REVIEW

The role of cystectomy for non-malignant bladder conditions: a review

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Introduction: *Few studies have adequately addressed the indications, efficacy, and quality-of-life for cystectomy performed for non-malignant bladder conditions. Patients with debilitating non-malignant bladder conditions who have failed all previous conservative therapies may undergo various forms of cystectomy, including partial, simple or radical cystectomy. We provide a review of the current literature and recommendations for cystectomy for various non-malignant bladder conditions.*

Materials and methods: *A systematic review of MEDLINE was conducted to find prospective and retrospective studies using the keywords "cystectomy", "benign", and "non-malignant". Articles were reviewed and triaged, background articles were added as supplements, leaving a final review of 67 papers.*

Results: *Data from the final review suggests that common benign indications for cystectomy are interstitial cystitis/painful bladder syndrome (IC/PBS), neurogenic bladder, hemorrhagic/radiation cystitis, infectious diseases of the bladder and miscellaneous conditions of the bladder such as endometriosis and total refractory incontinence. The most common perioperative complications include urinary tract and wound infections. Efficacy of cystectomy in patients with IC/PBS is greater than 80%, while efficacy in patients with neurogenic bladder is greater than 90%. Finally, improved urinary quality-of-life has been demonstrated in patients with neurogenic bladder post-cystectomy.*

Conclusion: *Cystectomy for non-malignant conditions can be considered for patients who have failed previous conservative therapy. The limited data in existence suggests fertility can be adequately preserved after cystectomy in younger males. The data regarding the forms of urinary diversion suggests no significant advantage between any of the major forms of urinary diversion. Finally, while newer pharmacologics and technological advances are widely used in the treatment of various benign urological conditions, their role in preventing or treating refractory benign bladder conditions have not been fully characterized.*

Key Words: interstitial cystitis, neurogenic bladder

Introduction

Cystectomy is a widely employed surgical procedure for removal of the urinary bladder. The procedure has been in practice since the late 19th century for malignant bladder diseases; however, it wasn't until the latter part of the 20th century when cystectomy became an acceptable surgical option for patients with non-malignant processes affecting the urinary bladder.[1] Even with improvements in outcomes, the mortality of cystectomy today is between 1%-2%,[1] and the perioperative morbidity of this procedure remains high. There is limited data regarding perioperative morbidity and mortality rates for simple or partial cystectomies, derived mainly from small case series. Rowley and colleagues examined the late complication rates of simple cystectomy and found a 39% late complication rate in 23 patients who underwent this procedure for non-malignant bladder conditions.[2]

The most common non-malignant indications for cystectomy include interstitial cystitis/painful bladder syndrome (IC/PBS), neurogenic bladder, hemorrhagic/radiation cystitis, infectious diseases of the bladder, and other miscellaneous conditions such as bladder endometriosis and refractory total incontinence, Table 1. Medical management is the first line treatment for these conditions; however, in cases refractory to medical therapy, surgical management

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TABLE 1. **Indications for cystectomy for non-malignant bladder conditions**

Interstitial cystitis/painful bladder syndrome
Neurogenic bladder
Hemorrhagic/radiation cystitis
Infectious diseases of the bladder
Endometriosis
Refractory genitourinary fistulae

includes partial, simple, and radical cystectomy. If the primary outcome is urinary diversion, it is important to remove a defunctionalized bladder due to complication rates as high as 60%, and a subsequent cystectomy rate of 20% due to conditions such as pyocystis, persistent hematuria, pelvic pain, and even increased rates of malignancy.[3] More recently, Lawrence and colleagues reported a 7% complication rate related to retaining a defunctionalized bladder and suggested that a concomitant cystectomy is not necessary for patients who require urinary diversion, at least for intractable urinary incontinence.[4]

Patients undergoing cystectomy for non-malignant bladder conditions face many of the same challenges as patients undergoing radical cystectomy for malignant urothelial carcinoma of the bladder. Stein and colleagues examined the long term results of 1054 patients undergoing radical cystectomy and report the perioperative morbidity to be approximately 14% in both males and females.[5] In a more recent study, Prasad and colleagues re-examined the major 30-day postoperative morbidities in 154 patients undergoing radical cystectomy by a single surgeon and found a rate of 26%.[6] Additionally, the two most common postoperative complications include myocardial infarction and pulmonary embolism, followed closely by anastomotic leaks.[6] These numbers, however, are for patients undergoing radical cystectomy, most commonly for urothelial carcinomas.

