary continence may also impact body image which can lead to isolation and depression for patients who receive an ileal conduit [39]. Anxiety associated with fear of urinary leakage and odor impacts patient quality of life significantly after both conduit and continent urinary diversion. Not surprisingly, urinary incontinence and leakage are the most commonly investigated domain among HRQOL in bladder cancer patients [40]. Leakage with conduit diversions is most commonly due to poor external appliance adherence or suboptimal stoma placement. Among ileal conduit patients, urinary leakage rates during daytime and nighttime have been reported as high as 40%, and patient anxiety related to leakage appears even higher [41, 42]. Improvements in surgical techniques as well as enterostomal nurse education have decreased some of these issues [43]. Although continent urinary diversions are most often used to preserve normal urinary function, incontinence rates and urine leakage are still relatively high, particularly at night, and may be related to infrequent catheterization or uninhibited contractions [44].

Changes in sexuality and sexual health may be underestimated among men and women after urinary diversion, particularly in cases of concurrent cystectomy. In men, erectile dysfunction has been reported in up to 80% of patients after cystectomy and ileal conduit [45]. Many factors contribute substantively to sexual dysfunction after urinary diversion, including physical and functional changes that result from collateral tissue injury or loss in the case of cystectomy (e.g., erectile dysfunction, altered vaginal anatomy), changes in body image related to the urinary diversion itself, and attendant emotional and psychological concerns that follow physical and functional insult. As discussed later in the chapter, some of the currently available bladder cancer-specific questionnaires integrate both physical and psychosocial aspects of sexual dysfunction. However, many factors such as quality of erections, decrease in penile length, impaired sexual function even before surgery, partner response to changes in function and appearance, and overall psychological issues are often overlooked [46]. As with other types of pelvic surgery, post-diversion sexual function depends on a number of factors, including age, initial sexual function before surgery, and surgery-specific factors such as nerve and vaginal sparing. Hekal and colleagues reported that a majority of men achieved adequate erections after nerve-sparing cystectomy and urinary diversion without needing other sexual dysfunction treatments [47]. Other studies suggest that prostate-sparing cystectomy and urinary diversion may preserve sexual function postoperatively [48–50].

The role of urinary diversion type on post-diversion sexual and erectile dysfunction has not been fully elucidated. While Hedgepeth and colleagues identified a potential benefit in men who received neobladder diversion, others have not shown a difference in recovery of sexual function between continent and conduit diversions [10, 51–53]. In females, sexual dysfunction after urinary diversion is primarily related to either nerve damage affecting sensation, changes to vaginal anatomy that effect compliance and/or capacity, and decreased lubrication [54]. Among women treated with vaginal-sparing cystectomy and urinary diversion, 80% remained sexually active in one study [55]. In contrast, others have reported more disappointing results. Zippe and colleagues found that less than half of patients were sexually active with the most commonly reported complaints consisting of inability to achieve orgasm (45%), decreased lubrication (41%), decreased sexual desire (37%), and dyspareunia (22%) [56]. Another recent study reported that in vaginal-sparing cystectomy patients more than 65% were sexually active [57].

Recognizing the relationship between psychological stresses related to urinary diversion and sexual dysfunction is critical. Altered body image after undergoing either a conduit or continent urinary diversion and the anxiety associated with potential urinary incontinence can further negatively impact sexual function. In addition to patients' perceived psychological distress, partners experience stress related to urinary diversion. The presence of a stoma, external urostomy appliance, or catheterizable channel may contribute to sexual dysfunction or a lack of sexual interest among couples. While repulsion and lack of interest in sexual intimacy among urinary diversion patients has not been well studied, it has been demonstrated among colorectal cancer patients living with ostomies [58].

Bowel function and dysfunction represent another area of concern among urinary diversion patients. Diversion can impact both short-term and long-term gastrointestinal function. While several studies have examined short-term changes in and recovery of bowel function after urinary diversion, relatively few have investigated long-term bowel changes to bowel or their impact on quality of life among urinary diversion patients. Several prior studies have reported normal bowel function after urinary diversion [59, 60]. Although a recent study investigating bowel changes 1 year after cystectomy found that more than 70% of patients were satisfied with bowel function at 1 year, a relatively large group of patients experienced more frequent diarrhea, defecation frequency, fecal incontinence, and life restriction from bowel disease [61]. Further research is needed to identify and prevent morbidity associated with bowel issues and improve the urinary diversion patient's quality of life.

Body image has been defined as the way patients perceive themselves [62]. Regardless of type of urinary diversion received, long-lasting or permanent changes in the body and body image are common for many patients. However, some studies suggest that despite dramatic differences in external body changes between diversion types, body image is important in all diversion patients [51, 63]. Nevertheless, patients with conduits and stomas clearly experience a more dramatic alteration in their body's appearance. A recent Korean study suggests that neobladder patients report relatively better body image compared to patients managed with ileal conduits, which may reflect not only differences in individuals' perceptions of their body but also cultural values and norms [64].

Assessing Health-Related Quality of Life

A number of instruments are available to evaluate health-related quality of life among patients treated with urinary diversion. These include general – or generic – instruments, such as the Medical Outcomes Study Short Forms (SF-36 and SF-12) and EuroQol five dimensions questionnaire (EQ-5D), as well as more specific condition-oriented measures that target symptoms, functional complications, and health problems that are particularly germane to urinary diversion [65–67]. Of note, most condition-specific instruments that assess issues associated with urinary diversion have been developed in the context of bladder cancer. Examples of these include the Functional Assessment of Cancer Therapy-Bladder (FACT-BL) cancer subscale, the Vanderbilt Cystectomy Index (VCI), the Bladder Cancer Index (BCI), and the European Organization for Research and Treatment of Cancer Quality-of-Life Bladder Module (EORTC QLQ-BLM30) [68–71]. The use of general health surveys to assess health-related quality of life and well-being after urinary diversion has several limitations. Early studies on health-related quality of life after cystectomy and urinary diversion typically used generic QOL questionnaires supplemented with add-on questions in an attempt to improve the sensitivity to diversion-related health outcomes. Because these makeshift questionnaires did not undergo full psychometric evaluation, their reliability and validity are uncertain. (Table 11.1)

Table 11.1 Key components of HRQOL instruments [72–74]

Psychometric property	Description
Construct validity	Assess how well an instrument measures the intended construct/concept
Criterion validity	Assess how well an instrument correlates with an existing criterion measure of the intended construct/concept
Reliability	Assesses how consistently an instrument estimates the construct/concept with repeated measures given stable disease
Responsiveness	Assesses how well an instrument identifies meaningful changes in quality of life and/or health states

The condition-specific instruments that have been developed thus far contain items (questions) that focus on symptoms, complications, and health impairments that can occur after cystectomy and urinary diversion and therefore cover many of the health domains that were reviewed earlier in the chapter. The Vanderbilt Cystectomy Index (VCI) utilizes the general FACT as its core questionnaire with the addition of supplemental bladder cancer-specific questions derived from FACT-BL, FACT-colorectal, and Functional Assessment of Incontinence Therapy-Urinary. It contains urinary, bowel, and sexual function components. The FACT-BL consists of 39 questions inclusive of the general FACT core. Twelve diversion-specific questions have been added to the general questions that cover body image, stoma care, and sexual function. The Bladder Cancer Index (BCI) is a validated and reliable questionnaire developed with patient and physician feedback that includes urinary, bowel, and sexual function components. It consists of 36 questions and contains function and bother subdomain scores. The BCI has been validated across stages of bladder cancer and for different urinary diversion modalities. The EORTC-QLQ-BM30 is modified from the EORTC-QLQ-C30 and includes 30 additional items specific to bladder cancer. This instrument has not been fully validated yet but is in the late phases of validation. A 23-item neobladder HRQOL instrument called the IONB-PRO was recently developed to provide more discrete information gathering for issues and concerns that are specific to neobladder patients [77]. Although tailored to neobladder diversion, it may not provide reliable or responsive information for other diversion types, likely limiting its use in comparative studies.

In addition to the condition-specific instruments that are currently available to assess health-related quality of life after cystectomy and urinary diversion (FACT-Bl, VCI, BCI, EORTC QLQ-BLM30), several new measures are in development, such as the Bladder Utility Symptom Scale (BUSS) and the Memorial Sloan Kettering Idiographic Model [75, 76]. The BUSS is a ten-question survey designed to measure quality of life in all stages of bladder cancer patients. The questionnaire has undergone validity and reliability testing and consists of both generic and bladder cancer-specific questions [75]. A limitation with this instrument is that it does not contain any diversion-specific components, in part because it was designed to apply to all stages of bladder cancer. More recently, researchers at Memorial Sloan Kettering Cancer Center outlined the limitations of the aforementioned standard HRQOL instruments, noting that while they can be implemented and used fairly easily, they fail to capture individual patient concerns and also fail to account for the impact of response shift [76, 78]. The authors proposed adding idiographic measures of progress toward goal achievement and difficulty with activities among patients prior to cystectomy and urinary diversion and found that these additional metrics improved estimation of health-related quality of life. Further validation of this approach is necessary in the postoperative setting. A summary of available condition-specific HRQOL measures is shown in Table 11.2.

