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THE INFLUENCE OF SPECIFIC FACTORS ON POSTEROPERATIVE COMPLICATIONS IN PEDIATRIC AUGMENTATION ENTEROCYSTOPLASTY

TESI DI MASTER
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SUMMARY

AE is a reconstructive procedure developed to reduce storage pressures in the bladder, preserve renal function, increase bladder capacity, and improve continence, often with the addition of a continent catheterizable channel. In children it is mainly indicated for patients with spinal dysraphism and BEEC. The procedure is associated with the high number of early and late complications, both related to the surgical procedure and to the continued contact of the intestinal mucosa with urine.

The aim of this work is to identify any specific preoperative or intraoperative factors that can be associated to early postoperative complications after augmentation enterocystoplasty in pediatric population. The patients that benefit from this procedure represent a diverse population, with different primary diagnostics and specific physiological and anatomic characteristics, which could lead to different risk factors for particular early postoperative complications. Identifying these risks factors could lead to better management of the patients' postoperative care and also of their expectations.

In our retrospective series of 28 patients, 8 (28,6%) presented with 15 postoperative complications. According to the Clavien-Dindo classification of postoperative complications there were 9 grade II, 5 grade IIIb and 1 grade V complications. We were able to demonstrate a statistically significant association between the presence of a postoperative complication and the identification of intra-abdominal anatomical variants or adhesions from previous surgery (p=0,015).

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ABBREVIATIONS

Augmentation Enterocystoplasty	AE
Electronical medical records	EMR
Chronic kidney disease	CKD
Intensive care unit	ICU
Small bowel obstruction	SBO
Urinary tract infection	UTI
Total parenteral nutrition	TPN
Renal replacement therapy	RRT
Bladder exstrophy-epispadias complex	BEEC
Clean intermittent catheterization	CIC
Continent catheterizable channel	CCC
Genitourinary	GU
Gastrointestinal	GI

INTRODUCTION

Bladder augmentation is a complex reconstructive procedure that aims reproduce a functionally normal lower urinary tract in terms of storage, voiding, continence and preservation of renal function in patients with diverse urologic conditions (1). The procedure is indicated in patients with a reduced functional or anatomic bladder capacity that leads to deteriorating renal function due to high filling or voiding bladder pressures (as seen in neurogenic bladder disorders) or intractable incontinence. In the adult population the mains candidates are patients with neurogenic bladder dysfunction and functional bladder disorders who have failed to achieve improvement of their condition with conservative measures (2). In the pediatric population the main indications are neurogenic bladder disorder (resulting from congenital conditions associated with spinal dysraphism in the vast majority but also from acquired disorders resulting from spinal cord traumatic injury or infection) and complex congenital malformations involving the bladder (such as bladder exstrophy-epispadias complex) (3)(4).

Historical Evolution of Bladder Augmentation and Alternative Procedures

In 1888 Tizzoni and Foggi from Bologna described the replacement of the bladder after cystectomy in dogs by anastomosing an isolated ileal loop with the ureters and urethra, thus creating a continent urinary diversion(5). In the following year, both Rutkowski and Mikulicz independently reported the application of bladder ileocystoplasty in a patient with bladder exstrophy (6) Bladder augmentation using reconfigured intestinal segments (ileum or colon) has proven to be a reliable method of increasing bladder capacity and reducing bladder pressures, but at the risk of long-term complications due to the prolonged contact of urine with functioning intestinal mucosa (6,7). In 1956 Sinaiko first

reported using the stomach for urinary diversion in a dog model, and gastrocystoplasty was introduced clinically by Leong and Ong in the 1970's. The procedure was initially adopted as an alternative for bladder augmentation in children with chronic renal failure (as it did not worsen the metabolic acidosis as typically seen with intestinal segments) and in cases where using bowel is not a viable option such as short bowel syndrome (as seen in some patients with cloacal exstrophy). However, some specific and troublesome complications became apparent, such as intermittent hematuria, metabolic alkalosis and the hematuria-dysuria syndrome, which led to the disuse of the procedure.

Many alternatives have been explored with the goal of eliminating the incorporation of the gastrointestinal mucosa into the urinary tract in order to achieve a better bladder capacity. The utilization of a variety of natural or synthetic material as alternatives for bladder augmentation has been reported, but all have been disappointing and none have been adopted in clinical practice (7,8). In an effort to maintain the physiologic integrity of the reconstructed bladder, several techniques that preserve the urothelium as the sole component of the augmented bladder have been reported. Procedures such as ureterocystoplasty, auto augmentation with detrusorectomy or detrusorotomy, or detrusorectomy covered with a reconfigured segment of gastric wall, ileum or colon stripped of the mucosa lining have been reported. However, these procedures imply a very selective patient population, and the only that have shown some evidence or urodynamic effectiveness are ureterocystoplasty and seromuscular colocystoplasty lined with urothelium (7).

Another investigative approach has been pursued in order to avoid the complications related to bladder augmentation with intestinal tissue. The research regarding tissue engineering technology application for bladder reconstruction has shown interesting and promising advances towards creating a functional bladder wall (9,10). Tissue-engineering technology could provide

novel treatment options for bladder augmentation by regenerating epithelium and muscle using a variety of biomaterial scaffolds, along with autologous, or allogeneic cells and growth factors, leading to the regeneration of partial bladder tissue or construction of a neo-bladder. The regeneration of tissue derived from a patient's own cell is particularly interesting for pediatric patients, as their regenerative capacity is significantly greater than in adults. Nonetheless, the successful transfer of these approaches into clinical routine still represents a major challenge. And in the specific case of pediatric patients, the issue of functional tissue replacements with a good growth potential and a long life span is also of paramount importance.

