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# Augmentation cystoplasty in neurogenic bladder

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The aim of this review is to update the indications, contraindications, technique, complications, and the tissue engineering approaches of augmentation cystoplasty (AC) in patients with neurogenic bladder. PubMed/MEDLINE was searched for the keywords "augmentation cystoplasty," "neurogenic bladder," and "bladder augmentation." Additional relevant literature was determined by examining the reference lists of articles identified through the search. The update review of of the indications, contraindications, technique, outcome, complications, and tissue engineering approaches of AC in patients with neurogenic bladder is presented. Although some important progress has been made in tissue engineering AC, conventional AC still has an important role in the surgical treatment of refractory neurogenic lower urinary tract dysfunction.

#### Keywords: Augmentation; Bladder; Neurogenic urinary bladder

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## INTRODUCTION

Bladder augmentation cystoplasty (AC) is used in the adult population for neurogenic bladder dysfunction, as well as for inflammatory conditions such as tuberculosis cystitis that result in a severely contracted bladder, interstitial cystitis, and reconstruction of iatrogenic bladder injury [1].

AC can be performed by using different bowel segments. Enterocystoplasty is a generic terminology indicating that a bowel segment is used to increase the bladder capacity. Based on what part of the bowel is used a different terminology applies. The most frequently used bowel segment for AC is a detubularised patch of ileum [2]. Augmentation enterocystoplasty is a procedure with long-term durability and high rates of patient satisfaction but not without risk of complications and potential increased risk of malignancy [3,4].

Recent studies demonstrated that the use of bladder augmentation procedures has been declining in the United Kingdom and the United States [2,5]. Although the exact cause for this decline was unknown potential reasons might be multifactorial as shown in Table 1 [2,5].

Editorial comment on the study of Schlomer et al. asked a critical question 'whether this declining trend was beneficial by decreasing the risk of AC related complications, or were the urologists delaying an inevitable operation or risking irreversible upper tract damage' [5,6].

This review aims to update the indications, techniques, outcome, complications, and the future of AC.

After the first publication of canine model of AC by Tizzoni and Foggi in 1888, von Mikulicz described its first use in humans in 1889 [2]. The introduction of clean intermittent self catheterisation (CISC) by Lapides et al. [7], resulted in more widely use of AC. The first use of the gastric segment for bladder augmentation in humans was reported by Leong [8] in 1978. Apart from bowel segments and stomach other natural tissues such as free fascial grafts, peritoneum,

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omentum, lyophilised human dura, skin, and pericardium, materials such as gelatin, sponge, teflon, polyvinyl sponge, resin coated paper, collagen/polyglactin membrane and silastic were used with dissappointing results [2].

## INDICATIONS OF AUGMENTATION CYS-TOPLASTY

International Consultation on Incontinence (ICI) in 2012 stated that bladder augmentation was indicated wherever bladder capacity and compliance was reduced, or in the event of detrusor overactivity, when all conservative treatments (medical treatments, detrusor injections of botulinum toxin and/or neuromodulation of posterior sacral roots) have failed [9].

According to the European Association of Urology guidelines, bladder augmentation is a valid option to decrease detrusor pressure and increase bladder capacity, whenever more conservative approaches have failed [10].

Bladder augmentation was found to be beneficial especially with underlying neurological disorders such as spinal cord injury, multiple sclerosis and myelodysplasia [11-15].

## **CONTRAINDICATIONS**

Inflammatory and congenital bowel disease (Crohn disease, congenital anomalies such as cloacal exstrophy, and radiotherapy induced enteritis), or conditions resulting in short bowel (wide bowel resections), and malignant bladder disease constitute contraindications for AC (Table 2) [2]. Inability to perform CISC because of reduced manual dexterity or cognitive function is a relative contraindication for AC [15].

## **SURGICAL TECHNIQUE**

Various augmentation techniques using different gastrointestinal tract (GIT) segments, and the alternatives to GIT have been described.

#### 1. Use of gastrointestinal segments

AC can be performed by using several bowel segment which is called augmentation enterocystoplasty. The most widely used bowel segment for AC is a detubularised patch of ileum [2,14]. When ileum is not suitable for augmentation because of short ileal mesentery and obvious ileal pathology, sigmoid colon is the most common alternative [2,14]. The caecum can be used in its original tubular shape or as a detubularised patch which is called augmentation caecocystoplasty. Where bowel is unavailable or unsuitable, and in patients with metabolic acidosis, stomach is an alternative to bowel, and this procedure is called augmentation gastrocystoplasty [2,8]. Recently there has been an increase in reports of malignancy associated specifically with gastrocystoplasty [2,16]. Recent increase in the incidence of malignancy, complications of the haematuria-dysuria syndrome, and high incidence of reoperations has reduced the use of stomach for augmentation [2,16].