Table 11.2 Condition-specific HRQOL instruments

Instrument	Items	Domains/attributes	Validity testing
FACT-BL [68]	41 (FACT-G + 12 additional questions)	Single items covering urinary, sexual and bowel questions, ostomy care, body image and appetite	Information on validity and reliability evaluation not available
VCI-15 [69]	15 (total of 43 co-administered with FACT-G)	General cancer related domains plus urinary, bowel, ostomy and sexual questions	Reliability and validity testing performed
BCI [70]	36	Bowel, sexual and urinary domains with function and bother subdomains	Reliability and validity testing performed
EORTC-QLQ-BLM30 [71]	30	Single items covering urinary symptoms, sexual function, urostomy issues, body image	In phase 3 of reliability and validity evaluation
IONB-PRO [77]	23	Neobladder diversion-specific questions covering symptoms, self-management, activities of daily living, emotional and social issues, and sleep fatigue	Reliability and validity testing performed
BUSS [75]	10	Single item covering urinary, bowel, and sexual issues, as well as body image, psychological problems, pain, and medical care	Reliability and validity testing performed

Review of Current HRQOL Literature

As noted earlier, most early studies that explored health-related quality of life in cystectomy and urinary diversion patients used either general quality-of-life instruments or informal, un-validated questionnaires. Porter and Penson noted that of 15 quality-of-life studies identified in a systematic review of studies published between 1966 and 2004, few consisted of HRQOL assessment with either a condition-specific or validated instrument, and most omitted baseline or serial longitudinal data, making results difficult to interpret [79]. General assessment tools such as EQ-5, Sickness Impact Profile, SF-12 and SF-36, and FACT have been used to measure quality of life in urinary diversion patients with similar scores noted on average between neobladder and ileal conduit patients [80]. More recently, a greater number of studies have compared health-related quality of life among diversion patients using condition-specific validated assessment tools such as VCI, BCI, FACT-BL, QLQ-BLM30, and IONB-PRO. The vast majority of more recent studies, although methodologically improved, have been retrospective and cross-sectional, suggesting continued room for improvement in the area of research and clinical assessment [81].

From a clinical and research perspective, the most interesting and relevant HRQOL comparisons are between different types of urinary diversion (e.g., ileal conduit vs.

neobladder vs. catherizable colon pouch), and while many prior studies have compared HRQOL across urinary diversion types, almost none have demonstrated a significant difference in health-related quality-of-life outcomes between continent and incontinent diversions [51–53, 63, 82–87]. Notably, Anderson and colleagues reported higher quality of life at 1 year postoperatively in ileal conduit urinary diversion patients compared to neobladder patients [69]. Conversely, Singh et al. reported better physical and social function among neobladder patients compared to patients who received an ileal conduit in a prospective study, with scores diverging between 6 and 18 months after surgery, despite similar baseline assessment [87]. A recent multicenter Italian study investigating quality of life in neobladder patients using the IONB-PRO and EORTC QLQ-BLM30 reported that longer follow-up and lack of urinary incontinence were predictors of better emotional/relational health [88]. This study, however, lacked baseline data and did not consist of a comparison group. A more recent study reported higher quality-of-life scores among ileal conduit patients compared to neobladder patients more than 10 years after urinary diversion [89]. In contrast, a recent systematic review suggested that improved reconstructive techniques representative in modern comparison studies favor ileal neobladder in terms of higher quality-of-life scores after urinary diversion surgery [90]. In contrast, a relatively large meta-analysis of observational HRQOL studies that used validated questionnaires reported by Cerruto et al. identified modest but insignificantly higher health-related quality-of-life scores after neobladder diversion compared to ileal conduit. Quality-of-life outcomes were significantly better among patients treated with orthotopic neobladder in a sub-analysis of studies based on the EORTC QLQ-C30 [91].

Confounding, biases, and patients' preferences are a major if not fatal limitation in past and likely future efforts comparing health-related quality-of-life outcomes between continent diversions and conduits, principally because randomization is not feasible to address the question of which is "better" and because patients who select neobladder reconstruction tend to be younger, healthier, and more engaged and motivated regarding their diversion selection [16]. All of the comparative studies presented and discussed thus far must be viewed and interpreted through a cautionary lens for this reason. Table 11.3 summarizes an update of the most currently available HRQOL studies comparing outcomes between different urinary diversion groups.

Future Research Areas and Clinical Application

Quality-of-life assessment after urinary diversion is a crucial element of fully evaluating patient-reported outcomes and gauging the impact and success of diversion surgery. There has been long-standing interest in health-related quality-of-life evaluation and research among patients who receive urinary diversion, mainly in the form of comparative studies examining outcomes following ileal conduit and continent diversions. Results to date have been mixed, with few studies showing any significant HRQOL differences across diversion type. This may be in part related to shortcomings in research methods and study design. Prior studies have predominantly used general HRQOL instruments or informally developed, un-validated diversion questionnaires.

Table 11.3 Summary of comparative urinary diversion HRQOL studies since 2000

References	Instrument	No. pts	Year	Population	Findings
McGuire et al. [92]	SF-36	76	2000	United States	Lower mental QOL scores in IC patients compared to population norm
Fujisawa et al. [93]	SF-36	56	2000	Japan	No differences detected between groups
Hobish et al. [14]	EORTC-QLQ-C30	102	2000	Austria	Higher QOL scores in NB patients
Hara et al. [94]	SF-36 + informal questionnaire	85	2002	Japan	No differences detected in general HRQOL
Dutta et al. [15]	SF-36 FACT-G	100	2002	United States	Marginally higher HRQOL scores detected in NB group
Protogerou et al. [41]	EORTC-QOL-C30, informal questionnaire	108	2004	Greece	Urinary and sexual function impairments present following cystectomy but no HRQOL differences between groups
Kikuchi et al. [63]	FACT-BL	35	2006	Japan	Lower body image scores among ileal conduit patients
Gilbert et al. [52]	BCI	315	2007	United States	Decreased urinary HRQOL among NB group
Saika et al. [95]	EORTC-QLQ-C30	78	2007	Japan	No significant difference between IC and NB
Autorino et al. [96]	SF-36	79	2008	Italy	No difference between IC and NB, but physical, emotional, and social QOL scores below population norm
Sogni et al. [84]	EORTC-QLQ-C30 + EORTC-QLQ-BLM30	34	2008	Italy	Global health status higher in NB group but not significant
Philip et al. [42]	SF-36, informally developed questionnaire	52	52	England	NB group had significantly better physical functioning
Somani et al. [11]	EORTC-QLQ-C30 + SWLS	32	2009	England	No HRQOL difference before or after cystectomy
Hedgepeth et al. [51]	BCI	224	2010	United States	No difference between IC and NB groups
Erber et al. [85]	EORTC-QLQ-C30 + EORTC-QLQ-BLM30	58	2012	Germany	Higher HRQOL scores among NB vs. IC patients

(continued)

Table 11.3 (continued)

References	Instrument	No. pts	Year	Population	Findings
Gacci et al. [97]	EORTC-QLQ-C30 + EORTC-QLQ-BLM30, FACT-BL	25	2013	Italy	No HRQOL differences among female patients
Metcalfe et al. [98]	FACT-VCI	84	2013	Canada	No HRQOL differences between IC and NB groups
Singh et al. [87]	EORTC-QLQ-C30	164	2014	India	General HRQOL better in NB group compared to IC group
Huang et al. [39]	BCI	294	2015	China	No difference in long-term HRQOL between IC and NB

Even in cases where condition-specific measures have been used, direct comparisons have been flawed and results difficult to fully interpret because of methodological issues such as cross-sectional data collection and missing assessment points (e.g., lack of baseline QOL assessment), and the unavoidable confounding that accompanies differences is patient fitness and preferences that fundamentally separate patients who elect and receive ileal conduit or content diversions. Nevertheless, there are several fronts where health-related quality-of-life research and clinical assessment can and will improve moving forward. Several prospective studies that focus on longitudinal health-related quality-of-life assessment among cystectomy and urinary diversion patients as primary outcomes are currently ongoing. As the results of these studies become available, our understanding of the factors that contribute to and drive health-related quality-of-life in this patient population will undoubtedly improve.

Beyond expanding our knowledge base in this area, practical applications of clinically integrated patient-reported outcomes such as health-related quality of life are underfoot. A future state of clinical care should include making HRQOL assessments available at the point of care for a number of reasons, including to help identify complications and health deficits, guide clinical management after surgery, and inform physician counseling and patient decision-making before surgery. Clinical integration of patient-reported outcomes has already begun in some clinical settings where access to actionable quality-of-life assessments has been shown to translate to superior symptom control and arguably better patient care [99, 100]. These future areas of work will further move health-related quality-of-life to the fore and help establish a clinical role for HRQOL assessment and outcomes.

References

1. Lee RK, Abol-Enein H, Artibani W, Bochner B, Dalbagni G, Daneshmand S, Fradet Y, Hautmann RE, Lee CT, Lerner SP, Pycha A, Sievert KD, Stenzl A, Thalmann G, Shariat SF. Urinary diversion after radical cystectomy for bladder cancer: options, patient selection, and outcomes. BJU Int. 2014;113(1):11–23.