There have been many studies that have examined the effectiveness of different types of urinary diversions, and this review will address the existing data. Additionally, patients undergoing cystectomy for non-malignant conditions may be younger than those with bladder cancers, and fertility preservation may be an important concern.

Cystectomy for IC/PBS

Originally defined by the Society of Urodynamics, Female Pelvic Medicine, & Urogenital Reconstruction (SUFU) and later adopted by the American Urological Association (AUA), interstitial cystitis is "an unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than six weeks duration, in the absence of infection or other identifiable causes."[7,8] The hallmark feature of IC/PBS is suprapubic discomfort related to the urinary bladder, but may also include diffuse pelvic pain and or pain within the lower back and abdomen.[8] Cystoscopic features for IC/PBS may include the "Hunner" lesion,[9] but this submucosal ulcer is identified in less than 7% of patients with IC/PBS.[10]

Due to its irreversibility, AUA guidelines state that surgical treatment of IC/PBS is only appropriate after all conservative treatment options have been exhausted or if the patient is found to have a small fibrotic bladder. Accordingly, surgical management has received a recommendation Grade C (based on level III evidence) from the AUA.[8] The European Association of Urology (EAU) also recommends surgical management only after a thorough evaluation and failure of conservative treatment; however, a Grade A recommendation (based on level I evidence) was ultimately assigned for cystectomy in this setting.[11]

There are very limited studies that have examined surgical management of IC/PBS, most of which are retrospective analyses with few patients. In 1998, Linn and colleagues retrospectively analyzed 31 patients with IC/PBS treated with either supratrigonal or subtrigonal cystectomy with Mainz pouch orthotopic bladder substitution.[12] Patients that underwent supratrigonal cystectomy were followed for an average of 32 months while patients that underwent subtrigonal cystectomy were followed for an average of 94 months. The supratrigonal method resects the bladder above the ureteral orifices while the subtrigonal method resects the bladder to within 1 cm-1.5 cm of the bladder neck and requires ureteral reimplantation. Success was defined by improvement of functional bladder capacity as measured by a voiding protocol 3 to 6 months postoperatively, while voiding frequencies and symptom alleviation were measured by a questionnaire. Both groups had clinically and statistically significant improvements in bladder capacity and daytime/nighttime frequency. Fourteen of 17 (82%) patients who had undergone subtrigonal cystectomy were completely symptom free versus 6/6 (100%) patients who had undergone supratrigonal cystectomy. The authors concluded that both methods of cystectomy provided similar relief of symptoms, but patients who underwent supratrigonal cystectomy had improved urinary rehabilitation.

Similarly, van Ophoven and colleagues reported statistically significant improvement in voiding

frequencies, bladder capacity and symptom scores in patients with IC/PBS who had undergone trigone-preserving cystectomy with substitution enterocystoplasty.[13] The authors reported a success rate of 83% (15/18 patients, mean follow up of 57 months), as defined by improvements in functional bladder capacity, voiding frequencies, postoperative voiding modality as well as patients' assessment of satisfaction with the procedure. The idea of trigone-preserving surgery and the potential for persistent pain has been addressed in the past. Christmas and colleagues described up to a 66% failure rate with supratrigonal cystectomy.[14] However, in a follow up study, Christmas and colleagues reported a 100% success rate for subsequent cystectomy with urinary diversion for patients who had failed previous surgical treatment including prior supratrigonal cystectomy.[14] Success in this study (mean follow up 30 months) was purely based on subjective pain relief. Advantages to trigonal preservation are many, however, and include avoiding the pitfalls of ureteral reimplantation as well as preservation of the autonomic innervation to the bladder neck necessary for continence after bladder reconstruction.[15]