#### 2. Alternatives to GIT

There are alternatives to gastrointestinal flaps for AC such as autoaugmentation and ureterocystoplasty. Autoaugmentation was first described by Cartwright and Snow [17] who reported their series in children with neurogenic voiding dysfunction. The authors resected detrusor muscle off the bladder to create a low-pressure bladder diverticulum. Most of the published series of autoaugmentation consist of children, and the results are

Table 1. Potential causes of the decline in augmentation cystoplasty rates

High risk of complications Potential increased risk of malignancy Newer less invasive treatment alternatives Sacral neuromodulation Intradetrusor onabotulinum toxin A injection therapy Increased availability and earlier use of anticholinergics and clean intermittent catheterization

#### Table 2. Contraindications for augmentation cystoplasty

Inflammatory bowel disease (Crohn disease) Congenital bowel anomalies (cloacal exstrophy) Radiotherapy induced enteritis Conditions resulting in short bowel (wide bowel resections) Malignant bladder disease Inability to perform clean intermittent self catheterisation because of reduced manual dexterity or cognitive function

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generally poor [9] The technique of extensive detrusorectomy withy rectus muscle hitch and backing to prevent shrinkage and retraction was described [18,19].

When there is pre-existing dilated ureter, ureterocystoplasty may be an option for augmentation mainly for children with neurogenic bladder [9]. A study reporting the long-term follow-up results associated with the bladder capacity and compliance demonstrated that 24% of the patients required revision surgery with ileocystoplasty for poorly compliant bladders [20].

ICI in 2012 stated that any segment of the GIT except jejunum might be used for bladder augmentation, while the ileum seemed to give the best results in terms of ease, risk of complications and efficacy, and recommended its use with grade B [9]. Detrusor myomectomy (autoaugmentation) was not recommended in neurological patients with impaired bladder function by ICI (grade D) [9].

#### 3. Technique

Classically, AC is performed as an open abdominal operation with coronal or sagittal bi-valving of the bladder down to the level of the ureteric orifices, with anastomosis of a detubularised segment of bowel onto the native bladder [2,21].

When the bladder wall is very fibrous and thickened supratrigonal cystectomy should be performed, since otherwise exclusion of the ileal patch may occur [9].

#### 4. Ureteric reimplantation

High pressures generated by the neurogenic bladder may result in vesicoureteral reflux (VUR) and may contribute to renal deterioration. Augmentation cystoplasty lowers intravesical pressure and increases bladder compliance during the storage phase, so generally in most of the cases, VUR resolves or improves after AC making an antireflux procedure unnecessary [2,14,22].

It was demonstrated that ureteric reimplantation during cystoplasty in children with neurogenic bladder might be required as VUR can persist after bladder augmentation without reimplantation, and be associated with febrile urinary tract infection (UTI) and upper tract scarring [23]. ICI in 2012 stated that bladder augmentation might resolve low grade VUR, while it recommended ureteric reimplantation in the case of grade 4 or 5 VUR with grade C level [9].

Several techniques such as seromuscular enterocystoplasty and reversed seromuscular ileocystoplasty have been tried both clinically and experimentally to reduce the reabsorbtion of urine from the intestinal mucosa. These techniques did not gain widespread use [9].

## COMPLICATIONS (EARLY AND LONG-TERM COMPLICATIONS)

#### **1. Early complications**

The mortality rate from AC was reported to be 0%-3.2% [2,9]. The most frequently reported early complication was prolonged postoperative ileus [9]. Transient urinary fistula (0.4%-4%), wound infection (5%-6.4%), bleeding requiring reoperation (0%-3%), and thrombo-embolic complications (1%-3%) consist of early complications (Table 3) [2,9,24].