2. Cody JD, Nabi G, Dublin N, McClinton S, Neal DE, Pickard R, Yong SM. Urinary diversion and bladder reconstruction/replacement using intestinal segments for intractable incontinence or following cystectomy. Cochrane Database Syst Rev. 2012 Feb 15;2:CD003306.
3. Gandaglia G, Popa I, Abdollah F, et al. The effect of neoadjuvant chemotherapy on perioperative outcomes in patients who have bladder cancer treated with radical cystectomy: a population-based study. Eur Urol. 2014;66:561.
4. Shansigh A, Korets R, Vora KC, et al. Defining early morbidity or radical cystectomy for patient with bladder cancer using a standardized reporting methodology. Eur Urol. 2009;55(1):164–74.
5. Gilbert SM, Lai J, Saigal CS, Gore JL. Urologic Diseases in America Project. J Urol. 2013;190(3):916–22.
6. Hautmann RE, de Petriconi RC, Volkmer BG. 25 years of experience with 1,000 neobladders: Long-term complications. J Urol. 2011;185(6):2207–12.
7. Taub DA, Dunn RL, Miller DC, Wei JT, Hollenbeck BK. Discharge practice patterns following cystectomy for bladder cancer: evidence for the shifting of the burden of care. J Urol. 2006;176(6 Pt 1):261207.
8. Tyson MD, Chang SS. Enhanced recovery pathways versus standard care after cystectomy: a meta-analysis of the effects on perioperative outcomes. Eur Urol. 2016;70(6):995–1003.
9. Kamat AM, Haung SF, Bermejo CE, Rosser CJ, Pettaway CA, Pisters PW, Guitreau D, Pisters LL. Total pelvic exenteration: effective palliation of perineal pain in patients with locally recurrent prostate cancer. J Urol. 2003;170(5):1868–71.
10. Månsson A, Johnson G, Månsson W. Quality of life after cystectomy: comparison between patients with conduit and those with continent caecal reservoir urinary diversion. Br J Urol. 1988;62:240–5.
11. Somani BK, Gimlin D, Fayers P, et al. Quality of life and body image for bladder cancer patients undergoing radical cystectomy and urinary diversion – a prospective cohort study with a systematic review. Urology. 2009;74:1138.
12. Kock NG, Nilson AE, Nilsson LO, Norlen LJ, Philipson BM. Urinary diversion via a continent ileal reservoir: clinical results in 12 patients. J Urol. 1982;128(3):469–75.
13. Hautmann RE, Egghart G, Frohneberg D, Miller K. The ileal neobladder. J Urol. 1988;139(1):39–42.
14. Hobisch A, Tosun K, Kinzl J, Kemmler G, Bartsch G, Holtl L, Stenzl A. Life after cystectomy and orthotopic neobladder versus ileal conduit urinary diversion. Semin Urol Oncol. 2001;19(1):18–23.
15. Dutta SC, Chang SC, Coffey CS, Smith Jr JA, Jack G, Cookson MS. Health related quality of life after radical cystectomy: comparison of ileal conduit with continent orthotopic neobladder. J Urol. 2002;168(1):164–7.
16. Evans B, Montie JE, Gilbert SM. Incontinent or continent urinary diversion: how to make the right choice. Curr Opin Urol. 2010;20(5):421–5.
17. Skinner EC. Choosing the right urinary diversion: patient's choice or surgeon's inclination? Urol Oncol. 2011;29(5):473–5.
18. Gore JL, Saigal CS, Hanley JM, Schonlau M, Litwin MS. Urologic Disease in America Project: Variations in reconstruction after radical cystectomy. Cancer. 2006;107(4):729–37.
19. Hautmann RE. Which patients with transitional cell carcinoma of the bladder or prostatic urethra are candidates for an orthotopic neobladder? Curr Urol Rep. 2000;1:173.
20. Hollenbeck BK, Dunn RL, Miller DC, Daignault S, Taub DA, Wei JT. Volume-based referral for cancer surgery informing the debate. J Clin Oncol. 2007;25(1):91–6.
21. Centers for Disease Control and Prevention, definition of Health-Related Quality of Life. https://www.cdc.gov/hrqol/. Accessed 9/5/2016.
22. National Institutes of Health, National Cancer Institute, Applied Research, Cancer Control and Population Sciences, Health-Related Quality of Life Assessment & Application. http://appliedresearch.cancer.gov/areas/assessment/. Accessed 9/6/2016.
23. Healthy People 2020, Foundation Health Measure Report, Health-Related Quality of Life and Well-Being. https://www.healthypeople.gov/sites/default/files/HRQoLWBFullReport.pdf. Accessed 10/7/2016.

24. World Health Organization, Mental Health Program. http://www.who.int/mental_health/publications/whoqol/en/. Accessed 10/1/2016.
25. International Society of Quality of Life, Health-Related Quality of Life Research. http://www.who.int/mental_health/publications/whoqol/en/. Accessed 9/8/2016.
26. Schipper J, Clinch JJ, Olweny CLM. Quality of life studies: definitions and conceptual issues. In: Spilker B, editor. Quality of Life and Pharmacoeconomics in Clinical Trials. Philadelphia: Lippincott-Raven Publishers; 1996. p. 11–23.
27. Cella D. Measuring quality of life in palliative care. Semin Oncol. 1995;22:73–81.
28. Bakas T, McLennon SM, Carpenter JS, Buelow JM, Otte JL, Hanna KM, Ellett ML, Hadler KA, Welch JL. Systematic review of health-related quality of life models. Health Qual Life Outcomes. 2012;10:134.
29. Bergner M. Measurement of health status. Med Care. 1985;23:696–704.
30. Johnson RJ, Wolinsky FD. The structure of health status among older adults: disease, disability, functional limitations, and perceived health. J Health Soc Behav. 1993;34:105–21.
31. Wilson IB, Cleary PD. Linking clinical variables with health-related quality of life: a conceptual model of patient outcomes. JAMA. 1995;273(1):59–65.
32. Ferrans CE, Zerwic JJ, Wilbur JE, Larson JL. Conceptual model of health-related quality of life. J Nurs Scholarsh. 2005;37(4):336–42.
33. Dumitrache M, Badescu DL, Rascu S, Balalau OD, Popescu B, Scaunasu RV, Balalau C. Considerations on the psychological status of the patients undergoing radical cystectomy. J Mind Med Sci. 2015;2(2):193–8.
34. Henningsohn L, Steven K, Kallestrup EB, Steineck G. Distressful symptoms and well-being after radical cystectomy and orthotopic bladder substitution compared with a matched control population. J Urol. 2002;168(1):168–74. discussion 174-65
35. Palapattu GS, Haisfield-Wolfe ME, Walker JM, BrintzenhofeSzoc K, Trock B, Zabora J, Schoenberg M. Assessment of perioperative psychological distress in patients undergoing radical cystectomy for bladder cancer. J Urol. 2004;172(5 Pt 1):1814–7.
36. Benner C, Greenberg M, Shepard N, Meng MV, Rabow MW. The natural history of symptoms and distress in patients and families following cystectomy for treatment of muscle invasive bladder cancer. J Urol. 2014;191(4):937–42.
37. Gerharz EW, Mansson A, Hunt S, Skinner EC, Mansson W. Quality of life after cystectomy and urinary diversion: an evidence based analysis. J Urol. 2005;174(5):1729–36.
38. Thulin H, Kreicbergs U, Wijkstrom H, Steineck G, Henningsohn L. Sleep disturbances decrease self-assessed quality of life in individuals who have undergone cystectomy. J Urol. 2010;184(1):198–202.
39. Huang Y, Pan X, Zhou Q, Huang H, Li L, Cui X, Wang G, Jizhong R, Yin L, Xu D, Hong Y. Quality-of-life outcomes and unmet needs between ileal conduit and orthotopic ileal neobladder after radical cystectomy in a Chinese population: a 2-to-1 matched-pair analysis. BMC Urol. 2015;15:117.
40. Perlis N, Krahn M, Alibhai S, Finelli A, Ritvo P, Bremner KE, Kulkarni G. Conceptualizing global health-related quality of life in bladder cancer. Qual Life Res. 2014;23(8):2153–67.
41. Protogerou V, Moschou M, Antoniou N, Varkarakis J, Bamias A, Deliveliotis C. Modified S-pouch neobladder vs ileal conduit and a matched control population: a quality-of-life survey. BJU Int. 2004;94(3):350–4.
42. Philip J, Manikandan R, Venugopal S, Desouza J, Javle PM. Orthotopic neobladder versus ileal conduit urinary diversion after cystectomy--a quality-of-life based comparison. Ann R Coll Surg Engl. 2009;91(7):565–9.
43. Li X, Fang Q, Ji H, Pan J, Zhang J, Li Z, Chen M, Wu X, Zhou Z, Chen Z. Use of urostomy bags in the management of perioperative urine leakage after radical cystectomy. Cancer Nurs. 2014;37(3):170–4.
44. El Bahnasawy MS, Osman Y, Gomha MA, Shaaban AA, Ashamallah A, Ghoneim MA. Nocturnal enuresis in men with an orthotopic ileal reservoir: urodynamic evaluation. J Urol. 2000;164(1):10–3.