It is worthwhile to note that surgical success may be related to the subtype of IC/PBS. First reported in 1998, Peeker and colleagues surmised that surgical outcomes of IC/PBS may differ according to whether the IC/PBS is of the classic "Hunner ulcer" type versus the non-ulcerative type.[16] In his study of 13 patients, ten with classic IC/PBS and three with the non-ulcerative type, Peeker reported 100% improvement with supratrigonal cystectomy in patients with classic IC/PBS and no improvement in all three patients with the non-ulcerative IC/PBS. This is corroborated by Rossberger and colleagues study where the author retrospectively evaluated the outcomes of 47 patients with IC/PBS.[17] In his study, 34 patients were identified as having the classic ulcerative subtype of IC/PBS and 13 patients with a non-ulcerative form. For patients with classic IC/PBS, 28/34 patients (82%) had symptom relief with the first surgical procedure with the remaining 4/6 obtaining symptom relief with subsequent surgical procedures (urinary diversion, cystectomy and or transurethral ulcer resection). On the other hand, only 3/13 patients (23%) with non-ulcerative IC/PBS obtained relief with their first surgical procedure. As such, a preoperative cystoscopic evaluation may be an important tool that can be used for patient counseling regarding potential surgical outcomes.

Patients should be informed that surgical interventions for IC/PBS may not improve their pain. Elzawahri and colleagues analyzed 11 patients with IC/PBS who had previously undergone enterocystoplasty (n = 7) or cystectomy with continent urinary diversion (n = 4) but continued to complain of persistent pelvic pain.[18] Patients then underwent takedown of the enterocystoplasty or continent diversion and a subsequent construction of an ileal conduit. The authors analyzed whether or not re-tubularization of the same intestinal segments would result in persistent pain and found that 10/11 patients (91%) reported relief of symptoms. As such, the authors reported that use of retubularized bowel segments for ileal conduit construction after initial failed surgical management for IC/PBS may be appropriate. Conversely, Luchey and colleagues reported a case series of two patients who had undergone cystectomy with urinary diversion persisting with pain whom did not achieve pain alleviation until a subsequent urethrectomy was performed.[19]

Objective outcome measures after cystectomy for benign conditions include functional bladder capacity and voiding frequencies. Post-void residuals have also been used as a measure of improvements in LUTS.[13] Subjective outcomes related to improvements in pain and quality-of-life are best assessed with questionnaires.

More recently, new treatment options have become available for IC/PBS, such as onabotulinum toxin A and sacral neuromodulation. In a review of studies published between 1950-2011, Srivastava and colleagues reported only one randomized controlled trial assessing pain relief with sacral neuromodulation in patients with IC/PBS, which showed a decrease in pain score by 49%.[20] According to the EAU, level I evidence supports the use of onabotulinum toxin A for the treatment of IC/PBS.[21] However, the EAU also conceded that the current heterogeneity of the pharmacological market for IC/PBS creates an environment where definitive conclusions are lacking.[22] It is still unknown how these newer treatment modalities will affect the cases of refractory IC/PBS and how many will eventually need cystectomy.

Key points regarding cystectomy for IC/PBS are shown in Figure 1.

- IC/PBS is defined as an unpleasant sensation perceived to be related to the urinary bladder.
- Supra-trigonal cystectomy may be as effective as sub-trigonal cystectomy for IC/PBS.
- Patients with the ulcerative form of IC/PBS may have improved surgical outcomes.
- Patients may have persistent pain despite surgical intervention.

Figure 1. Key Points: Cystectomy for interstitial cystitis/painful bladder syndrome (IC/PBS).