### 2. Long-term complications

#### 1) Metabolic complications

Reabsorption of acid and secretion of bicarbonate by the bowel segment resulted in acid-base and electrolyte disturbance nearly in all patients with enterocystoplasty, but this complication was not found to be clinically important in majority of the cases [2,9,24]. Varying degrees of villous atrophy in the mucosa of augmented ileal segments has been shown [25]. These changes may explain the limited acid-base and electrolyte disturbance in these patients. However, clinician must be careful when operating patients with low creatinine clearance levels, since metabolic acidosis is no longer compensated [9]. Since the colon patch secrete potassium into the urine, colocystoplasty may be occasionally associated with hypokalaemia [2]. Gastrocystoplasty was found to be associated with hypochloraemic hyponatraemic alkalosis in nearly 7% of the patients because of hydrochloric acid secretion by the gastric patch [26]. Haematuria-dysuria syndrome, peptic ulceration of the bladder, and perforation

Table 3. Complications of augmentation cystoplasty

Early complications	
Prolonged postoperative ileus	
Transient urinary fistula	
Wound infection	
Bleeding requiring reoperation	
Thrombo-embolic complications	
Long-term complications	
Metabolic complications	
Acid-base and electrolyte disturbances	
Hyperchloremic acidosis	
Hypochloraemic hyponatraemic alkalosis in gastrocystoplasty	
Haematuria-dysuria syndrome in gastrocystoplasty	
Peptic ulceration and/or perforation of the bladder	
Diverticulisation of the intestinal patch	
Urinary stone formation after augmentation	
The risk of malignancy	
Cystoplasty perforation	
Bowel disturbance	
Urologic surgery after augmentation cystoplasty	

of the gastric segment are the other complications of gastrocystoplasty due to hydrochloric acid secretion by the gastric patch [2,9].

#### 2) Diverticulisation of the intestinal patch

Inadequate bi-valving of the bladder may result in the diverticulisation of the intestinal patch, and surgical revision of the augmentation may be required [27].

#### 3) Urinary stone formation after augmentation

The formation of urinary tract stones, especially bladder stones, is a common complication of cystoplasty and occurs in 3%–40% [2]. Some factors such as bacterial cystitis with urease-producing bacteria (Proteus, *Klebsiella*), intravesical foreign bodies (staples, nonabsorbable sutures), excess mucus production, and hypocitraturia may play a role in stone formation [2].

Lower quantity of mucus production, and urinary pH, and the lower incidence of bacteriuria may result in lower incidence of urinary tract stones [28,29].

#### 4) The risk of malignancy

The general consensus is that the risk of malignancy is higher in augmented patients than in general population but still there remains controversy as to whether enterocystoplasty is an independent risk factor for cancer development [9,30,31]. The incidence of malignancy after augmentation is low and range from 1% to 4.6% [9]. Most of the published cases are adenocarcinomas located at the junction of intestinal and bladder mucosa. These tumors have long latency period after augmentation (over 10 years in most cases) [9]. Urinary stasis, bacterial conversion of urinary nitrates to nitrosamines, infection, bladder calculi, are the proposed risk factors for the development of malignancy [30,32,33]. Traditionally, malignancy incidence after gastrocystoplasty was found to be generally lower than after enterocystoplasty. However, recent studies report an increased incidence of malignancy associated specifically with gastrocystoplasty [16,34].

It was suggested to perform cystoscopy with or without biopsy and urinary tract imaging in the symptomatic patient with haematuria, suprapubic pain, and recurrent or unexplained UTIs [35].

Due to the risk of complications, ICI in 2012 recommended regular follow up for patients with augmentation cystoplastics with grade B [9].

#### 5) Perforation

The most serious and life threatening complication

is cystoplasty perforation with a reported incidence of 0.8%–13%, and with some reporting mortality rates of up to 25% [2,9]. Perforation usually occurs on the graft or at the junction of the bladder with the bowel, and often results from the high pressures within the enterocystoplasty, or rarely from traumatic catheterization or urodynamic investigations [9].

#### 6) Bowel disturbance

Resection of the large segments of terminal ileum may result in bile acid and fat malabsorption with consequent steatorrhoea and diarrhoea [36]. Furthermore this may expose the patients to a vitamin B12 deficiency with possible onset of megaloblastic anemia [37]. The use of ileocecal valve and terminal ileum should be avoided to prevent this complication. Since the use of terminal ileum was avoided, and generally small bowel segments less than 50 cm was used in augmentation enterocystoplasty, clinically overt vitamin B12 deficiency is rare after augmentation cysyoplasty [9].

Bowel disturbances after augmentation have been reported in 18%–54% of the patients [38-40]. It has been demonstrated that this high rate of intestinal transit disorder after augmentation resulted in nearly 10% of the patients to regret having undergone augmentation surgery [41].