45. Matsuda T, Aptel I, Exbrayat C, Grosclaude P. Determinants of quality of life of bladder cancer survivors five years after treatment in France. Int J Urol. 2003;10(8):423–9.
46. Mulhall JP. Defining and reporting erectile function outcomes after radical prostatectomy: challenges and misconceptions. J Urol. 2009;181(2):462–71.
47. Hekal IA, El-Bahnasawy MS, Mosbah A, El-Assmy A, Shaaban A. Recoverability of erectile function in post-radical cystectomy patients: subjective and objective evaluations. Eur Urol. 2009;55(2):275–83.
48. Nieuwenhuijzen JA, Meinhardt W, Horenblas S. Clinical outcomes after sexuality preserving cystectomy and neobladder (prostate sparing cystectomy) in 44 patients. J Urol. 2008;179(5 Suppl):S35–8.
49. Ong CH, Schmitt M, Thalmann GN, Studer UE. Individualized seminal vesicle sparing cystoprostatectomy combined with ileal orthotopic bladder substitution achieves good functional results. J Urol. 2010;183(4):1337–41.
50. Basiri A, Pakmanesh H, Tabibi A, Radfar MH, Tajalli F, Ahadi B, Eslami N. Overall survival and functional results of prostate-sparing cystectomy: a matched case-control study. Urol J. 2012;9(4):678–84.
51. Hedgepeth RC, Gilbert SM, He C, Lee CT, Wood Jr DP. Body image and bladder cancer specific quality of life in patients with ileal conduit and neobladder urinary diversions. Urology. 2010;76(3):671–5.
52. Gilbert SM, Wood DP, Dunn RL, Weizer AZ, Lee CT, Montie JE, Wei JT. Measuring health-related quality of life outcomes in bladder cancer patients using the Bladder Cancer Index (BCI). Cancer. 2007;109(9):1756–62.
53. Allareddy V, Kennedy J, West MM, Konety BR. Quality of life in long-term survivors of bladder cancer. Cancer. 2006;106(11):2355–62.
54. Modh RA, Mulhall JP, Gilbert SM. Sexual dysfunction after cystectomy and urinary diversion. Nat Rev Urol. 2014;11(8):445–53.
55. Game X, Mallet R, Guillotreau J, Berrogain N, Mouzin M, Vaessen C, Sarramon JP, Malavaud B, Rischmann P. Uterus, fallopian tube, ovary and vagina-sparing laparoscopic cystectomy: technical description and results. Eur Urol. 2007;51(2):441–6.
56. Zippe C, Nandipati K, Agarwal A, Raina R. Sexual dysfunction after pelvic surgery. Int J Impot Res. 2006;18(1):1–18.
57. Wishahi M, Elganozoury H. Survival up to 5-15 years in young women following genital sparing radical cystectomy and neobladder: oncological outcome and quality of life. Single-surgeon and single-institution experience. Cent European J Urol. 2015;68(2):141–5.
58. Popek S, Grant M, Gemmill R, Wendel CS, Mohler MJ, Rawl SM, Baldwin CM, Ko CY, Schmidt CM, Krouse RS. Overcoming challenges: life with an ostomy. Am J Surg. 2010;200(5):640–5.
59. Hautmann RE, Volkmer BG, Schumacher MC, Gschwend JE, Studer UE. Long-term results of standard procedures in urology: the ileal neobladder. World J Urol. 2006;24(3):305–14.
60. Fung B, Kessler TM, Haeni K, Burkhard FC, Studer UE. Bowel function remains subjectively unchanged after ileal resection for construction of continent ileal reservoirs. Eur Urol. 2011;60(3):585–90.
61. Kramer MW, von Klot CA, Kabbani M, Kabbani AR, Tezval H, Peters I, Herrmann TR, Kuczyk MA, Merseburger AS. Long-term bowel disorders following radial cystectomy: an underestimated issue? World J Urol. 2015;33(10):1373–80.
62. Hopwood P, Fletcher I, Lee A, Al GS. A body image scale for use with cancer patients. Eur J Cancer. 2001;37:189–97.
63. Kikuchi E, Horiguchi Y, Nakashima J, Ohigashi T, Oya M, Nakagawa K, Miyajima A, Murai M. Assessment of long-term quality of life using the FACT-BL questionnaire in patients with an ileal conduit, continent reservoir, or orthotopic neobladder. Jpn J Clin Oncol. 2006;36(11):712–6.
64. Shim B, Kim KH, Yoon H, Park YY, Lee DH. Body image following radical cystectomy and ileal neobladder or conduit in korean patients. Korean J Urol. 2014;55(3):161–6.

65. Ware Jr JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. Med Care. 1992;30:473–83.
66. Ware Jr JE, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care. 1996;34(3):220–33.
67. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol group. Ann Med. 2001;33:337–43.
68. Functional Assessment of Cancer Therapy, Bladder Cancer module. http://www.facit.org/FACITOrg/Questionnaires. Accessed 10/9/2016.
69. Anderson CB, Feurer ID, Large MC, Steinberg GD, Barocas DA, Cookson MS, Penson DF. Psychometric characteristics of a condition-specific, health-related quality-of-life survey: the FACT-Vanderbilt Cystectomy Index. Urology. 2012;80(1):77–83.
70. Gilbert SM, Dunn RL, Hollenbeck BK, Montie JE, Lee CT, Wood DP, Wei JT. Development and validation of the Bladder Cancer Index: a comprehensive, disease-specific measure of health related quality of life in patients with localized bladder cancer. J Urol. 2010;183(5):1764–9.
71. European Organization for Research and Treatment of Cancer, Quality of Life, EORTC-QLQ-BLM30 module. http://groups.eortc.be/qol/bladder-cancer-eortc-qlq-nmibc24-eortc-qlq-blm30. Accessed 10/9/16.
72. Somani BK, MacLennan SJ, N'Dow J. Quality of life with urinary diversion. Eur Urol Suppl. 2010;9(10):763–71.
73. Roach KE. Measurement of health outcomes: reliability, validity and responsiveness. JPO J Prosthet Orthot. 2006;18(6):P8–P12.
74. Hays RD, Hadorn D. Responsiveness to change: an aspect of validity, not a separate dimension. Qual Life Res. 1992;1(1):73–5.
75. Perlis N, Boehme K, Jamal M, Bremner K, Alibhai S, Finelli A, Ritvo P, Krahn M, Gandhi R, Kulkarni G. MP31-17 validating the bladder utility symptom scale (BUSS): a novel patient reported outcome quality of life measure for all patients with bladder cancer. J Urol. 2016;195(4):e426.
76. Anderson CB, Rapkin B, Reaves BC, Sun AJ, Morganstern B, Dalbagni G, Donat M, Herr HW, Laudone VP, Bochner BH. Idiographic quality of life assessment before radical cystectomy. Psychooncology. 2015, ahead of print.
77. Siracusano S, Niero M, Lonardi C, Cerruto MA, Ciciliato S, Toffoli L, Visalli F, Massidda D, Iafrate M, Artibani W, Bassi P, Imbimbo C, Racioppi M, Talamini R, D'Elia C, Cacciamani G, De Marchi D, Silvestri T, Verze P. Belgrano E (2014) Development of a questionnaire specifically for patients with Ileal Orthotopic Neobladder (IONB). Health Qual Life Outcomes. 2014;12:135.
78. Morganstern BA, Bochner B, Dalbagni G, Shabsigh A, Rapkin B. The psychological context of quality of life: a psychometric analysis of a novel idiographic measure of bladder cancer patients' personal goals and concerns prior to surgery. Health Qual Life Outcomes. 2011;9:10.
79. Porter MP, Penson DF. Health related quality of life after radical cystectomy and urinary diversion for bladder cancer: a systematic review and critical analysis of the literature. J Urol. 2005;173(4):1318–22.
80. Ali AS, Hayes MC, Birch B, Dudderidge T, Somani BK. Health related quality of life (HRQoL) after cystectomy: comparison between orthotopic neobladder and ileal conduit diversion. Eur J Surg Oncol. 2015;41(3):295–9.
81. Ahmadi H, Lee CT. Health-related quality of life with urinary diversion. Curr Opin Urol. 2015;25(6):562–9.
82. Mansson A, Davidsson T, Hunt S, Mansson W. The quality of life in men after radical cystectomy with a continent cutaneous diversion or orthotopic bladder substitution: is there a difference? BJU Int. 2002;90(4):386–90.
83. Yoneda T, Adachi H, Urakami S, Kishi H, Shigeno K, Shiina H, Igawa M. Health related quality of life after orthotopic neobladder construction and its comparison with normative values in the Japanese population. J Urol. 2005;174(5):1944–7.
84. Sogni F, Brausi M, Frea B, Martinengo C, Faggiano F, Tizzani A, Gontero P. Morbidity and quality of life in elderly patients receiving ileal conduit or orthotopic neobladder after radical cystectomy for invasive bladder cancer. Urology. 2008;71(5):919–23.

