UNIVERSIDADE FEDERAL DE MINAS GERAIS

Faculdade de Medicina Programa de Pós-graduação em Ciências da Saúde da Criança e do Adolescente

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ACHADOS CLÍNICOS E URODINÂMICOS EM CRIANÇAS E ADOLESCENTES COM BEXIGA NEUROGÊNICA REFRATÁRIA SUBMETIDOS À CISTOPLASTIA DE AUMENTO

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UNIVERSIDADE FEDERAL DE MINAS GERAIS FACULDADE DE MEDICINA - CENTRO DE PÓS-GRADUAÇÃO PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DA SAÚDE SAÚDE DA CRIANÇA E DO ADOLESCENTE ATA DE DEFESA DE DISSERTAÇÃO

Às quatorze horas do dia seis de dezembro de dois mil e vinte e quatro, na sala 062 (Auditório Prof. Amílcar Vianna), andar térreo da Faculdade de medicina da Universidade Federal de Minas Gerais, realizou-se a defesa de dissertação de mestrado do aluno OTÁVIO AUGUSTO FONSECA REIS, número de registro 2023651306, graduado no curso de MEDICINA, como requisito parcial para a obtenção do grau de Mestre em CIÊNCIAS DA SAÚDE - SAÚDE DA CRIANÇA E DO ADOLESCENTE pelo Programa de Pós-Graduação em Ciências da Saúde-Saúde da Criança e do Adolescente. A Presidência da sessão coube a Prof.º Flávia Cristina de Carvalho Mrad, orientadora (UFMG). Inicialmente a Presidente após dar conhecimento aos presentes sobre o teor das Normas Regulamentares do trabalho final de Pós-Graduação, fez a apresentação da Comissão Examinadora, assim, constituída pelos Professores Doutores: Flávia Cristina de Carvalho Mrad - Orientadora (UFMG), Marcelo Esteves Chaves Campos (UFMG), Eliney Ferreira Faria (FCMMG) e Mônica Maria de Almeida Vasconcelos - Coorientadora (UFMG). Em seguida a Presidente autorizou o aluno a iniciar a apresentação de seu trabalho final intitulado "ACHADOS CLÍNICOS E URODINÂMICOS EM CRIANÇAS E ADOLESCENTES COM BEXIGA NEUROGÊNICA REFRATÁRIA SUBMETIDOS À CISTOPLASTIA DE AUMENTO". Seguiu-se à arguição pela comissão Examinadora, com a respectiva defesa do aluno. Logo após a Comissão reuniu-se sem a presença do candidato e do público para julgamento e expedição do resultado da avaliação do trabalho final do aluno e considerou a dissertação Aprovada. O resultado final foi comunicado publicamente ao aluno pela Presidente da Comissão. Nada mais havendo a tratar, a Presidente encerrou a sessão e lavrou apresente ata que, após lida, será assinada eletronicamente por todos os membros da Comissão Examinadora presente através do SEI (Sistema Eletrônico de Informações) do Governo Federal.