Despite all attempts, the ideal tissue and technique for bladder augmentation remains elusive, and for now the clinical experience suggests that standard bladder augmentation techniques with intestinal reconfigured segments are the most reliable choice.

Indications for Augmentation Enterocystoplasty

As stated, bladder augmentation is a reconstructive procedure developed to reduce storage pressures in the bladder, preserve renal function, increase bladder capacity, and improve continence. It is not designed to simply expand the size of the bladder, but it aims to correct the physical properties of the bladder. As the augmented bladder suffers from poorly coordinated voiding, the addition of a continent catheterizable channel (CCC) is usually needed if the patient cannot catheterize via urethra.

Bladder filling and storage require accommodation of increasing volumes of urine without increase of intravesical pressure, a bladder capacity that allow storage of an adequate volume of urine, absence of involuntary bladder contractions, and competent outlet that remains closed during filling(3). This

process can be disrupted by poor bladder compliance, a reduced bladder capacity or detrusor overactivity.

Poor bladder compliance leads to an increase in detrusor pressure as the bladder volume increases, and the elevation of filling pressures places the upper urinary tract at risk. Values over 40cm H2O in detrusor pressure without leakage during bladder filling are considered a risk for vesicoureteral reflux and consequent upper urinary tract deterioration. This may be due to neurologic conditions (as seen in spinal dysraphism), where sympathetic facilitation of bladder compliance is altered and increased afferent input leads to decreased compliance. Changes in the viscoelastic properties of the bladder can also lead to poor compliance, as seen in after pelvic radiation or in BEEC (11,12).

Reduced bladder capacity, either anatomical or functional, is another frequent indication for AE, as patients suffer from incontinence, frequent urination or need to perform clean intermittent catheterization (CIC). This reduced capacity may be functional, as found in conjunction with poor bladder compliance or severe detrusor overactivity, or anatomical, as seen in patients with BEEC or previous partial cystectomy due to pelvic tumors.

Detrusor overactivity, characterized by involuntary detrusor contraction during bladder filling, can cause lower urinary tract symptoms as frequency, urgency and incontinence and lead to a substantial impact in the patients' quality of life. It can be associated with neurogenic bladder disorders or functional bladder disorders, and patients who are refractory to conservative management (anticholinergics, intravesical injections of botulin toxin or neuromodulation) are candidates for AE.

Regarding the voiding phase of micturition, bladder emptying requires a coordinated contraction of the bladder of adequate magnitude and duration coupled with the lowering of resistance of the bladder sphincters. The voiding process can be disrupted by detrusor muscle contraction concurrent with a

concomitant involuntary urethral sphincter activation as seen in detrusor sphincter dyssynergia (13,14). This is frequently seen in patients with neurogenic bladder dysfunction, and can lead to high bladder pressures associated with vesicoureteral reflux, UTI and progressive renal damage. Usually managed by conservative measures, when associated with concurrent bladder filling and storage difficulties it may be addressed by AE (3).

In the pediatric population the most frequent indications for AE are neurogenic bladder dysfunction (spinal dysraphism being the main cause) and BBEC. The primary goal of treatment in neurogenic bladder dysfunction is to preserve renal function and prevent urinary tract infection, and achieving urinary continence a secondary goal. In this patient population AE addresses the issue of overactive bladder with a small capacity or poor compliance, and with the option of a CCC for those com cannot perform urethral catheterization(15). In the BBEC population AE may be needed when the bladder fails to gain adequate capacity due to various reasons (such as after failed repair, failure of the bladder to grow after initial reconstruction or bladder neck repair) leading to urinary incontinence or deterioration of the upper urinary tract. For these patients AE and CCC has become the most reasonable option to achieve continence(4,11,16).

Despite being considered the most adequate surgical procedure, AE is reserved for patients who have failed or who are not candidates for conservative treatment, namely clean intermittent catheterization (CIC), anticholinergics, intravesical instillation of medication, and intravesical injection of botulinum toxin (3,12). The increasing efficacy of these treatments in improving bladder compliance and capacity, namely in patients with neurogenic and functional bladder disorders, associated with the concerns for long term complications associated with the surgical procedure, has been suggested as a reason for the decrease observed in the number of AE performed in the United States and

United Kingdom in the early 2000's (8,17). In the pediatric population, the early proactive conservative management of congenital neurogenic bladder disorders may also be responsible for the decrease observed (18). In patients with the bladder exstrophy-epispadias complex the improvement of the surgical techniques has led to a better continence rate, leading to fewer candidates for AE (11).

COMPLICATIONS ASSOCIATED WITH AUGMENTATION ENTEROCYSTOPLASTY

Augmentation enterocystoplasty provides durable clinical and urodynamic improvements; however, it does also carry substantial and life-long morbidity.

The early postoperative complications associated with AE are the same as those associated with any major abdominal procedure, with some particularities related the specific nature of the procedure (8,19). The long term complications are mostly related with the prolonged contact of urine with the intestinal mucosa in the augmented bladder and with patient non-compliance with the management plan needed in this particular situation (20,21). However, some specific complications, such as bladder perforation, can present both in the very early postoperative period or late in the follow up (20,22). This entails an added difficulty when reporting the postoperative complication of AE.