Cystectomy for neurogenic bladder

Conditions that can lead to neurogenic bladder dysfunction include congenital anomalies such as meningomyelocele, spina bifida, and acquired diseases/trauma of the central nervous system such as spinal cord injury, multiple sclerosis, stroke and Parkinsonism.[23] The sequelae of untreated neurogenic bladder dysfunction include upper tract damage, recurrent urinary tract infections, breakdown of skin and fistulaization due to urinary leakage and the social ramifications of incontinence.[23,24] The conservative management of neurogenic bladder includes patient education, pharmacotherapy, timed voiding, incontinence pads, and catheterization. The preferred method of management of neurogenic bladder is intermittent catheterization.[23] Surgical management of neurogenic bladder has also been described, but the type of surgery depends on the nature of bladder dysfunction (detrusor underactivity/overactivity versus incomplete emptying versus sphincteric insufficiency) and includes sacral nerve stimulation, artificial urinary sphincters, augmentation cystoplasty, ileovesicostomy, and cystectomy with urinary diversion.[23,25]

Indications for urinary diversion in the patient with neurogenic bladder include upper-tract damage from high-pressure voiding, urethro-cutaneous fistulas, perineal ulcers and recurrent infections.[26] Additionally, urinary diversion is usually performed with a concomitant cystectomy due to complications of retaining a defunctionalized bladder.[3]

The success of cystectomy and urinary diversion for patients with neurogenic bladder has been studied in both young adults and older individuals. Over a 30 year period, Stein and colleagues analyzed 129 children and young adults with neurogenic bladder who underwent cystectomy and urinary diversion (colonic conduit 46%, orthotopic bladder substitution 9%, and continent Mainz pouch 45%) and found a 97% upper tract preservation rate in patients with colonic conduits or Mainz pouches, and 95% upper tract preservation in patients with orthotopic bladder substitutes.[27]

Because spinal cord injury comprises a major portion of patients presenting with neurogenic bladder, several groups have analyzed varying techniques of surgical management, including enterocystoplasties, supratrigonal cystectomies and simple cystectomies with subsequent analysis of urinary function and quality-of-life in this patient population. Gobeaux and colleagues have described supratrigonal cystectomy with Hautmann pouch for patients with neurogenic bladder (61 patients with neurogenic detrusor overactivity subtype) and reported 90% and 74% achievement of partial or total continence, respectively, over a mean follow up of almost 6 years.[28]

Over an 11 year period, Cheng and colleagues identified 2569 patients with acute traumatic spinal cord injuries in a Urology spinal cord unit.[29] While 21 patients (0.8%) received enterocystoplasties, only 14 patients (0.5%) with neurogenic bladder required cystectomies. Of these 14, five (36%) required cystectomies for non-malignant reasons, including high-pressure voiding, urethro-cutaneous fistulas, and recurrent urosepsis.

Quality-of-life is an important factor in the decision to undergo cystectomy for the management of intractable neurogenic bladder. Using the PGI-I scale,[30] a seven-point validated survey to evaluate quality-of-life as it relates to urinary function, Cheng et al reported a 2.4 unit improvement of urinary quality-of-life in a benign cohort requiring cystectomy.[29] Guillotreau and colleagues analyzed the urinary and overall quality-of-life changes associated with cystectomy and ileal conduit by using two validated surveys, Qualiveen (urinary quality-of-life) and SF36-v2 (general quality-of-life) pre- and 6 months post-cystectomy + ileal conduit.[31] In his prospective cohort of 48 patients (multiple sclerosis 79%, spinal cord injury 15%, other 6%), Guillotreau et al reported a significant improvement of urinary quality-of-life but no improvement of overall quality-of-life. The Qualiveen survey has also been used in patients with multiple sclerosis with end-stage neurogenic bladder requiring cystectomy and ileal conduit. Legrand and colleagues applied the Qualiveen survey to 53 patients with multiple sclerosis and reported a significant improvement in post-cystectomy urinary quality-of-life.[32]

Key points regarding cystectomy for neurogenic bladder are shown in Figure 2.