#### 7) Urologic surgery after AC

A recent retrospective, population based cohort study using administrative data records of adults who underwent enterocystoplasty between 1993 and 2009, identified 243 patients, of whom 61% had a neurogenic bladder, 20% had a simultaneous incontinence procedure and 18% underwent creation of a catheterizable channel [3]. This study concluded that repeat urological surgery was common after enterocystoplasty. Patients who had a simultaneous incontinence procedure at enterocystoplasty were more likely to require future surgery, and patients with catheterizable channels were at significant risk for future cystolitholapaxy [3]. A large retrospective cohort of children who underwent AC identified 2,831 patients. Ten-year cumulative incidences of cystolitholapaxy and reaugmentation were found to be in the ranges of 13.3%–35.1%, and 5.2%–13.4%, respectively [4].

## FUNCTIONAL OUTCOME OF AUGMENTATION CYSTOPLASTY

ICI in 2012 concluded that all series of patients undergoing AC for neurogenic bladder reported an improvement

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in bladder capacity. More than 90% of patients achieved nocturnal and diurnal continence with high satisfaction rates [9]. Recent retrospective study demonstrated that protection of renal function, adequate bladder capacity and low detrusor pressure could be achieved using supratrigonal cystectomy and augmentation ileocystoplasty in patients suffering from refractory neurogenic lower urinary tract dysfunction [42]. In our series of AC with 69 patients marked improvement of the upper tracts was documented in 79% of the patients in the neuropathic and 73% in the nonneuropathic group. High continence rates were also achieved in both groups (82% and 94%, respectively) [14].

### **CONCOMITANT PROCEDURES**

Surgical correction of concomitant urethral sphincteric deficiency is usually required if demonstrated preoperatively in patients with neurogenic bladder [2,14,15]. Several surgical treatment alternatives such as artificial urinary sphincter (AUS) implantation, conventional, and midurethral tension free slings are available to treat coexisting urodynamic stress urinary incontinence (SUI) [2,14,15]. These procedures can be performed concomitantly with AC, or after AC if urinary incontinence persists [14]. Closure of the bladder outlet may be performed if above mentioned procedures to manage sphincteric deficiency have failed. On this occasion continent catheterisable stoma using the Mitrofanoff principle must be added to AC for urinary drainage. Closure of bladder outlet in patients with neurogenic bladder, and especially in female patients seemed to be a challenging surgical reconstruction. A single operation did not usually solve all the problems but persistence did almost always resulted in continence [43]. ICI in 2012 recommended bladder outlet closure to patients who had persistent neurogenic stress incontinence after the other alternatives of sphincter enhancing procedures (grade B) [9].

Good results of concomitant insertion of an AUS cuff only with AC was reported in patients with neurogenic bladder who appeared to need both procedures. The authors deferred insertion of the remaining AUS components at a second procedure if incontinence persisted [24].

If for any reason a patient with neurogenic bladder who appear to need AC, and is not able to perform transurethral clean intermittent catheterization, augmentation with stoma using Mitrofanoff or Monti channel may be required [14,15].

# KIDNEY TRANSPLANTATION, AND BLADDER AUGMENTATION

A low-pressure, good capacity, and compliant bladder is a prerequisite for a favourable outcome from renal transplantation. Graft failure might occur due to highpressures inside the bladder. In patients with neurogenic bladder who have high pressure bladders during filling, and resultant end stage renal failure, renal transplantation must be performed in conjunction with bladder augmentation. However the timing of AC in combination with renal transplantation remains controversial. AC before transplantation aims to avoid complications of systemic infection and delayed wound healing associated with immunosuppression [44-46]. On the other hand AC after transplantation avoids the rare complication of pyocystitis secondary to an under-filled bladder [2]. Little statistical difference has been found in terms of acute or chronic rejection between the groups [45].

The concern with cystoplasty in patients with kidney transplantation is the increased risk of UTI in these immunosuppressed patients, which could lead to urosepsis and ultimately graft rejection [2].

## **PREGNANCY AND AUGMENTATION**

Vaginal delivery should be recommended to women with AC. Caesarean section should be reserved for obstetric indication only, to avoid possible injury to the pedicle of the augmenting bowel preferably with the involvement of an urologist [2]. Elective caesarean section should be offered to those women with an AC in conjunction with bladder outlet procedure, to avoid pressure and ischaemic damage to the continence mechanism during vaginal delivery [47]. On the other hand, Creagh et al. [48] demonstrated that vaginal delivery has also been proven safe in this subset of patients.