The most common reported in the adult population are small bowel obstruction requiring reintervention (3 -5,7%), wound infection or dehiscence (5-6,4%), bleeding requiring reoperation (0-3%) and infection of ventriculo-peritoneal shunt (0-20%) (8,19). In the pediatric series the most common complications were UTI (9,6-10,7%), wound complications (7,4-8,7%), and urine leaks (12,7%) (23–25). Although the most common primary diagnosis in all pediatric series is neurogenic bladder, in many cases associated with spinal dysraphism and who might need a ventriculo-peritoneal shunt, infection of the

shunt was not reported in the early complications of the pediatric population. Also, spontaneous bladder perforation has been reported as an early complication in a pediatric series, but no in the adult literature (22).

As for the long term complications, the most commonly reported are bladder urolithiasis, bladder perforation, metabolic complications and malignant transformation. The formation of bladder stones occurs in up to 52% of patients, and the main causes are poor emptying of the reservoir and mucous accumulation (19,22,23). Bladder perforation is frequently reported in both pediatric and adult series, ranging from 3 to 53%, and is also associated with poor patient compliance with catheterization (19,22,23) The metabolic complications are related to the reabsorption of urinary ammonia and ammonium with accompanying chloride, leading to chronic metabolic acidosis and results in the excessive waste of phosphate from bone for use as a urinary buffer for the excreted acid (19,26). Although there are concerns that this will have an adverse result on bone health and growth potential of children over the long term, this has not been observed. Malignant transformation is one of the main concerns regarding AE, and even though there are reports of this being a significant risk, there are no reports of malignancy in the pediatric literature (22,23,27). Husmann followed 385 patients during a mean follow up of 26 years (range 2-56 years) has shown a total of 8 cases of neoplasia. The median age at the time of tumor diagnosis was 51 years (range 30-64), and median time from AE to tumor development was 39 years.

Social and Clinical Considerations in Augmentation Enterocystoplasty

Augmentation enterocystoplasty is a major surgical procedure, and involves careful planning regarding several aspects of the patient's clinical and social history.

The patient and the family must be made aware that their cooperation is essential for the best outcome of the procedure and that they will need lifelong care. They should be prepared to performed CIC (either per urethra or via CCC). After augmentation voiding dysfunction is usually inevitable, as the integration of bowel in the bladder replaces the normal sustained detrusor contraction with the involuntary and unsustained contractions characteristic of the bowel. This results in poorly coordinated voiding, often associated with high postvoiding residue that may lead to UTI, stone formation, incontinence and in the presence of elevated bladder pressure upper tract damage(28).

Many patients will have suffered previous renal damage and developed chronic kidney disease, with need for renal replacement therapy in the most advanced stages. Careful planning and monitoring of renal function are paramount when considering the procedure and special precautions should be taken to reduce the risk of further decline in kidney function (29).

As discussed before, the main indications for pediatric AE are spinal dysraphism and BEEC. These patients may have been previously submitted to other genitourinary or abdominal procedures (like ventriculo-peritoneal shunt placement or bladder neck procedures) that renders them more likely to having pelvic and abdominal adhesions or anatomic alterations. The surgeon must be prepared to cope with these, adapting or changing the procedure if need be.

The need for another concomitant surgical procedure should be addressed beforehand, such as ureteral reimplantation or bladder neck procedure. Although it is not mandatory to perform these other procedures at the same operative time, it may prevent further interventions and complications. (29).

Technical Aspects of Augmentation Enterocystoplasty

The bladder is approached by a lower longitudinal or transversal incision (fig. 1). The bladder dome is opened transversally (in a clamshell fashion) with the incision being extended close to the trigonum in order to obtain a large circumference for bowel anastomosis and avoid an "hourglass" phenomenon.

In our hospital other bladder procedures (such as bladder neck section or ureteral reimplantation) are performed at this moment (fig. 2).

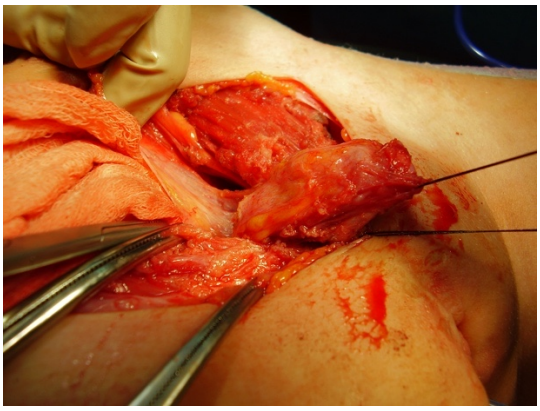

Fig. 1: identification of the bladder dome

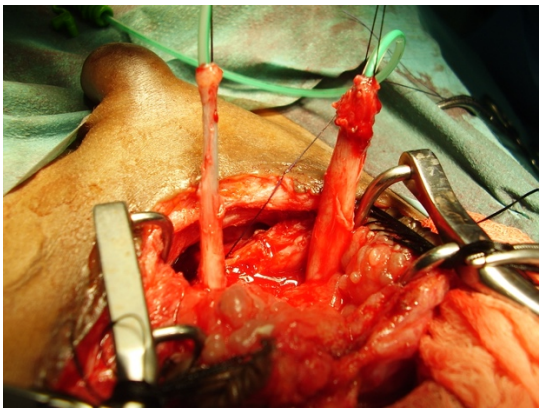

Fig. 2: ureteral reimplantation

Afterwards, a segment of ileum measuring between 20 to 30cm and at least 20 cm away from the ileocecal valve is chosen (fig. 3). Care should be taken to assure that the mesentery can easily reach down to the bladder and contains more than one vascular arcade to ensure adequate vascularization. The ileal segment is divided along the anti-mesenteric border and reconfigured by sewing the detubularized segment into a "U" shape, at the same time increasing the capacity of the bowel segment and desynchronizing the bowel contractions and lowering intraluminal pressure (fig. 4). If a continent catheterizable channel is to be created, either using the appendix or a reconfigured ileum segment, it is done at this time (fig. 5). The bladder is then anastomosed to the ileal segment (fig. 6 and 7).