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Resumo

Introdução: Transtornos neurológicos, particularmente defeitos do tubo neural como a espinha bífida, podem levar à bexiga neurogênica (BN) em crianças e adolescentes. A BN é caracterizada por um enchimento de alta pressão da bexiga e esvaziamento ineficiente, resultando em complicações como incontinência urinária (IU), infecções urinárias recorrentes, refluxo vesicoureteral (RVU) e aumento do risco de danos aos rins. Os tratamentos iniciais incluem cateterismo intermitente limpo, medicamentos anticolinérgicos ou a aplicação de toxina botulínica A. A cistoplastia de aumento (CA) é um procedimento cirúrgico destinado a criar um reservatório de bexiga de baixa pressão e alta capacidade para preservar a função renal e melhorar a qualidade de vida. É indicada quando os tratamentos minimamente invasivos falham. A ileocistoplastia e a colocistoplastia são métodos comumente utilizados para aumentar a capacidade e a complacência da bexiga. Objetivos: O objetivo principal deste estudo foi avaliar IU, RVU e parâmetros urodinâmicos em crianças e adolescentes com BN refratária após a CA e comparar esses achados com dados pré-operatórios. O objetivo secundário foi realizar uma revisão sistemática para analisar os achados clínicos e urodinâmicos em crianças e adolescentes com BN submetidos à CA. **Métodos:** Estudo de coorte retrospectivo que recrutou 42 pacientes consecutivos com BN refratária, submetidos apenas à CA entre fevereiro de 2009 e março de 2023. Os critérios de exclusão foram pacientes com anomalias não neurogênicas do trato urinário inferior e aqueles com vesicostomia prévia. Os parâmetros avaliados neste estudo, antes e depois da CA, com pelo menos um ano de acompanhamento, incluíram IU, RVU e dados urodinâmicos, como capacidade cistométrica máxima (CCM), capacidade vesical esperada (CVE), complacência vesical e pressão detrusora ao final do enchimento. **Resultados:** Dos 22 pacientes elegíveis (50% do sexo masculino, idade mediana de 12 anos, variando de 7 a 19 anos), 77,3% foram submetidos à ileocistoplastia com Mitrofanoff. Antes da CA, a IU foi diagnosticada em 81,8% dos pacientes, com 83,3% obtendo resolução completa após a CA (p<0,001). O RVU estava presente em 31,8% dos pacientes antes da CA. O RVU de alto grau foi resolvido em 90,9 a 100% dos pacientes. (p=0,001). A CCM aumentou de 120 ml para 405 ml (p<0.001) e CVE normalizou em 85,7% dos pacientes (p<0.001). A complacência da bexiga melhorou significativamente de 6,4 ml/cmH2O para 38,3 ml/cmH2O (p<0,001). A mediana da pressão detrusora ao final do enchimento diminuiu de 20,0 para 11,0 cmH2O (p<0,001). Conclusão: Após a CA, as crianças e adolescentes com BN refratária apresentaram melhora significativa na IU, RVU, CCM, complacência vesical e na pressão detrusora ao final do enchimento.

Palavras-chave: cistoplastia de aumento; bexiga neurogênic; incontinência urinária; refluxo vesicoureteral; urodinâmica.

Abstract

Introduction: Neurological disorders, particularly neural tube defects such as spina bifida, can lead to neurogenic bladder (NB) in children and adolescents. NB is characterized by highpressure filling of the bladder and inefficient emptying, resulting in complications such as urinary incontinence (UI), recurrent urinary infections, vesicoureteral reflux (VUR), and an increased risk of kidney damage. Initial treatments include clean intermittent catheterization, anticholinergic medications, or the application of botulinum toxin A. Augmentation cystoplasty (AC) is a surgical procedure aimed at creating a low-pressure, high-capacity bladder reservoir to preserve kidney function and improve quality of life. It is indicated when minimally invasive treatments fail. Ileocystoplasty and colocystoplasty are commonly used techniques to increase bladder capacity and compliance. Objectives: The primary objective of this study was to evaluate UI, VUR, and urodynamic parameters in children and adolescents with refractory NB after AC and compare these findings with preoperative data. The second objective was to conduct a systematic review to analyze the clinical and urodynamic findings in children and adolescents with NB who underwent AC. Patients and Methods: Retrospective cohort study that recruited 42 patients with refractory NB who underwent AC alone between February 2009 and March 2023. Exclusion criteria were patients with non-neurogenic lower urinary tract anomalies and patients with previous vesicostomy. The parameters evaluated in this study, before and after AC, with at least one year of follow-up, included UI, VUR and urodynamic data, such as maximum cystometric capacity (MCC), expected bladder capacity (EBC), bladder compliance and end filling detrusor pressure. Results: Of 22 eligible patients (50% male, median age 12 years- range from 7 to 19), 77.3% underwent ileocystoplasty with Mitrofanoff. Pre-AC, UI was diagnosed in 81.8% of patients, with 83.3% achieving complete resolution post-AC (p<0.001). VUR was present in 31.8% of patients' pre-AC; post-AC, high-grade VUR resolved in 90.9 to 100% of the patients (p=0.001). Median MCC increased from 120 ml to 405 ml (p<0.001), and EBC normalized in 85.7% of patients (18/21) (p<0.001). Bladder compliance significantly improved from 6.4 ml/cmH2O to 38.3 ml/cmH2O (p<0.001), while median end filling detrusor pressure. decreased from 20.0 to 11.0 cmH2O (p<0.001). Conclusion: After AC, children and adolescents with refractory NB showed significant improvement in UI, VUR, MCC, bladder compliance and end filling detrusor pressure.

Keywords: augmentation cystoplasty; neurogenic bladder; urinary incontinence; vesicoureteral reflux; urodynamics.