Close monitorization of women with AC and pregnancy was proposed because of higher rates of complications, including UTI, upper tract obstruction requiring intervention, and pre-eclampsia [49]. On the other hand, pregnancy has not been found to have any long-term deleterious effect on renal function and AC despite higher rates of complications [49].

## **FUTURE**

Although the AC is currently considered the gold standard surgical treatment of untractable poor compliance bladder, it is associated with serious complications such as

bowel and, metabolic disturbances, urolithiasis, cystoplasty perforation, and malignant diseases. To avoid these complications new therapeutic alternatives are needed [50]. Tissue engineering approaches might represent an interesting option. After considerable experience derived from preclinical bladder reconstruction studies using tissue engineering by use of biomaterials supplemented with cells and/or growth factors, some clinical studies of AC using tissue engineering have been reported [51].

Bladder tissue engineering uses biomaterials (scaffolds) classified as biological or synthetic [50]. Biological scaffolds are described in the 2 sections as naturally derived biomaterials (collagen and alginate), and acellular tissue matrices (bladder submucosa, small intestine submucosa, derma, bladder, and gallbladder) usually extracted from pigs. Synthetic scaffolds comprise several materials, such as polyvinyl sponges, teflon, vicryl (polyglycolic acid, PGA) matrices, silicone, and silk derivatives. Given the contrasting findings of biological and synthetic scaffold implantation, some authors suggested the use of cell adjunction (seeding) from several sources (autologous cells, stem cells, human cell reprogramming ) to improve bladder tissue regeneration and functional outcomes in bladder tissue engineering [50].

However, a recent systematic review of the preclinical tissue engineering bladder reconstruction studies found that scaffolds with seeding did not result in a better bladder volume than acellular constructs [51]. The systematic review showed a slight decrease in bladder volumes in the group with cellular constructs.

Furthermore this systematic review concluded that preclinical research in healthy animals appeared to show the feasibility of bladder augmentation by tissue engineering. The authors also stated that in view of the disappointing clinical results based on healthy animal models new approaches should also be evaluated in preclinical models using dysfunctional/diseased bladders [51].

In the first clinical study concerning AC by use of autologous cell seeded collagen or composite collagen-PGA scaffold in 7 young patients with myelomeningocele, Atala et al. [52] concluded that engineered bladder tissues wrapped in omentum after implantation, could be used in patients who need cystoplasty. On the other hand, in a recent clinical phase II prospective study in 10 children with refractory neurogenic bladder due to spina bifida, autologous cell seeded biodegradable scaffold was used for bladder augmentation, and the results were disappointing [53]. The authors concluded that autologous cell seeded biodegradable scaffold did not improve bladder compliance or capacity, and serious adverse events surpassed an acceptable safety standard [53]. Actually, when we had a closer look to the results of Atala et al. [52], it was evident that all patients except one had hypocompliance even after tissue engineered cystoplasty.

The bladder is a complex organ particularly because of its sophisticated innervation, and specific storage (good compliance [elasticity] in association with volume) and emptying functions (good and sufficient contractility). Although at present bladder tissue engineering is far away from achieving these functions, it might become a reality in the future [51].

## CONCLUSIONS

Bladder augmentation is indicated whenever bladder capacity and compliance is reduced, or in the event of detrusor overactivity, when all conservative and minimally invasive treatments have failed. Inflammatory and congenital bowel diseases, conditions resulting in short bowel, and malignant bladder disease constitute contraindications for AC. Various augmentation techniques using different GIT segments, and the alternatives to GIT have been described. The most widely used bowel segment for AC is a detubularised patch of ileum. Although many complications such as metabolic disorders, perforation, increased risk of malignancy, and urinary stone formation could be seen after AC, all series of patients undergoing AC for neurogenic bladder reported an improvement in bladder capacity. Several adjunctive surgical treatment alternatives are available to treat coexisting SUI. Augmentation with stoma using Mitrofanoff or Monti channel may be required in patients who are not able to perform transurethral CIC. To avoid these complications new therapeutic alternatives such as tissue engineering approaches are needed. Although at present bladder tissue engineering is far away from achieving normal storage and emptying functions of micturition, it might become a reality in the future.

## **CONFLICTS OF INTEREST**

The authors have nothing to disclose.

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