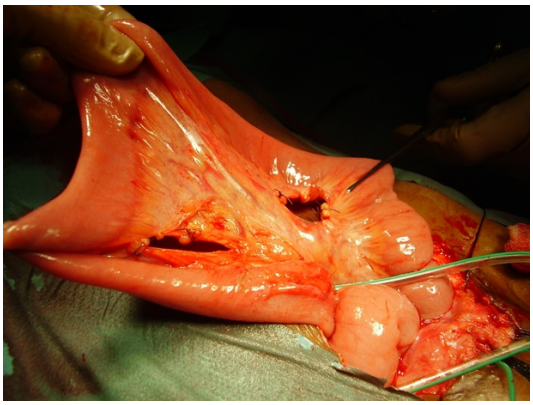

Fig. 3: choosing the ileal segment

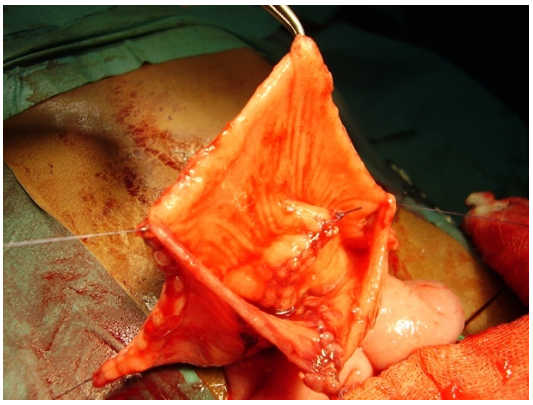

Fig. 4: reconfiguring the ileal segment

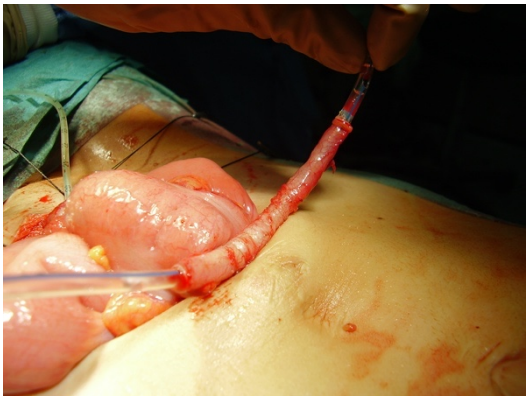

Fig. 5: fashioning the appendicovesicostomy

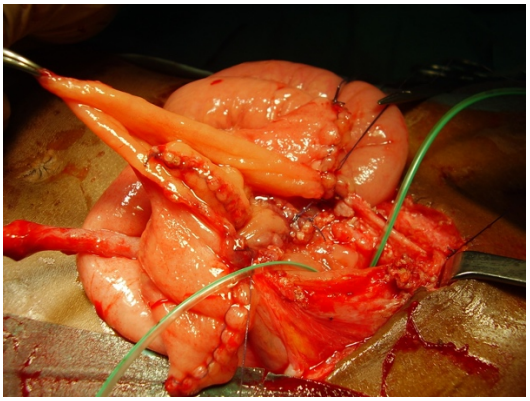

Fig. 6: the anastomosis of the ileum to the bladder

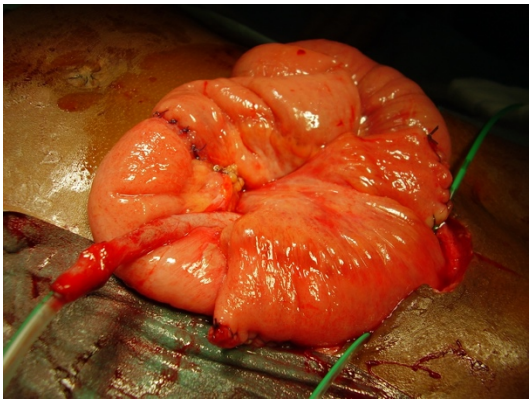

Fig. 7: the finished anastomosis

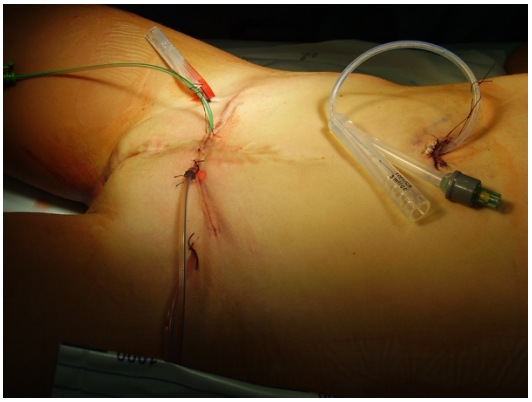

Fig. 8: the exterior aspect

In our institution the augmented bladder is drained by a transvesical Foley catheter, a silastic drain in the paravesical region and if possible a transurethral Foley catheter (fig 8). Most patients will be transferred to the Intensive Care Unit after the surgery and remain there until considered clinically stable.

Despite being a complex procedure, laparoscopic and robot-assisted laparoscopic augmentation enterocystoplasty have been reported with comparable outcomes to the conventional open procedure (30,31).