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LISTA DE ABREVIATURAS E SIGLAS

BN: Bexiga neurogênica

CA: Cistoplastia de Aumento

CCM: Capacidade Cistométrica Máxima

CIL: Cateterismo intermitente limpo

CVE: Capacidade vesical esperada

DLPP: Detrusor Leak Point Pressure

EUD: Estudo Urodinâmico

ITUs: Infecções do trato urinário inferior

IU: Incontinência urinária

MMC: Mielomeningocele

Pdet: Pressão detrussora

RVPM: Resíduo vesical pós-miccional

RVU: Refluxo vesicoureteral

Tc-99m DMSA: Ácido dimercaptosuccínico-tecnécio-99m

TUI: Trato urinário inferior

UCM: Uretrocistografia Miccional

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1 INTRODUÇÃO

O trato urinário inferior normal permite o enchimento coordenado de baixa pressão e o esvaziamento voluntário da bexiga. Lesões no sistema nervoso central ou periférico podem alterar essa função, levando a dissinergia detrusor esfincteriana, denominada bexiga neurogênica (BN)¹⁻⁵. A principal causa da BN em crianças e adolescentes é o disrafismo espinhal, com a mielomeningocele (MMC) sendo responsável por 85% dos casos^{3,5,6}. Aproximadamente 98% das crianças com MMC também apresentam BN⁷.

Crianças e adolescentes com BN podem apresentar diversos tipos de dissinergia detrusor esfincteriana, categorizados com base nos resultados urodinâmicos. Isso pode resultar em incontinência urinária (IU), infecções do trato urinário (ITU), refluxo vesicoureteral (RVU) e, finalmente, cicatrizes renais, que podem resultar em doença renal crônica, necessitando de terapia renal substitutiva e/ou transplante^{3-5,8,9}. Durante fases de rápido crescimento, como nos dois primeiros anos de vida e na puberdade, o padrão de BN pode se alterar, permitindo que a doença progrida^{3,8,10}.

Uma abordagem abrangente e multidisciplinar é essencial para o diagnóstico e monitoramento eficaz de pacientes com BN^{3,5,9,10}. A meta do manejo da BN é estabelecer um reservatório de pressão baixa e alta complacência, protegendo trato urinário superior de danos e preservando a função renal. Essa abordagem inclui seriadas avaliações clínicas, laboratoriais, além de exames radiológicos, como ultrassonografia renal e da bexiga, urografia, estudo urodinâmico (EUD), uretrocistografia miccional (UCM), e cintilografia renal estática com ácido dimercaptosuccínico-tecnécio-99m (Tc-99m DMSA)^{3,5,6,9}. Um diagnóstico tardio, ITUs recorrentes, espessamento da parede vesical, resíduo vesical pós-miccional (RVPM) elevado, RVU primário ou secundário, *detrusor Leak Point Pressure* (DLPP) >40 cmH2O e pressão detrusora ao final do enchimento (> 10 cm H2O cmH2O) podem aumentar o risco de deterioração do trato urinário superior^{6,11-13}.

Em relação a proposta terapêutica, ainda é controverso determinar a melhor abordagem^{6,14}. A abordagem proativa recomenda cateterismo intermitente limpo (CIL) precoce, medicamentos como anticolinérgicos desde o diagnoóstico. Por outro lado, a abordagem expectante é mais conservadora, com foco no monitoramento e avaliação de risco antes de iniciar o tratamento^{5,9}. Apesar dos estudos sobre o manejo da BN em crianças e adolescentes

identificar aqueles que se beneficiariam com o início precoce CIL o momento ideal para cada intervenção médica ou cirúrgica permanece desafiador^{3,5,9,12}. Se os tratamentos de primeira linha falharem, as opções de segunda linha, como beta-agonistas e toxina botulínica A, podem melhorar a continência urinária e manter pressões intravesicais adequadas⁵. Em alguns casos, os pacientes com BN podem precisar de intervenção cirúrgica, apesar de receberem tratamento adequado, devido a não resposta ou a baixa adesão ao tratamento^{3,15,16}.

A cistoplastia de aumento (CA) é um procedimento cirúrgico que foi descrito pela primeira vez no final do século XIX e foi aprimorado por Goodwin na década de 1950¹⁷. Durante a cirurgia, um segmento intestinal ou ureteral, juntamente com seu suprimento sanguíneo é detubulizado, reconfigurado em forma de uma placa e anastomosado na bexiga garantindo a expansão do reservatório e assim reduzindo a pressão vesical^{15,18}. A ileocistoplastia e a colocistoplastia são atualmente os procedimentos padrões utilizados para a CA, uma vez que o íleo e o colón são segmentos longos e possuem uma adequada capacidade de distensibilidade^{19,20}. Pacientes que se submetem à CA tem a necessidade de realização de CIL²¹. Durante a cirurgia pode-se realizar um conduto cutâneo continente utilizando o apêndice cecal (técnica de Mitrofanoff) ou um segmento de íleo (técnica de Yang Monti) para facilitar a realização deste procedimento de cateterização vesical^{22,23}.