85. Erber B, Schrader M, Miller K, Schostak M, Baumunk D, Lingnau A, Schrader AJ, Jentzmik F. Morbidity and quality of life in bladder cancer patients following cystectomy and urinary diversion: a single-institution comparison of ileal conduit versus orthotopic neobladder. ISRN Urol. 2012;2012:342796.
86. Large MC, Malik R, Cohn JA, Richards KA, Ganshert C, Kunnavakkum R, Smith ND, Steinberg GD. Prospective health-related quality of life analysis for patients undergoing radical cystectomy and urinary diversion. Urology. 2014;84(4):808–13.
87. Singh V, Yadav R, Sinha RJ, Gupta DK. Prospective comparison of quality-of-life outcomes between ileal conduit urinary diversion and orthotopic neobladder reconstruction after radical cystectomy: a statistical model. BJU Int. 2014;113(5):726–32.
88. Imbimbo C, Mirone V, Siracusano S, Niero M, Cerruto MA, Lonardi C, Artibani W, Bassi P, Iafrate M, Racioppi M, Talamini R, Ciciliato S, Toffoli L, Visalli F, Massidda D, D'Elia C, Cacciamani G, De Marchi D, Silvestri T, Creta M, Belgrano E, Verze P. Quality of life assessment with orthotopic ileal neobladder reconstruction after radical cystectomy: results from a prospective Italian Multicenter Observational Study. Urology. 2015;86(5):974–9.
89. Gellhaus P, Cary KC, Johnson C, Monn MF, Kaimakliotis H, Weiner M, Koch M, Bihrle R. MP38-13 long-term 10-year health-related quality of life outcomes following radical cystectomy. J Urol. 2016;195(4):e537–8.
90. Ghosh A, Somani BK. Recent trends in postcystectomy health-related quality of life (QoL) favors neobladder diversion: systematic review of the literature. Urology. 2016;93:22–6.
91. Cerruto MA, Elia CD, Siracusano S, Gedeshi X, Mariotto A, Iafrate M, Niero M, Lonardi C, Bassi P, Belgrano E, Imbimbo C, Racioppi M, Talamini R, Ciciliato S, Toffoli L, Rizzo M, Visalli F, Verze P, Artibani W. Systematic review and meta-analysis of non RTCs on health related quality of life after radical cystectomy using validated questionnaires: better results with orthotopic neobladder versus ileal conduit. Eur J Surg Oncol. 2016;42(3):343–60.
92. McGuire MS, Grimaldi G, Grotas J, et al. The type of urinary diversion after radical cystectomy significantly impacts on the patient's quality of life. Ann Surg Oncol. 2000;7:4.
93. Fujisawa M, Isotani S, Gototh A, et al. Health-related quality of life with orthotopic neobladder versus ileal conduit according to SF-36 survey. Urology. 2000;55:862.
94. Hara I, Miyake H, Hara S, et al. Health-related quality of life after radical cystectomy for bladder cancer: a comparison of ileal conduit and orthotopic bladder replacement. BJU Int. 2002;89:10.
95. Saika T, Arata R, Tsushima T, Nasu Y, Suyama B, Takeda K, Ebara S, Manabe D, Kobayashi T, Tamimoto R, Kumon H. Okayama Urological Research Group. Health-related quality of life after radical cystectomy for bladder cancer in elderly patients with an ileal conduit, ureterocutaneostomy, or orthotopic urinary reservoir: a comparative questionnaire survey. Acta Med Okayama. 2007;61(4):199–203.
96. Autorino R, Quarto G, Di Lorenzo G, De Sio M, Perdona S, Giannarini G, Giugliano F, Damiano R. Health related quality of life after radical cystectomy: comparison of ileal conduit to continent orthotopic neobladder. Eur J Surg Oncol. 2009;35(8):858–64.
97. Gacci M, Saleh O, Cai T, Gore JL, D'Elia C, Minervini A, Masieri L, Giannessi C, Lanciotti M, Varca V, Simonato A, Serni S, Carmignani G, Carini M. Quality of life in women undergoing urinary diversion for bladder cancer: results of a multicenter study among long-term disease-free survivors. Health Qual Life Outcomes. 2013;11:43.
98. Metcalfe M, Estey E, Jacobsen NE, Voaklander D, Fairey AS. Association between urinary diversion and quality of life after radical cystectomy. Can J Urol. 2013;20(1):6626–31.
99. Berry DL, Hong F, Halpenny B, Partridge AH, Fann JR, Wolpin S, Lober WB, Bush NE, Parvathaneni U, Back AL, Amtmann D, Ford R. Electronic self-report assessment for cancer and self-care support: results of a multicenter randomized trial. J Clin Oncol. 2014;32(3):199–205.
100. Cleeland CS, Wang XS, Shi Q, Mendoza TR, Wright SL, Berry MD, Malveaux D, Shah PK, Gning I, Hofstetter WL, Putnam Jr JB, Vaporciyan AA. Automated symptom alerts reduce postoperative symptom severity after cancer surgery: a randomized controlled clinical trial. J Clin Oncol. 2011;29(8):994–1000.

Considerations for Urinary Re-diversion

12

Richard E. Hautmann and Bjoern G. Volkmer

Abbreviations

BC	Bladder cancer
IC	Interstitial cystitis
OBS	Orthotopic bladder substitute
RC	Radical cystectomy
UD	Urinary diversion

Introduction

Performing a second urinary diversion (UD) is not only a major surgical challenge but also requires creative surgical problem solving. Very few publications exist about conversion or re-diversion surgery [1–5]. With the exception of one paper [5], all patients underwent (radical) cystoprostatectomy (RC) before the option of orthotopic bladder substitution (OBS) was offered, and all had difficulties with their cutaneous UD and were seeking alternative options.

R.E. Hautmann (✉)
University of Ulm, Boschstrasse 4a, 89231 Neu-Ulm, (Donau), Germany
e-mail: richard.hautmann@uni-ulm.de

B.G. Volkmer
Department of Urology, Klinikum Kassel Mönchebergstrasse 41-43,
Kassel, D-34125, Germany

S. Daneshmand (ed.), *Urinary Diversion*, DOI 10.1007/978-3-319-52186-2_12

Indications for Conversion in the Pre-neobladder Era

In a study by Boyd et al. [2], indications for prior RC included transitional cell carcinoma of the bladder in nine patients and multiple failed bladder reconstructions secondary to megacystis and pyocystis in two. All nine cancer patients were free of disease and none had received perioperative radiation therapy.

Six men had prior conduit diversion. One had a continent cutaneous diversion, three had prior conduit that subsequently had been converted to a cutaneous Kock ileal reservoir, and one had a prior ureterosigmoidostomy that had previously been converted to a continent cutaneous diversion. Of the six patients with existing conduits, four were seeking conversion to some form of continent UD because of dissatisfaction with a cutaneous stoma and appliance problems. One patient suffered recurrent stomal stenosis, and one demonstrated renal deterioration more than 20 years after RC and loop diversion. Of the five men with a previously created continent cutaneous reservoir, one underwent undiversion to an OBS because of a parastomal hernia with difficulty in catheterization and right ureteroileal stenosis. One patient experienced recurrent large stones associated with the efferent nipple valve and difficult catheterization. The final three patients underwent undiversion for problems with the efferent nipple and incontinence.

In the Ahlering et al. [3] report, the major reasons for conversion were patient preference in 11 cases, surgical correction of an existing problem (stomal stenosis or parastomal hernia) in ten, and pyonephrosis due to ureteral obstruction in two. After a complete discussion of options, the latter patients with existing problems requested conversion simultaneously with correction of the underlying problem. The two patients with pyonephrosis had an anastomotic stricture, and the nonfunctioning kidney was removed at conversion.

In the report from Mainz [4] on 39 patients, indications for UD were neurogenic bladder (38%), bladder exstrophy and epispadias (28%), tumors (18%), and anatomical/functional bladder loss (15%). A total of 13 patients presented with recurrent urinary infection, 11 with stoma problems such as dermatitis or stenosis, and 13 with ureteral obstruction. In addition, 20 patients had undergone surgery of the upper urinary tract before conversion to continent UD. There were 11 patients with epispadias/exstrophy who underwent bladder surgery before primary UD. Five patients with malignant tumors had radiation therapy, and in two radiotherapy was combined with chemotherapy.

In Pow-Sang et al. [1] report, a total of 20 patients underwent conversion from different types of external (requiring an appliance) or internal diversion to a Florida pouch (type I or II). There were 11 men and 9 women between 17 und 66 years old (average age 40 years). Previous methods for diversion included an ileal conduit in 15 patients, a suprapubic tube in 1, sigmoid conduit in 1, cecal conduit in 1, ureterosigmoidostomy in 1, and cutaneous ureterostomy in 1. All patients requested the continent UD, and among them three presented with recurrent symptomatic urinary tract infections, three presented with complications with the stoma and external appliance, and five presented with ureteral obstruction in seven ureters. Three patients with ureteral obstruction presented with a diverting nephrostomy tube. The patient who had undergone ureterosigmoidostomy had recurrent urinary tract infection and was concerned about the risk of malignancy.

In summary These surgeons [1–4] offered the conversion option to highly select male patients who had previously undergone cystoprostatectomy and some form of cutaneous diversion. All of these patients underwent their primary operations before the option of orthotopic reconstruction was offered, and all had difficulties with the cutaneous diversion and were seeking alternative options. The main impetus to conversion has been patients with problems resulting from cutaneous diversions such as parastomal hernia with difficult catheterization and incontinence with continent diversion, or patient dissatisfaction with a continent stoma and cutaneous appliances. For the Mainz report [4], younger patients, particularly adolescents, desired conversion from conduit to continent cutaneous diversion.

Contemporary Indications for Conversion in the Neobladder Era

Since the need for a second diversion is an infrequent problem after RC, there are limited number of patients from most single institutions. As a result, there is a paucity of data in the literature to characterize the need for a second diversion. We evaluated this risk in patients who underwent RC in the setting of BC or a non-oncologic disease and determined differences in the requirement of a secondary diversion, reporting the largest series of patients [5].

The primary UD in our series of 1614 patients undergoing cystectomy was an ileal neobladder in 71.9% of male patients and 42.3% of female patients, a conduit in 17.6% and 38.6%, and (trans)ureterocutaneostomy in 9.5% and 12.5%, respectively, while continent pouches and diversions to the intestinal tract were limited to a small number of patients. In the complete series of 1614 patients treated with RC, the underlying disease was non-oncologic in 92 patients (15.7%), mainly defunctionalized bladders from radiation therapy, interstitial cystitis (IC), neurologic diseases, or as a reaction to cytotoxic medication. Overall 94.3% of patients had UC. There were 25 females and 23 males for a total of 51 second/third UDs among 48 of the 1614 patients (3.2%). In 29 of 48 patients, RC and first diversion were performed at our institution, while we performed the second/third diversions in 41 of the 48 patients. The primary UD of the reoperation group was performed at a mean patient age of 50 years compared to a mean age in the complete series of 65 years, with a mean interval between first and second UD of 57 months. Indications for conversion are listed in the table (Table 12.1).