OBJECTIVES

The aim of this work is to identify any specific preoperative or intraoperative factors that can be associated to early postoperative complications after augmentation enterocystoplasty in the pediatric population. The patients that benefit from this procedure represent a diverse population, with different primary diagnostics and specific physiological and anatomical characteristics, which could lead to different outcomes in the early postoperative complications.

Primary objective

To identify preoperative (related to the primary diagnosis, previous surgical interventions or degree of kidney damage) or intra-operative factors (such as length of surgery, identification of intra-abdominal anatomical variant or adhesions from previous surgery or concomitant surgical procedures) that are associated with postoperative complications identified in the early postoperative period after augmentation enterocystoplasty in a pediatric population of a single tertiary center.

Secondary objective

1. To compare the preoperative and intra-operative factors associated with early postoperative complications in this series to those described in the literature.
2. To compare the rate of complications in this population to those described in the literature.

METHODS

PATIENT SELECTION

The patient selection was established by a convenience sample of all patients identified as having had an augmentation enterocystoplasty performed by the same pediatric urology in the Hospital Dona Estefânia, since January 2010, with a minimum of three months of follow up.

DATA COLLECTION

A retrospective observational study was performed by reviewing the electronic medical records (EMR) of patients submitted to augmentation enterocystoplasty (AE) in a single tertiary care pediatric hospital in a ten-year period between January 2010 and October 2021. The EMR were reviewed for the following variables:

A. Patient variables

1. Sex (nominal variable)
2. Age at surgery (continuous quantitative variable)
3. Duration of follow-up in months (continuous quantitative variable)
4. Primary diagnosis: dysraphism; bladder exstrophy; central nervous system tumor; pelvic tumor; spinal trauma (categorical variable)
5. Presence or absence of Chronic Kidney Disease (CKD), as defined by the KIDGO 2012 guidelines: abnormalities of kidney structure or function, present for more than three months, with implications for health (categorical variable)

6. Staging of CKD grade 1 to 5, if present, as defined by the KIDGO 2012 guidelines (categorical variable)
7. Presence or absence of renal replacement therapy (RRT) (categorical variable)
8. Type of renal replacement therapy, if present: peritoneal dialysis, hemodialysis, renal transplant (categorical variable)
9. Presence or absence of previous surgical interventions (categorical variable)
10. Type of previous surgery: bladder closure; ureteral reimplantation; continent catheterizable conduit; bladder neck procedure; ventriculo-peritoneal shunt; open dysraphism closure; other gastrointestinal or genitourinary procedure (categorical variable)
11. Number of previous surgeries (discrete quantitative variable)

B. Intra-operative variables

1. Duration of surgery in minutes (continuous quantitative variable)
2. Presence or absence of intra-operative blood transfusion (categorical variable)
3. Presence or absence of intra-abdominal anatomical variant or adhesions from previous surgery (categorical variable)
4. Presence or absence of concomitant surgical procedures in the same operative time of the augmentation enterocystoplasty (categorical variable)
5. Presence or absence of construction of a continent catheterizable conduit in the same operative time of the augmentation enterocystoplasty (categorical variable)

6. Presence or absence of unilateral or bilateral ureteral reimplantation in the same operative time of the augmentation enterocystoplasty (categorical variable)
7. Presence or absence of construction of a bladder neck procedure in the same operative time of the augmentation enterocystoplasty (categorical variable)
8. Other surgical procedure in the same operative time of the augmentation enterocystoplasty (categorical variable)
9. Number of concomitant surgical procedures in the same operative time of the augmentation enterocystoplasty (discrete quantitative variable)

C. Postoperative variables

1. Admission or no admission to the Intensive Care Unit (ICU) after the surgery (categorical variable)
2. Length of stay in ICU in days, if admitted after the surgery (discrete quantitative variable)
3. Need of invasive mechanical ventilation in the 30 days following surgery (categorical variable)
4. Need of blood transfusion in the 30 days following surgery (categorical variable)
5. Identification of urinary tract infection in the 30 days following surgery (categorical variable)
6. Identification of intra-abdominal hemorrhage in the 30 days following surgery (categorical variable)

7. Identification of peritonitis in the 30 days following surgery (categorical variable)
8. Identification of small bowel obstruction (SBO) requiring surgical intervention in the 30 days following surgery (categorical variable)
9. Identification of enteric or vesical fistula in the 30 days following surgery (categorical variable)
10. Identification of surgical site infection in the 30 days following surgery (categorical variable)
11. Identification of major thromboembolic event in the 30 days following surgery (categorical variable)
12. Need for total parenteral nutrition (TPN) in the 30 days following surgery (categorical variable)
13. Need for initiation of RRT in the 30 days following surgery (categorical variable)
14. Need for hospital readmission after discharge in the 30 days following surgery (categorical variable)
15. Need for surgical reintervention in the 30 days following surgery (categorical variable)
16. Death (categorical variable)
17. Presence of absence of postoperative complications in the 30 days following surgery, as one or more of the following: need of blood transfusion; UTI; intra-abdominal hemorrhage; peritonitis; SBO; vesical or enteric fistula; surgical site infection; major thromboembolic event; need for TPN; need for initiation of RRT; surgical reintervention; hospital readmission or death (categorical variable)
18. Total length of hospital stay in days (discrete quantitative variable)

STATISTICAL ANALYSIS

The data collected was anonymized and registered in a digital database. The descriptive statistics were reported as absolute frequencies and percentages for the qualitative data. Median, mean and range were used for quantitative data. The association between preoperative and intra-operative variables and postoperative complications was tested with the Fisher's exact test. A p-value less than 0.05 was considered statistically significant. Statistical analysis was performed with EasyMedStat (version 3.12; www.easymedstat.com).