- The preferred method for management of neurogenic bladder is intermittent catheterization.
- Indications for urinary diversion in the patient with neurogenic bladder include upper tract damage from high pressure voiding, urethra-cutaneous fistulae, perineal ulcers, and recurrent infections.
- Cystectomy can improve urinary quality-of-life in patients with neurogenic bladder.

Figure 2. Key Points: Cystectomy for neurogenic bladder.

Cystectomy for hemorrhagic/radiation cystitis

Hemorrhagic cystitis is a broad term used to describe hematuria accompanied by lower urinary tract symptoms such as frequency, urgency and dysuria. It may be caused by trauma, infection, or as a result of treatment such as chemotherapy and radiation. When caused by radiation, it is often termed "radiation cystitis" and is commonly encountered in patients with prostate cancer who undergo radiation as primary therapy.[33] Hemorrhagic cystitis can be further classified as acute or chronic.

Acute hemorrhagic cystitis is frequently seen in the pediatric population and highly associated with viral infections typically caused by adenovirus.[34] Additionally, immunocompromised patients including those who have undergone bone marrow transplantation or other organ transplants are also susceptible to viral hemorrhagic cystitis. The virus isolated in these patients is usually BK Polyoma virus.[35]

Chronic hemorrhagic cystitis can be associated with drug-induced causes as well as post-radiation. Cyclophosphamide, an alkylating agent used for treating both malignant and non-malignant conditions, is a frequent cause of drug-induced hemorrhagic cystitis[36] with a reported incidence of 20%-25%.[37] The administration of Mesna has been proposed to prevent cyclophosphamide-induced hemorrhagic cystitis; however, the outcomes may be equivalent to simple hyperhydration.[38] Conversely, radiation cystitis is a late direct sequela of radiation therapy for prostate and cervical malignancies that occurs as early as 90 days after treatment. It may also present as late as 10 years later following treatment.[39] Radiation damage may induce an obliterative endarteritis leading to mucosal ischemia, ulceration and bleeding as shown in Figure 3.[40] A literature review of 309 articles by Crew and colleagues estimate an incidence of less than 5% for severe hematuria after radiation therapy.[41]

Surgical treatment for hemorrhagic and radiation cystitis may be considered in patients who have failed conservative therapy. Withdrawal of the offending agent, continuous bladder irrigation, intravesical instillations, hydrodistension, and hyperbaric oxygen therapy are often attempted before cystectomy is considered.[41] In a retrospective analysis of 100 patients with cyclophosphamide-induced hemorrhagic cystitis, Stillwell and colleagues noted that five patients (5%) required cystectomy for intractable hematuria.[36] Cystectomy with neobladder substitution may be an acceptable form of surgical management;[42] however, subtotal cystectomy with the preservation of the bladder neck and urethra may be favored for preservation of urinary continence and improved quality-of-life.[43] Laparoscopic approaches have been performed, but surgeons should be aware of the difficulty identifying surgical planes in patients that have undergone radiation therapy for prostate cancer. Fergany and colleagues proposed that dissection of the posterior prostate should not occur until certain landmarks such as the obliterated umbilical ligaments along the lateral planes and the endopelvic fascia have been identified.[44]