The indication for RC was oncologic in 28 patients and nononcologic in 23. Conversions were continent to continent (14), incontinent to continent (14), continent to incontinent (13), and incontinent to incontinent (10). Twelve patients had tumor recurrence impacting the initial diversion. In eight patients the indication was abscess or necrosis of the diversion or radiation damage. Six patients with renal failure required conversion. All patients with conversion from incontinent to continent had a strong desire to avoid a stoma. Four patients died perioperatively, and

Table 12.1 Indications for second diversion

Oncologic
Upper tract recurrence/involvement
Transitional cell carcinoma of the ureter
Local recurrence infiltrating the ureter
Recurrence at ureteral implantation site
Urethral recurrence/second tumor
Neobladder, male
Neobladder, female, Morbus Paget urethra
Neobladder female, obstructive local recurrence
Recurrence invading diversion/tumor in diversion/ invasion
Neobladder
Colon conduit, adenocarcinoma of the colon
Augmentation with neobladder, transitional cell carcinoma of the trigone
Neobladder, vaginal carcinoma
Emergency
Pelvic abscess
Ischemia of the mesenteric artery
Radiogenic damage
Necrosis of conduit
Necrosis of neobladder
Malfunction of initial diversion
Persisting symptoms from IC after supratrigonal RC
Persistent pain
Ureteroenteric stricture
Conduit stenosis
Conduit stricture/neurogenic tract/failed bladder reconstruction
Anatomical functional bladder loss
Renal failure
Obstruction
Dislike of initial diversion
RC for benign disease
RC for malignant disease + no evidence of disease
For more than 12 months

short bowel syndrome developed in one patient. In summary the contemporary indications reflect real-world situations as they will be seen at any major bladder cancer center. Patient dislike of the stoma plays only a minor role.

The potentially greatest diversion-related complication is one that requires a second diversion [5]. Even in the most experienced hands, at least five scenarios may require an alternative diversion, including (1) emergency UD for complications requiring immediate take down of the initial UD, (2) tumor recurrence impacting the urinary tract or the UD, (3) progressive impairment of renal function (in patients with a continent UD), (4) malfunction/complications of the initial UD, and (5) patient dislike of a stoma.

The Dilemma of the Intestine-Ureteral Anastomosis

The major motivation in patients with a conversion from incontinent to continent diversion was dislike of the initial UD. Overall nine male and three female patients in the Hautmann series [5] underwent conversion to an OBS. In seven patients the underlying disease was non-oncologic, and the other five had UC but had no evidence of disease for 1 year. In three of the male patients, the apex/prostate had been left behind at RC. Of the three female patients, two underwent cystectomy at the second UD. In the other six male and female patients, the urethra and the striated sphincter were spared during cystectomy, but the urethral remnant had been closed.

All patients were informed about the risk of postoperative hypercontinence (requiring clean intermittent catheterization) or incontinence. In patients with remnants of the prostate, resection of the residual prostatic tissue was performed without any problems. In a case of an ileal conduit, we left the ureterointestinal anastomoses intact and incorporated this intestinal segment in the neobladder as an afferent tubular segment and part of the lateral wall [5] (See Fig. 12.1)

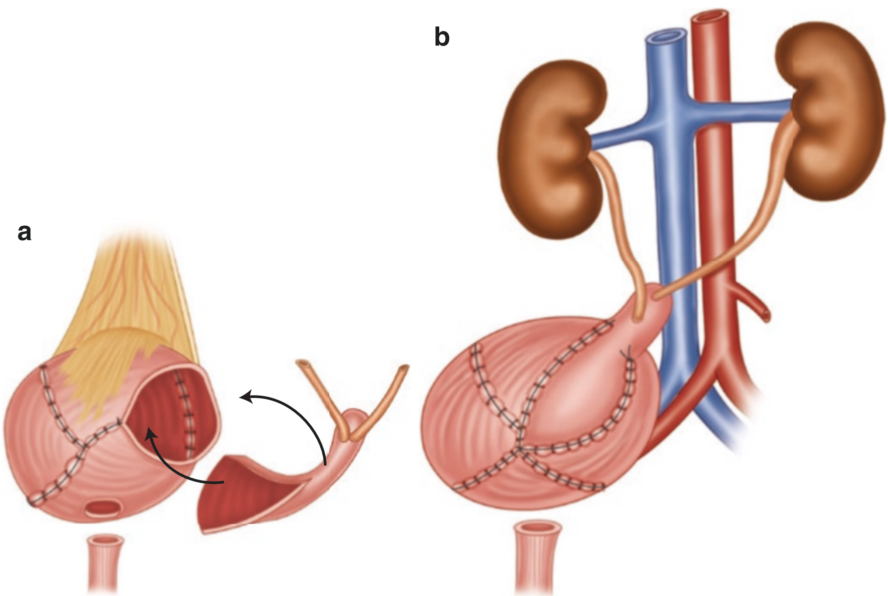


Fig. 12.1 Principle of bowel preservation: (**a**) Ileal conduit is opened along the antimesenteric wall. Proximal portion of the conduit and ileo-ureterostomies are left undisturbed. *Arrows* indicate attachment sites. (**b**) Completion of conversion of ileal conduit to ileal neobladder. Afferent limbs and left side wall of the neobladder are spared, i.e., 25 cm of ileum length

In the long term, all female patients experienced hypercontinence [5]. All men with initial complete resection of the prostate and closure of the urethral remnant experienced subneovesical obstruction and underwent transurethral resection of the neovesicourethral anastomosis, or performed clean intermittent catheterization. Male patients who had at least remnants of the prostate had excellent functional long-term results [2]. The results from the series described by Hautmann et al. [5] are consistent with the USC experience [2].

The precision of the anastomosis to the urethra and the presence of a retained apex of the prostate were major factors in the technical success of the operation, degree of continence, and satisfaction of the patients. All four patients who had some portion of retained prostate enjoy excellent continence without anastomotic stricture. In two of the early undiversion patients with direct membranous urethral anastomoses, strictures occurred, and they subsequently chose to proceed with continent cutaneous diversion. The other five patients with anastomoses to the membranous urethral stump did well, but two required an artificial urinary sphincter for continence. These latter five patients had more extensive pelvic mobilization of the urethra for more precise anastomoses. The satisfaction level of all nine continuing neobladder patients, even if an artificial urinary sphincter was necessary, has been exceptional [2].

An occasional bladder cancer patient will have undergone cystoprostatectomy with an inadvertent portion of the prostatic urethra left intact. Many patients with a history of a neurogenic bladder or congenital urinary tract anomalies have undergone cutaneous diversion with only simple cystectomy. These men are ideal candidates for undiversion because the remaining apex of the prostate allows the urethral anastomosis to be performed well above the urogenital diaphragm, and in all four of our cases, a satisfactory anastomosis was accomplished, and good continence has been achieved. These patients must be aware, however, that they are still at risk for prostate cancer in the remaining prostate apex and must continue to be followed with prostate-specific antigen levels and examination.

In the male patient, urethroscopy should be performed preoperatively. The patency of the urethra must be assessed and the membranous urethral zone visualized. Coaptation of the sphincter must be noted, and the residual apex should be identified by some portion of retained verumontanum. In the absence of any prostatic apex, and when mobilization of the urethra from the urogenital diaphragm is required, an artificial urinary sphincter may be necessary for continence. All patients in whom this procedure is being considered should be clearly aware of the risks and options and only proceed if they accept these risks completely. The satisfaction level of these patients, however, even if an artificial sphincter is required, is usually high [2].

Bowel Preservation

Uniformly, all institutions that report their experience in conversion of diversions [1–5] stress the need and the principle of bowel preservation. Individuals who have undergone creation of a conduit have already had resection of a large or small bowel segment. The resection of the right colon and associated ileocecal valve as part of the pouch construction represents a risk to some patients for the development of a short gut malabsorptive syndrome [1].

In six patients with a nonobstructed ureterointestinal reimplantation and a conduit with adequate blood supply, the intestinal segment was preserved after detubularization, and the ureteral anastomoses were left undisturbed. In these patients the conduit was opened at its antimesenteric edge and was simply patched into the detubularized extended right colonic segment without attempting to mobilize, resect, or implant ten renoureteral units [1]. To preserve as much bowel as possible, Ahlering et al. [3] adopted this technique to incorporate the existing ileal conduit into the Indiana pouch (Fig. 12.1). Hence, when preoperative radiography of the loop or excretory urography shows normal ureterointestinal anastomoses, the remaining normal ileal conduit can be incorporated as part of the reservoir. Using part of the ileum to augment, the reservoir allows us to decrease the 33–36 cm length of the right colon to 25–28 cm. Avoiding dissection of the proximal conduit and ureteral anastomoses can dramatically simplify the procedure.

To preserve as much small bowel length as possible, the Mainz group [5] adopted the technique of incorporating the existing ileal conduit into the Mainz pouch. A pre-existing colonic conduit with antireflux implantation of the ureter is generally incorporated into the ileocecal pouch without reimplantation of the ureter. An ileal conduit commonly requires reimplantation of the refluxive ureters.

Therefore, the ileal conduit may be either incorporated into the pouch or used for construction of the continent outlet (e.g., intussuscepted nipple). With respect to fecal frequency, repeat bowel resection and exclusion of the ileocecal valve from bowel continuity can shorten the intestinal transit time. Patients with risk of fecal frequency developing after bowel resection such as those with myelomeningocele, previous bowel resection, or irradiation underwent reconstruction of the ileocecal valve. For conversion from a pre-existing colonic or ileal conduit to a continent cutaneous diversion, the existing conduit may be incorporated into the new reservoir or be used to create an intussusception nipple for the continent outlet.

Figure 12.2 presents another representative case: The patient with IC had a trigone-sparing cystectomy with ileal augmentation (length of augment 20 cm). (Fig. 12.2a). Since pain and urge persisted, she underwent a second UD (Fig. 12.2b). The trigone was resected, the augmentation was preserved, and an additional ileal loop (15 cm) was detubularized in its middle third and interposed between the urethra and the augment. The ureters were implanted into the tubular ends using the Wallace technique. The augment was attached to the interposed loop. After 13 months the patient still had a low-compliance neobladder. A third UD was performed, Fig. 12.2c. The augmentation was removed and replaced, while the segment with the ureteral and urethral anastomosis remained in place. The patient has now been alive for more than 8 years without any voiding problems.