RESULTS

During the study period 28 patients underwent augmentation enterocystoplasty, of which 17 (60,7%) were female. The mean age at surgery was 11,7 years (range 3,4 to 19,7), with a mean time of follow up of 83,7 months (range 3-132). The most common primary diagnosis was spinal dysraphism in 18 patients (64,3%), followed by BEEC in 6 (21,4%). Two patients had a primary diagnosis of pelvic tumor (1 rhabdomyosarcoma of the prostate and 1 sacrococcygeal teratoma type II), 1 patient central nervous system tumor (medullar astrocytoma) and 1 patient spinal trauma. Sixteen (57,2%) patients had evidence of CKD, but only 1 patient need RRT (hemodialysis). Twenty seven out of the 28 patients (96,4%) had previous surgery before AE, with a median of 3 previous procedures (range 0-8). The most frequent procedures were open dysraphism closure and other gastrointestinal or genitourinary procedure, with 11 patients each (39,2%), followed by ureteral reimplantation in 8 (28,6%), insertion of a ventriculo-peritoneal shunt in 5 (17,9%). One patient had a previous appendicovesicostomy and one patient had a previous bladder neck procedure.

The surgical intervention had a mean time of 390 minutes (range 240-660). Five patients required intraoperative blood transfusion, and in 5 patients intra-abdominal anatomical variants or adhesions from previous surgery were identified. Another surgical procedure in the same operative time was performed in 22 patients (78,6%), and the mean number of concomitant procedures in those patients was 1,7 (range 1-4). Ten patients (35,7%) 2 or more had more concomitant procedures. The most common concomitant procedure was creation of continent catheterizable channel in 16 patients (57,1%), followed by ureteral reimplantation in 11 (39,3%), bladder neck procedures in 5 (17,9%) and other procedures in 4 patients (14,3%).

After the surgical intervention 24 patients (85,7%) were admitted to the ICU, with a mean length of stay of 3 days (range 1-7). Of these patients 4 were invasively ventilated after surgery. In the 30 days following the AE none of the patients needed blood transfusions or de novo renal replacement therapy, and no peritonitis, postoperative hemorrhage or deep operative wound infection were identified. In that time period 8 patients (28,6%) presented with 15 postoperative complications (4 patients had 1 complication, 4 had 2 complications and 1 had 3 complications). Five patients (17,9%) were reinterventioned.

As for the complications: 2 patients had an ITU and 1 patient had a surgical site infection; 5 patients required parenteral nutrition (4 patients for prolonged postoperative ileus and 1 because of vesico-enteric fistula); 3 patients had small bowel obstruction (all required reintervention); 3 patients presented with urinary or enteric fistula (1 required reintervention with a divertive colostomy for a vesico-enteric fistula; 2 were managed conservatively, 1 with a urethral fistula after bladder neck closure concomitant with AE, 1 with a vesico-enteric fistula identified after a reintervention for SBO); 1 patient had a CCC complication requiring surgery and 1 patient had a major thromboembolic event that resulted in the only death registered in this series.

The indications for reintervention were small bowel obstruction in 3 patients, a vesico-enteric fistula requiring divertive colostomy and ischemia of a continent catheterizable conduit of the appendix that required its disassembly.

A statistically significant association was identified between the presence of a postoperative complication and the identification of intra-abdominal anatomical variants or adhesions from previous surgery (p=0,015). No other statistically associations were found, namely between the preoperative and intraoperative variables (primary diagnosis, presence of CKD, previous surgery or more than 3 previous surgical procedures and length of the surgical procedure)

and the postoperative complications encountered (UTI; SBO; vesical or enteric fistula; surgical site infection; major thromboembolic event; need for TPN; surgical reintervention or death).

The mean length of stay after AE was 26,5 days (range 9-93). No patients were readmitted to the hospital after initial discharge. There was only 1 death registered due to a major thromboembolic event that occurred 17 hours after the AE.

DISCUSSION

Postoperative complications have adverse effects on patient's health and are associated with increased length of stay and postoperative costs (32). They are traditionally used as a surrogate marker of quality in surgery, but the direct cause and effect relationship between surgery and complications is often difficult to assess (33) Also, there is no standardized method for reporting the severity of complications, although the modified Clavien-Dindo has been considered a valid grading system for urological procedures both in adults and in the pediatric population (33,34).

Several strategies have been proposed to evaluate a patient's risk for surgical complications since the introduction of the ASA score in 1941, in an attempt to create more objective predictors of complications (35). However, most of these are targeted to an adult population, and are poorly generalizable to the pediatric populations. Two very interesting papers published by the Clinical Research Program in The Children's Hospital in Boston proposed to address this problem by identifying perioperative risk factor for surgical complication in both pediatric urology and pediatric surgery in the early postoperative period (35,36). The findings were different in both studies. In the pediatric urology population, a multivariate analysis showed that weight in less than the fifth percentile, pulmonary and hematologic comorbidity, being on "other" medication, operation duration greater than 2 hours, intraoperative heart rate less than the second percentile for age, and the use of IV anesthesia were independent risk factors for complications(35). In the pediatric surgery population 4 preoperative (gestational age less than 36 weeks, ASA score >3, undergoing cardiovascular and neurological surgery) and 1 intraoperative variable (albumin transfusion) were found to be independent predictors of surgical complications (36). Interestingly, other variables such as duration of surgery and estimated blood

loss (even adjusted for weight) were not found to be significant in the pediatric surgery study. These observations highlight the importance of using a specific risk assessment based on the patient population, as undergoing different surgical procedures may have differing risks.