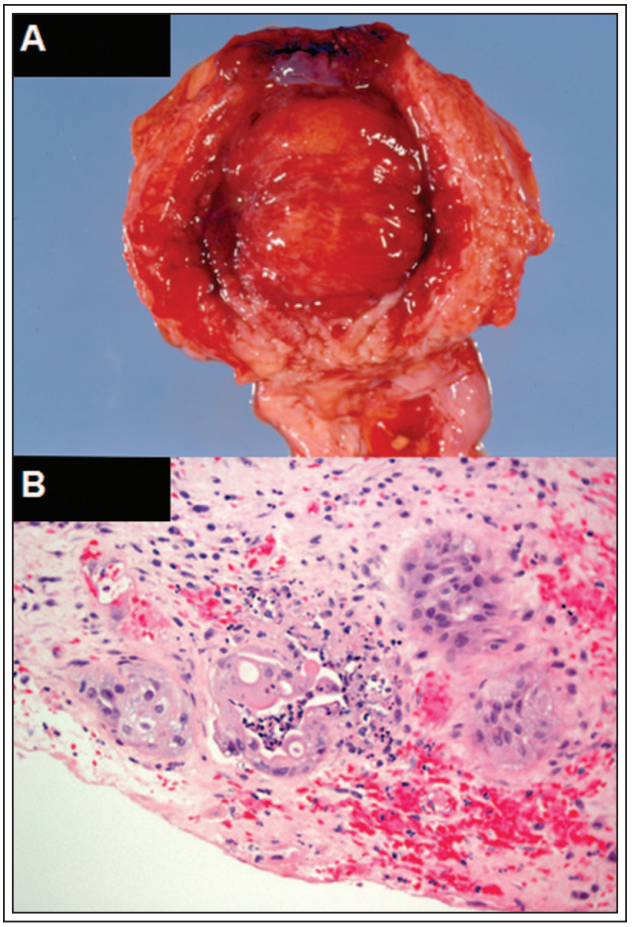

Figure 3. **(A)** Gross photograph of a urinary bladder showing diffusely hemorrhagic, smooth mucosa with no focal lesions, characteristic of hemorrhagic cystitis. **(B)** Microscopic image of radiation cystitis showing partially denuded surface urothelium and lamina propria with extravasated red blood cells and inflammation. There is radiation atypia within the urothelium, characterized by enlarged cells with abundant cytoplasm and vacuolated, degenerating appearing nuclei (hematoxylin and eosin stain, x 200). Images: courtesy of VCUHS Department of Pathology Archives.

- Acute hemorrhagic cystitis is most commonly caused by viral infections such as BK polyoma and adenoviruses.
- Chronic hemorrhagic cystitis is most commonly caused by radiation and chemotherapeutic agents such as cyclophosphamide.
- Approximately 5% of patients with severe hemorrhagic radiation cystitis will require cystectomy.

Figure 4. Key Points: Cystectomy for hemorrhagic cystitis.

Technological advances in radiation therapy such as intensity-modulated radiation therapy (IMRT) direct small beams of radiation to precisely target a tumor and may decrease the incidence of genitourinary toxicities. Spratt and colleagues examined the long term survival and toxicities for patients who underwent IMRT for localized prostate cancer.[45] Genitourinary toxicity was graded according to the Common Terminology Criteria for Adverse Events (CTCAE) with hemorrhagic cystitis reported as late-grade 3. Over the course of 7 years, 1002 patients were treated to a dose of 86.4 Gy using a 5-7 field IMRT technique and only 2.1% had a late-grade 3 genitourinary toxicity consisting of hemorrhagic cystitis.[45] Cystectomy for refractory hemorrhagic radiation cystitis should be reserved for patients with CTCAE grade 4 including perforations, fistulizations, or refractory hematuria.[46] There are no existing studies which have examined the percentage of patients post-IMRT who require cystectomy, nor are there any recommendations on bowel segments appropriate for urinary reconstruction post-IMRT.[47]

Key points regarding cystectomy for hemorrhagic cystitis are shown in Figure 4.

Cystectomy for infectious diseases of the bladder

Genitourinary tuberculosis and bilharziasis are infectious processes which can result in severe urinary dysfunction. These agents continue to be endemic in certain developing nations and the late diagnosis of these conditions leads to complications which may eventually obliterate bladder function and or destroy the upper tracts.