Only 1/48 patients experienced a short bowel syndrome. In 25/48 patients, parts of the initial diversion were incorporated into the second diversion [5].

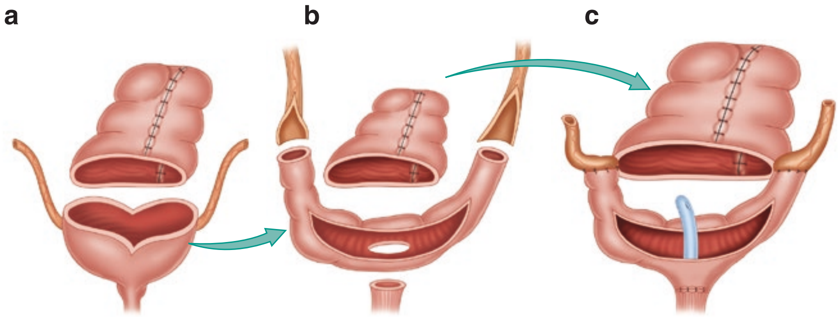


Fig. 12.2 Principle of bowel preservation. (**a**) First. (**b**) Second. (**c**) Third diversion. For details see text

Ureteral Reimplantation

After exclusion of patients without the use of intestinal segments, the ureterointestinal anastomosis of the initial UD was included in the second diversion in 19 of 29 diversions [5]. Only one patient experienced a short bowel syndrome [5].

Nonobstructive (antireflux) implantation of dilated or fibrotic ureters is a challenge in any form of UD.

Nearly 40% of the renoureteral units of patients presenting for conversion to continent urinary diversion were dilated. Since 1994 dilated ureters were generally reimplanted by the serous-lined extramural tunnel technique [4].

Among 38 ureters 28 were reimplanted and 10 were left undisturbed as part of the Florida pouch II [1]. Among the reimplanted ureters, six became obstructed postoperatively. Five of these ureters were obstructed preoperatively, and their units could not be salvaged with a new reimplantation procedure. The salvage rate with a new reimplantation of seven renal units preoperatively obstructed was low, that is, 5 units (28.5%). The incidence of postoperative obstruction in the preoperatively nonobstructed units was 4.2%.

In summary, the high percentage of recurrent obstruction after a new reimplantation indicates that the fibrotic process that caused the initial obstruction continues during the secondary procedure. The already shortened ureter, particularly on the left side, often, precludes adequate mobilization and the use of a healthier segment with better vascular supply. Perhaps in some situations, construction of a transverse colon reservoir and the use of the upper ureter might decrease the incidence of postoperative obstruction in scarred and dilated ureters.

Surgical/Technical Aspects

Ahlering et al. [3] placed the stoma at the original conduit site in their initial two patients. Neither patient had an underlying problem with a parastomal hernia, but a hernia developed in each. In experience with the Indiana pouch, they have seen no parastomal hernias, presumably due to fixation of the reservoir immediately superior and lateral to the stoma. With the pouch adherent to the abdominal wall at this site, the small bowel does not physically have access to the stomal area. This maneuver prevents parastomal hernias as long as they used a virgin site for the new stoma. Helal et al. reported the importance of using a new stomal site in patients with a Florida pouch who require parastomal hernia repair [6]. Of 23 patients 4 were initially referred for a parastomal hernia associated with the conduit. To date conversion by this technique has prevented further development of recurrent parastomal hernias.

Another aspect of interest is the total length of the bowel removed. Removing the right colon is usually well tolerated provided a substantial length of the ileum is not also removed. When a modification of the Indiana (Lundiana) pouch is used in which 10 cm of the ileum is removed, patients admit to some changes in bowel habits postoperatively, but serious problems are rare. As in the current technique, the loss of longer segments of the distal ileum substantially increases this risk. The authors mention that this increase is most obvious in neuropathic groups and in these with previous irradiation [7].

Individuals who have undergone creation of a conduit have already had resection of a large or small bowel segment. The resection of the right colon with the associated ileocecal valve as part of the pouch represents a definite risk to some patients for the development of a short gut malabsorptive syndrome as previously mentioned. Of Pow-Sang et al.'s [1] 20 patients, one had chronic diarrhea (an adult with left colectomy for left colonic cancer in whom an ileal conduit was constructed and who had also received radiation therapy to the pelvic cavity). Two other patients had temporary diarrhea that was controlled after several months of controlled diet and loperamide hydrochloride therapy. In their experience with continent diversion, the incidence of initial diarrhea is greater in this converted group of patients than with patients in whom normal bowel was diverted for other etiologies [8]. The elimination of 15–20 cm of the ileum in association with the entire right colon and ileocecal valve obviously increases the risk for the development of chronic diarrhea.

Problematic diarrhea developed in one young patient who received high-dose radiation for pelvic malignancy. We recommend counselling irradiated patients who are considering conversion about the possibility of complications with diarrhea, but we do not believe that conversion is contraindicated in such individuals [3]. Other metabolic problems include the development of hyperchloremia in 15 of their patients (75%) and acidosis in 2 (10%). Hyperchloremia occurred in patients who were otherwise doing well clinically and had normal renal function. Acidosis, however, was observed in one patient who presented with bilateral ureteral obstruction and in one who was borderline acidotic before the ileal conduit. Decreased red blood cell folic acid was observed in one patient who presented with acidosis. The serum vitamin B12 and folic acid levels were normal, but the decrease in serum red blood cell folic acid required treatment. This abnormality has not been observed in other patients in this group.

Second diversion rates in patients with non-oncologic indications are considerably higher (25%) than in patients with oncologic indications (1.8%). Clinical observations have raised the suspicion that non-oncologic cases have more complications leading to reoperations than oncologic cases, although there are no reports in the literature to confirm this. However, in a population-based assessment of enterocystoplasty complications in adults, Welk et al. reported a 40% rate of patients who required a subsequent urological procedure, including 13 of 243 (5%) who required UD [9]. This outcome is also not often reported in the enterocystoplasty literature.

In conclusion, secondary urinary diversion is a complex procedure that requires meticulous surgical planning, patient preparation, and vigilant postoperative follow-up to minimize complications. In select patients, functional results can be excellent with resultant improvement in quality of life. Patient counselling is key and the cornerstone to successful urinary re-diversion.

References

1. Pow-Sang JM, Helal M, Figureoa E, Sanford E, Persky L, Lockhart J. Conversion from external appliance wearing or internal urinary diversion to a continent urinary reservoir (Florida pouch I and II): surgical technique, indications and complications. J Urol. 1992;147:356.
2. Boyd SD, Esrig D, Stein JP, Freeman JA, Skinner DG. Undiversion in men following prior cystoprostatectomy and cutaneous diversion. Is it practical? J Urol. 1994;152:334–7.
3. Ahlering TE, Gholdoian G, Skarecky D, Weinberg AC, Wilson TG. Simplified technique with short and long term followup of conversion of an ileal conduit to an Indiana pouch. J Urol. 2000;163:1428.
4. Pahernik S, Stein R, Hohenfellner M, Thürhoff JW. Conversion from colonic or ileal conduit to continent cutaneous urinary diversion. J Urol. 2004;171:2293.
5. Hautmann RE, de Petriconi R, Schwarz J, Volkmer B. Single Center Experience with Secondary Urinary Diversion after Initial Radical Cystectomy and Primary Urinary Diversion. J Urol. 2016;195:406–12.
6. Helal M, Austin P, Spyropoulos E, Pow-Sang J, Persky L, Lockhart J. Evaluation and management of parastomal hernia in association with continent urinary diversion. J Urol. 1997;157:1630–2.
7. Mansson W. Editorial Comment, following: Ahlering TE, Gholdoian G, Skarecky D, Weinberg AC. Wilson TG. Simplified technique with short and long term followup of conversion of an ileal conduit to an Indiana pouch. J Urol. 2000;163:1428
8. Lockhart JL, Pow-Sang JM, Persky L, Kahn P, Helal M, Sanford E. A continent colonic urinary reservoir: Florida pouch. J Urol. 1990;144:864.
9. Welk B, Herschorn S, Law C, Nam R. Population based assessment of enterocystoplasty complications in adults. J Urol. 2012;188:464.