Augmentation enterocystoplasty is a complex reconstructive surgery with proven benefits, but places the patient at risk of both early and late complications. The aim of this study was to identify preoperative or intraoperative factors that could be associated with early postoperative complications. The decision to focus on the first 30 days after surgery, accepted in the surgical community as the early or immediate postoperative period, was influenced by the fact the evaluation of pediatric urologic complications has shown that most complications are related to "technical" issues (such as urine leak, anastomotic failure, surgical site complications and damage to surrounding structures) and mostly occur within 7 days of surgery (35). Also, in the particular case of augmentation enterocystoplasty, patient compliance is a major factor in the long term outcome, and difficult to assess or modify(20,23,37).

The bibliographic review for this work identified several papers regarding the complications after pediatric AE. Khishna et al reported their 5-year experience with 39 children, focusing on urodynamics outcome and complications with a mean follow up of 3,3 years (38). With a mean follow up of 3,3 years they reported 10 complications in 7 patients (17,9%), with 4 (10,3%) bladder perforations, 4 (10,3%) intestinal obstructions (3 requiring reintervention), 1 patient presented with bladder urolithiasis and 1 with wound dehiscence. They state that no deaths or significant morbidity occurred in the immediate postoperative period, despite not defining the time interval that this applies to. Ross et al analyzed their 28 year and 54 patients experience in a tertiary hospital with a mean follow up of 7,6 years, reviewing their complication rate and the need for postoperative cystogram(22). The series encompassed a heterogeneous population as 49

underwent ileocystoplasty and the remaining 7 augmentation with another gastrointestinal segment. The mean time of follow up was 7,6 years. During that time period 37 (68,5%) of patients experience at least 1 UTI, 8 (14,8%) had bladder urolithiasis and 2 (3,6%) a bladder perforation. Of the 28 patients who had a catheterizable continent channel fashioned at the same time as the augmentation procedure, 13 presented with complications of the stoma, 10 of which required a second intervention. In total 19 (35,2%) returned to the operating room due to postoperative complications. The timing of postoperative complications was variable depending on the type of complication. Bladder perforation was singled out as seen almost immediately in both cases (3 and 8 days postoperatively), while the other complications were seen well over one year postoperatively on average. Taghavi et al focused on short- and long-term complications of 71 consecutive operative cases in a 20-year span and a mean follow-up of 4,5 years (23). As in the series presented by Ross et al, different tissues were used in bladder augmentation, ileum being the most frequent (57,7%). The complications were considered as immediate (less than 30 days after the surgery) or long term. In the former category, 14 patients (19,7%) presented with 3 wound infections and 5 urine leaks that did not require reintervention; and 6 (8,4%) patients required reintervention associated with leaks from the anastomotic lines. In the latter group, the complications identified were symptomatic UTI in 36 patients (51%), bladder urolithiasis in 13 (18%), bladder perforation in 3 (4%), SBO also in 3 patients (4%). Of the 46 patients who had a CCC 28 (61%) developed a complication associated with it during follow up. All these publications are retrospective analysis, with a relatively small sample, as is expected due to the particular patient population for whom this surgery is indicated. Furthermore, only one clearly distinguishes between early and late complications (23), but all show the burden of postoperative complication in the

long term outcome of these patients, and emphasize the importance of long term follow up.

In the United States of America, the use of large national databases designed to measure and analyze outcomes of surgical interventions with prospectively collected data has allowed for studies with a larger population and a more refined statistical analysis. Schlomer et al analyzed 2810 patients identified in the Kids' Inpatient Database by the procedure code for augmentation cystoplasty from 2000 to 2009 (39). This database contains information pertaining to 1 hospital stay, so even though it is not stated in the paper the assumption can be made that the complications assessed occurred in the immediate postoperative period. They identified that 30% of patients had a potential complication after the procedure, with 14% having a major surgical complication (defined as SBO, blood transfusion, hemorrhagic technical or fistulous complications). Also, older age and BEEC diagnosis were associated with greater length of stay and increased odd of having any complications. The number of patients presenting with these complications is not stated in the paper. Two additional papers analyzed the data from the National Surgical Quality Improvement Program (NSQIP) Pediatric regarding the 30-day outcomes after enterocystoplasty. Du et al focused on perioperative factor and complications for enterocystoplasty, analyzing the data from 114 patients who underwent the procedure in 2012(24). In this population the 30-day complication rate was 33,3%, with the most common complications being UTI (9,6%), wound complications (8,7%), blood transfusions (6,1%) and sepsis (3,5%). Unplanned reintervention rate was 9,6%, and readmission was 13,2%. They found no statistically significant differences in perioperative characteristics in patients with or without postoperative complications. In turn, McNamara et al proposed to report on the 30-day complication, readmission and reoperation rate after AE and appendicovesicostomy identified in the NSQIP Pediatric database from 2012 and

2013 and explore the association between preoperative and intraoperative characteristics and occurrence of any 30-day event (25) In their series of 461 patients, 245 had an appendicovesicostomy, 97 patients had AE and 119 had both procedures. In the total population any 30-day event was seen in 27,8% of patients. Taking into consideration only the patients who had AE or AE and appendicovesicostomy (a total of 216 patients), 23 (10,7%) had an UTI, 16 (7,4%) a surgical site incision complication, 13 (6,0%) need a transfusion, 27 (12,5%) were readmitted after initial discharge and 17 (7,9%) underwent an unplanned reoperation. Operative time e number of concurrent procedures were associated with higher odds of complications, readmission and/or reoperation. Overall, these studies show a complication rate of about 30% in the early or immediate postoperative period. Older age, a primary diagnosis of BEEC, a longer operative time and the number of concurrent procedures are the only preoperative or intraoperative characteristics that have shown some associations or higher odds of complications, despite the high number of characteristics evaluated.