Up to 30% of all extra-pulmonary tuberculosis may present as genitourinary tuberculosis,[48] and the kidney is secondarily seeded after the mycobacterium tuberculosis is absorbed in the bloodstream.[49] Most ureteral and bladder lesions are secondary to renal shedding.[49] The initial acute bladder lesions of genitourinary tuberculosis appear as reddened, inflamed and edematous lesions around the ureteral orifices which later involve the entire bladder mucosa and may be indistinguishable from an acute cystitis.[49] Tuberculosis of the bladder may also be indistinguishable from interstitial cystitis.[50] Chronic genitourinary tuberculosis of the bladder can lead to bladder scarring, wall thickening, fibrosis and decreased compliance.[49,50]

In a case review of 174 patients, Gokce and colleagues reported the most common symptoms of genitourinary tuberculosis to be flank pain (44%), dysuria (43%), hematuria (40%) and frequency (34%).[51] All patients were treated with triple-therapy (isoniazid, rifampin and ethambutol). Nineteen patients ultimately required nephrectomy but only two required ileal conduit urinary diversion.[51] The surgical management of tuberculosis of the bladder may include bladder augmentation or cystectomy and bladder replacement; however, these are only indicated in cases of a severely retracted bladder or severe reflux that damages the upper tracts.[52]

Another genitourinary infection, bilharziasis, is caused by Schistosoma hematobium and affects over 100 million individuals worldwide.[53] The human immune reaction to the bilharzial eggs results in healing by fibrosis and may progress to mucosal, submucosal or muscular lesions.[54] These may include chronic ulcers, granulomas, leukoplakia, strictures, contracted bladder and squamous metaplasia leading to squamous cell carcinoma.[54] Radical cystectomy for bilharziasis-induced squamous cell carcinoma of the bladder has been extensively described in the literature, but there is limited information on surgical management for benign lesions of the bladder caused by bilharziasis. Augmentation cystoplasty is indicated in a severely contracted bladder (< 100 mL);[55] however, subtotal cystectomy combined with ileocystoplasty has also been previously described for bladder lesions coexisting with a contracted bladder.[56]

Cystectomy for bladder endometriosis

In certain instances, infiltrative bladder endometriosis may be considered an indication for cystectomy; however, this is dependent on the depth of infiltration into the bladder and partial cystectomy is most commonly employed. The prevalence of endometriosis of the urinary tract is about 1% and is defined as infiltration of the endometrial tissue into the detrusor muscle.[57] Laparoscopic partial cystectomy for focal

endometriosis was described by Nezhat and colleagues in two patients with bladder endometriosis in 1993.[58] Subsequently, these authors published a follow up series of 15 patients over the course of a 10 year period[59] with acceptable outcomes, demonstrating the feasibility of this approach. It has been previously emphasized that a laparoscopic partial cystectomy should only be attempted if the lesion is distant from the ureters, trigone and bladder neck.[60] Cystoscopy is commonly employed if a mucosal lesion is suspected.[61] In a series of 21 patients with endometriosis of the bladder, Kovoor and colleagues reported ten patients who required a partial cystectomy (48%). Major complications related to bowel resection occurred in three patients (14%), but there were no reported disease recurrence.[61]

Complications of cystectomy for benign bladder conditions

In 2013, Cohn and colleagues investigated the 30 and 90 day perioperative outcomes of cystectomy and urinary diversion for benign diseases of the urinary system in their cohort of 26 patients.[62] Similar to the previously described studies, the patients in Cohn et al's study who had to undergo cystectomy had conditions such as infection, fistulas, hematuria, incontinence, pain or neurogenic bladder. The authors reported a 73% complication rate within the first 30 days, with the most common complications being urinary tract infections (23%) and wound infections (23%). Seventy-three percent of these patients later had resolution of their original urological complication. Interestingly, the authors noted that cystectomy for radiation-induced fistulas were significantly more likely to result in complications (100%) versus those with non-radiation induced fistulas (78%). This is in comparison to patients who underwent cystectomy and urinary diversion for neurogenic bladder, whose complication rate was much lower (44%).

Special considerations: fertility preservation in men

Most cystectomies performed today are for malignant urothelial carcinoma of the bladder, which occurs primarily in older individuals in whom the preservation of fertility is not desired. As such, there exist very few studies that have examined the effects of cystectomy on fertility in men. A traditional or radical cystectomy requires a concurrent prostatectomy with removal of the entire prostate, seminal vesicles and vas deferens, precluding conception through natural means. Newer, fertility sparing approaches have been described for younger patients undergoing cystectomies who request fertility preservation.