Index

A
Adipose stem cells (ASCs), 88–89
Adult stem cells, 88
Alvimopan, 19

B
Bladder Utility Symptom Scale (BUSS), 160
Bone marrow-derived MSCs (BM-MSCs), 88
Bowel complications
  fistulas, 111
  obstruction, 65, 110–111
  pouch perforation, 111
Bowel preservation, 176–178
Bowel segment, 57
Bowel-to-bowel anastomosis, 58
BUSS. *See* Bladder Utility Symptom Scale (BUSS)

C
Cancer, 111–112
CCUD. *See* Continent cutaneous urinary diversion (CCUD)
Cellular immunogenicity, 86
Continent cutaneous diversion (CCD)
  difficult catheterization, 137–138
  efferent channel, necrosis of, 137
  parastomal hernia, 136–137
  preventing complications, 130–131
  rates, 129–130
  stomal stenosis
    incontinence, 134
    overdistention, 133
    pouch stones, 136
    U-shaped vascularized flap, 134–135
  surgical technique, 131–132
  urinary incontinence, 132–133
Continent cutaneous urinary diversion (CCUD)
  advantages, 39
  complications, 53
  disadvantages, 39
  double T-pouch, 50–52
  Indiana pouch, 41–45
  patient selection, 40
  postoperative care, 53
  right colon pouch, 45–50
  surgeons' choice, 39–40
  surgical preparation, 41
Cystectomy, 101

D
Diarrhea, 179
Double T-pouch, 50–52

E
Embryonic stem cells (ESCs), 87
Enterocutaneous fistula, 66
External urethral sphincter (EUS), 25

F
Fistulas, 111

G
Genital-sparing cystectomy, 33

H
Hautmann pouch, 13
Health-related quality of life (HRQOL)
  assessment, 161
  body image, 159
  bowel function and dysfunction, 158
  BUSS, 160
  clinical and research perspective, 161–162

S. Daneshmand (ed.), *Urinary Diversion*, DOI 10.1007/978-3-319-52186-2

Health-related quality of life (HRQOL) (*cont.*)
- clinical application, 162, 164
- components, 159
- definition, 154
- framework, 154–156
- functional and metabolic complications, 153
- functional domains, 157
- future research areas, 162, 164
- in females, 158
- instruments, 160–161
- long-staging interest, 153–154
- meta-analysis, 162
- outcomes, 162–164
- physical function, 156
- psychometric evaluation, 159
- reconstructive surgery, 153
- sexuality and sexual health, 157–158

I

Ileal conduit, 1, 122–123

Ileal conduit diversion, complications
- anastomotic bowel leak, 66–67
- bowel obstruction, 65
- chronic acidosis, 75
- conduit necrosis, 67
- construction, 64
- postoperative ileus, 65
- radiographic imaging, 65
- after stoma maturation, 64
- stomal stenosis, 67–68
- symptomatic metabolic acidosis, 74–75
- terminal ileum, 75
- ureterointestinal strictures, 74

Incontinent stoma
- complications, 121–122
- ileal conduit, 122–123
- IRCC, 124
- ischemia, 123
- parastomal hernia
  - diagnosis, 124–125
  - incidence, 125
  - laparoscopic placement, 127
  - prevention, 125
  - prophylactic placement, 126–127
  - randomized trials, 127
  - repair, 126
  - risk factors, 125
- perioperative, 122
- RARC, 124
- stomal stenosis
  - hyperkeratosis, 128–129
  - incidence, 127–128
  - prevent retraction, 128
  - surgical management, 129

Indiana pouch, 41–45
- bowel continuity, 41
- CCD, 131, 133
- colonic segment, 41, 42
- ileal segment, 41, 43
- ileal-colonic segment, 41, 42
- imbricating sutures, 41, 44
- robotic radical cystectomy, 45
- ureterocolonic anastomoses, 44
- urinary re-diversion, 179

Induced pluripotent stem cells (iPSCs), 88

Insulin-like growth factor-1 (IGF-1), 90

Internal urethral sphincter (IUS), 25

International Robotic Cystectomy Consortium (IRCC), 124

Intestinal bowel obstruction, 110–111

Intracorporeal ileal conduit. *See* Marionette technique

IRCC. *See* International Robotic Cystectomy Consortium (IRCC)

L

Levator ani muscle (LAM), 25–26, 143–145

M

Marionette technique. *See also* Robot-assisted radical cystectomy (RARC)
- bowel segment, 57
- bowel-to-bowel anastomosis, 58
- Marionette Stitch, 57
- stoma, 58
- ureteroileal anastomosis, 57–58

Mesenchymal stem cells (MSCs), 86

N

Nerve-sparing radical cystectomy, 28–33

Nutritional and metabolic complications
- altered sensorium, 113–114
- bone metabolic, 114
- electrolyte and acid-base disturbances, 113
- infection, 115
- renal function deterioration, 115–116
- short bowel syndrome, 112
- urolithiasis, 114–115

O
Orthotopic bladder substitution (OBS)
  in women
    anatomical considerations, 25–26
    functional prerequisites, 27–28
    genital-sparing cystectomy, 33
    nerve-sparing radical cystectomy, 28–33
    oncological prerequisites, 26–27
    treatment, 33–34
  RARC, 56
Orthotopic urinary diversion
  in men
    discharge and postoperative care, 20
    functional outcomes, 20–21
    Hautmann neobladder, 13
    in elderly patients, 21–22
    modified Studer pouch, 13–15
    neobladder reconstruction, 12, 22
    pain management, 20
    perioperative management, 17–19
    postoperative management, 19–20
    preoperative preparation, 12
    T pouch modification, 15–18
  in women
    anatomical considerations, 25–26
    functional prerequisites, 27–28
    genital-sparing cystectomy, 33
    nerve-sparing radical cystectomy, 28–33
    oncological prerequisites, 26–27
    treatment, 33–34

P
Parastomal hernia
  CCD, 136–137
  CT scan, 107
  etiology of, 70
  incontinent stoma (*see also* Incontinent stoma)
    diagnosis, 124–125
    incidence, 125
    laparoscopic placement, 127
    prevention, 125
    prophylactic placement, 126–127
    randomized trials, 127
    repair, 126
    risk factors, 125
  management, 108
  prophylactic mesh placement, 70–73
  risk factors, 108
  subtypes, 108
Patient selection
  absolute contraindications, 2
  cancer-related factors, 4–5
  CCUD, 40
  locally advanced tumor stage, 6
  relative contraindications, 2–4
  shared decision-making, 6–8
Pelvic floor muscles (PFM)
  behavioral modifications, 150–151
  biofeedback and PT modalities, 147, 149–150
  dysfunction, 144
  iliococcygeus, 143, 144
  levator ani, 143–145
  pubococcygeus, 143, 144
  puborectalis, 143, 144
  return to sexual function, 150–151
  training program, 146–148
  urinary incontinence, 145–146
Postoperative ileus, 65
Prior radical prostatectomy, 22

R
Radical cystectomy (RC), 12, 17, 22
  contemporary indications, 173–175
  indications, 172–173
  long-term voiding function, 103–104
  OBS, 26–27
  robot-assisted approach
    closure of neobladder, 60
    intracorporeal ileal conduit, 57–58
    modified Studer neobladder, 59–60
    neobladder-urethral anastomosis, 59
    outcomes, 60
    positioning and port placement, 56
    preoperative preparation, 56
    ureteral-neobladder anastomosis, 60
RARC. *See* Robot-assisted radical cystectomy (RARC)
Regenerative tissue uses. *See* Tissue-engineered urinary diversions (TEUDs)
Renal function deterioration, 115–116
Right colon pouch
  appendix, 45, 46
  approach for surgeons, 45
  colonic segment, 47
  ileal mesenteric division, 45
  medial colon, 47
  mesenteric window, 46
  stoma site, 47
  Yang-Monti channel, 47, 49, 50

Robot-assisted radical cystectomy (RARC)
closure of neobladder, 60
incontinent stoma, 124
intracorporeal ileal conduit
bowel segment, 57
bowel-to-bowel anastomosis, 58
Marionette Stitch, 57
stoma, 58
ureteroileal anastomosis, 57–58
modified Studer neobladder, 59–60
neobladder-urethral anastomosis, 59
outcomes, 60
positioning and port placement, 56
preoperative preparation, 56
ureteral-neobladder anastomosis, 60
Robotic radical cystectomy, 45

S
Scaffolds
acellular matrices, 82–83
biomaterials, 82
collagen I-based, 83
ideal, 82
materials, 83
seeded collagen, 84, 85
synthetic, 83–84
Second urinary diversion (UD). *See* Urinary re-diversion
Short bowel syndrome, 112
Small intestinal submucosa (SIS), 91
SMCs. *See* Smooth muscle cells (SMCs)
Smooth muscle cells (SMCs), 84, 87
Stem cells, 87–88
Stoma, 58, 64
classification, 68–69
complications
bowel segment elongation, 106–107
in continent cutaneous diversion, 129–138
incontinent, 121–129
parastomal hernia, 107–109
stomal stenosis, 106
radiologic evaluation, 68
Stomal stenosis, 106
CCD
incontinence, 134
overdistention, 133
pouch stones, 136
U-shaped vascularized flap, 134–135
incontinent stoma
hyperkeratosis, 128–129
incidence, 127–128
prevent retraction, 128
surgical management, 129
Stress urinary incontinence (SUI), 146
Studer neobladder, 59–60
Studer pouch, 13–15

T
T pouch, 15–18
Tissue-engineered urinary diversions (TEUDs)
cells, 84
adipose stem, 88–89
smooth muscle, 87
stem, 87–88
urine-derived stem cells, 89
urothelial, 86–87
clinical experience, 90–91
components, 82
gastrointestinal tract, 81
growth factor, 89–90
ideal cell type, characteristics
cell proliferative capacity, 86
cellular immunogenicity, 86
harvest, 85
SMCs, 84
UCs, 84
preclinical experiences, 91
scaffolds
acellular matrices, 82–83
biomaterials, 82
collagen I-based, 83
ideal, 82
materials, 83
seeded collagen, 84, 85
synthetic, 83–84
vascularization, 90

U
UCs. *See* Urothelial cells (UCs)
Ureteral reimplantation, 178
Ureteral strictures, 109–110
Ureteroileal anastomosis, 57–58
Ureterosigmoidostomy, 111–112
Urinary incontinence (UI)
CCD, 132–133
PFM, 145–146
Urinary re-diversion, 171. *See also* Radical cystectomy (RC)
bowel preservation, 176–178
indications, 173, 174
intestine-ureteral anastomosis, dilemma of, 175–176
surgical/technical aspects, 178–180

Urine-derived stem cells, 89
Urolithiasis, 114–115
Urothelial cells (UCs), 84, 86–87

V
Vascular endothelial growth factor (VEGF), 90
Voiding dysfunction, in orthotopic neobladder construction, 102
failure to empty, 104–105
failure to store, 102–104
management, 105–106
risk factors, 104–105

W
Wilson–Cleary framework, 155