The demographic characteristics of our series are in line with those reported in the literature, with the most frequent primary diagnosis being the various forms of spinal dysraphism, followed by BEEC (22–24,38–40). The mean age at surgery at 11,7 years old was slightly older than in most series (9,3 to 9,7).

In our series previous surgeries were observed in a vast majority of patients (96,4%), with a median of 3 procedures (range 0-8), and 5 patients had intra-abdominal anatomical variants or adhesions from previous surgery. No other series mentioned these characteristics. The intra-operative identification of intra-abdominal anatomical variants or adhesions from previous surgery was the only characteristic found to be statistically significant in regards to the presence of a postoperative complication (p=0,015), and surgical experience dictates that these factors can be associated in clinical practice. This factor has not been taken

into consideration in any of the other published series regarding possible risk factor for early complications. Considering that a large majority of the patients who underwent AE had already had previous surgery, this factor may in fact be of relevance and further investigation in this area would certainly yield interesting information.

The mean length of surgery, 390 minutes, was in line with those reported by Du et al (393,5 minutes) and McNamara et al (372 minutes). The latter reported that longer operative time showed higher odds of complications, and in our series showed a statistically significant associations with the presence of a postoperative complication. Another surgical procedure in the same operative time was performed in 22 patients (78,6%), and the mean number of concomitant procedures in those patients was 1,7 (range 1-4). Ten patients (35,7%) 2 or more had more concomitant procedures. These findings are in line with the published literature, with concomitant procedures being done in 59 to 92% of patients undergoing AE. Although in our series there was no significant statistical association between the having concomitant procedures or the number of concomitant procedures, McNamara et al demonstrated that the number of concurrent procedures were associated with higher odds of complications, readmission and/or reoperation.

A systematic review and meta-analysis by Hang et al concluded that prolonged operative time is associated with an increase in the risk of complications, which go in line with what was by McNamara (41). In this paper it is hypothesized that longer operative times can be indicative of more complex or difficult surgeries or of intraoperative complications. In the particular case of AE, besides being in itself a complex reconstructive intervention, the concurrent surgical procedures often done can contribute to the prolonged operative time, as well as the intraoperative difficulties encountered as result of previous operations or anatomical variations.

Eight patients (28,5%) presented with 15 early postoperative complications in our series. In spite of Khrishna's affirmation that there were no significant immediate postoperative complications in his paper, the larger published series focusing on early complications reported complications in 27,8 to 33% of patients. As for the unplanned reinterventions, 5 (17,9%) patients were identified, compared to the 7,9 to 9,6% of reoperations reported. In the pediatric early complication series, the reasons for abdominal revision and exploration are not explicit (24,25). Three patients had SBO requiring intervention; this complication has been reported in 3 -5,7% of adult patients. One patient that had previous pelvic radiation therapy for rhabdomyosarcoma of the prostate had vesico-enteric fistula requiring divertive colostomy. This was a very particular situation, and was not described in other series. One patient had ischemia of a continent catheterizable conduit of the appendix that required its disassembly. Complications with the CCC are among the most frequent complication reported, but in the early post-operative period (23).

According to the Clavien-Dindo classification of postoperative complications there were 9 grade II, 5 grade III and 1 grade V complications. We can state that even if the complication rate was larger than the other series, most of the complications may be considered as minor, required only minimal intervention and were not life-threatening, as has also been demonstrated in other series (22,35).

The mean length of stay after AE was 26,5 days, which is considerably longer than others have reported (7,5 to 9,8 days). This may be due to an outlier value, as our range was from 9 to 93 days, with a median of 14 days.

There was only 1 death registered due to a major thromboembolic event that occurred 17 hours after the AE. In the early complication series reported in the literature there are no deaths reported(24,25) We can infer from the high

morbidity and low morbidity reported that although AE is fraught with life-long complications, life-threatening complications are very rare.

Given the rarity of the procedure and the fact that most single centers have a limited experience, and the possibility of having even fewer candidates in the future as conservative measures become more efficient, future works in this subject should focus on multicentric studies. Pursuing the influence of previous surgeries and of intra-operative findings that may contribute to early complications appears to be an interesting challenge.

CONCLUSION

Augmentation enterocystoplasty is a complex reconstructive procedure with potential to greatly improve the health and quality of life of children with particular storage or voiding issues. However, it is not devoid of risks, and many early and long term complications have been reported, as well as the need for life-long care and patient compliance.

In this work it was demonstrated that even tough early complications occur in almost 30% of the patients, most of the complications were minor, requiring only minimal intervention and were not life-threatening. There were major complications in 6 patients, including one death.

We were able to demonstrate a statistically significant association between the intra-operative identification of intra-abdominal anatomical variants or adhesions from previous surgery and the presence of a postoperative complication (p=0,015). This factor has not been taken into consideration in any of the other published series regarding possible risk factor for early complications. We believe that further investigation should be done regarding the influence of these factors in the postoperative outcome.

Our results have proven to be in line with those in the published literature regarding the complications in the early postoperative period.

Further investigation regarding the influence of previous surgical interventions and intra-operative findings, especially in a multicentric setting, may yield interesting information regarding the risk of early postoperative complications.

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