Spitz and colleagues examined the effects of a "radical" cystectomy on fertility in younger males (median age 26) requiring removal of their bladder and prostates for nonurothelial carcinomas.[63] Outcomes measured included erectile function, ejaculatory ability, and offspring produced. The surgical approach preserved the ejaculatory ducts and involved transection of the prostate at an oblique angle to spare the posterior prostate, and thus, the nerves necessary for erectile function.[63] In this four patient series, all patients regained erectile function immediately post-operatively and 75% were able to ejaculate anterograde. In addition, one patient fathered a child, demonstrating the ability to preserve fertility.

In a more radical approach, Salem and colleagues described a technique originally used for younger males (n = 4, median age 45) with invasive transitional cell carcinoma of the bladder who wanted to preserve their fertility.[64] Because these individuals had muscle invasive disease, a radical surgical approach was required. To provide the continuity for sperm transit, the vas deferens were preserved and reanastomosed to the bulbar urethra in the perineum. Salem and colleagues reported that 50% of patients were able to ejaculate anterograde, of which one was able to father a child. These two studies described fertility preservation in radical surgical approaches. Unfortunately, there are currently no studies that have examined fertility preservation in patients undergoing cystectomy for non-malignant conditions. It is thus a logical conclusion to surmise that the absolute bare minimum to preserve fertility in patients receiving cystectomy for any indication is preservation of the vas and adequate reanastomosis to allow for sperm transit.

Special consideration: urinary diversion after cystectomy

There are many types of urinary diversions and data is conflicting as to whether there is a preferred method for patients who require a cystectomy. Over the last decade, orthotopic bladder substitution has become increasingly popular, and, as a result, numerous comparative studies have been performed. Nabi and colleagues reviewed 3370 abstracts from January 1990 to January 2003, with 32,795 patients included in their analysis. They concluded that there were no differences between a continent diversion versus a conduit diversion and that there were no differences between a diversion using segments of ileum versus using segments of colon.[65] In an updated systematic review that expanded on this

initial study and included 46,921 patients, the authors concluded that there was no evidence to support the superiority of any type of diversion.[66]

In 2012, The Cochrane Collaboration used more selective inclusion criteria by including only randomized or quasi-randomized controlled trials to address the same issue. In their study, Cody and colleagues included studies that examined the different types of urinary diversion as well as the type of intestinal segment in patients who required urinary diversion after cystectomy for malignant as well as non-malignant indications.[67] Only five studies totaling 355 patients met their inclusion criteria and the review did not find any substantial evidence as to the superiority of a continent vs. incontinent diversion in relation to frequency of urinary tract infections, upper tract preservation and daytime/nighttime incontinence.[67] While one small study of ileal segment vs. an ileocolonic segment for nocturnal incontinence achieved statistical significance in favor of the ileal segment, the authors remained skeptical.[67] Regardless, additional immeasurable factors such as patient preference and the variety of disease processes make this a very difficult topic to quantify.

Conclusion

Due to its irreversibility, high morbidity and mortality rate, cystectomy for non-malignant conditions should only be considered if patients have failed all conservative therapies. Decisions regarding the surgical approach should take into consideration the individual patient needs and the type of bladder pathology. In addition, the decision to perform a cystectomy should address the known safety and efficacy of the procedure as well as the potential to improve quality-of-life. Common non-malignant indications for cystectomy include IC/PBS, neurogenic bladder, radiation/hemorrhagic cystitis, infectious diseases of the bladder, bladder endometriosis and total refractory incontinence. For patients wishing to preserve their fertility, even radical surgical approaches are feasible. Additionally, there is no definitive data demonstrating the superiority of any particular type of urinary diversion. Finally, although there is widespread use of newer pharmacologics and technology in the treatment of various benign urological conditions, their role in preventing or treating refractory benign bladder conditions have not been fully characterized. □

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