A CA pode melhorar significativamente a qualidade de vida de pacientes com BN. Estudos demonstraram que ela pode aumentar a adesão ao tratamento em 69-100%, restaurar a continência em 75-100% e reduzir o risco de envolvimento do trato urinário superior. No entanto, é essencial observar que essa cirurgia também apresenta alguns riscos²⁴. Complicações a longo prazo podem surgir devido a diferenças funcionais entre o epitélio urinário e intestinal. Essas complicações podem incluir infecções do trato urinário recorrentes, urolitíase, produção de muco, deficiência de vitamina B12, desequilíbrios metabólicos por absorção de eletrólitos urinários (como íons de hidrogênio, amônio e cloreto) através do segmento intestinal ^{19,25}. Isso pode causar acidose metabólica hiperclorêmica, afetando negativamente o crescimento ósseo e a saúde ¹⁵. Além disso, lesões malignas e perfuração da bexiga podem ocorrer. A perfuração da bexiga pode acontecer devido a vários fatores, incluindo trauma externo, cateterização, má adesão aos regimes de cateterização, isquemia crônica e distensão aguda ou crônica da bexiga ²⁶. A CA apresenta uma taxa de mortalidade variando de 0 a 2,7%, e as taxas de morbidade precoce também são significativas¹⁵. Segundo Szymanski et al. ²⁷, aproximadamente 7,6% das crianças

e adolescentes com espinha bífida submetidos à CA, morreram com uma mediana de 10,6 anos após o procedimento^{28,29}. Curiosamente, foi constatado que as principais causas de morte nesses pacientes foram infecções não urológicas, em vez de complicações associadas à CA ou doença renal crônica²⁹.

Com base no exposto, este estudo se propôs a analisar a IU, RVU e parâmetros urodinâmicos após a CA em crianças e adolescentes com BN refratária e compará-los com os dados pré-cirúrgicos. A CA foi realizada pelo mesmo cirurgião, na mesma instituição, e os mesmos examinadores foram encarregados dos exames de seguimento.

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2 OBJETIVOS

2.1 Objetivo primário

Avaliar a incontinência urinária, o refluxo vesicoureteral e os parâmetros urodinâmicos em crianças e adolescentes com bexiga neurogênica refratária após cistoplastia de aumento e comparar esses achados com dados pré-operatórios.

2.2 Objetivo secundário

Realizar uma revisão sistemática da literatura sobre achados clínicos e urodinâmicos em crianças e adolescentes com bexiga neurogênica refratária, submetidos à cistoplastia de aumento.

3 REVISÃO DA LITERATURA

A revisão da literatura será apresentada como uma revisão sistemática que utilizou três grandes bases de dados eletrônicas até março de 2024. A estrutura *PICO (Patients, Interventions, Comparison, and Outcomes)* foi utilizado para desenvolver a busca por uma resposta à questão central desta revisão sistemática: "Quais as principais alterações clínicas e urodinâmicas após cistoplastia de aumento em crianças e adolescentes com bexiga neurogênica?"

SYSTEMATIC REVIEW/META-ANALYSIS



Clinical and urodynamic findings in children and adolescents with neurogenic bladder undergoing augmentation cystoplasty: a systematic review

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Abstract

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Background Augmentation cystoplasty (AC) is a procedure to improve the clinical and urodynamic parameters of neurogenic bladder (NB) in children and adolescents refractory to other treatments. We performed a systematic review to investigate these parameters in children and adolescents with NB undergoing AC.

Methods We followed PRISMA guidelines and searched electronic databases until March 2024 for studies involving patients aged three to 19 years diagnosed with NB undergoing AC. We assessed clinical and urodynamic parameters before and after surgery, focusing on improvements in urinary incontinence, vesicoureteral reflux (VUR), bladder capacity, compliance, and end filling detrusor pressure (EFP).

Results A total of 212 NB patients underwent AC and were evaluated for urinary incontinence before and after surgery. Two studies showed a 76.5% to 78.9% improvement in incontinence without bladder outlet procedures (BOP). Another study found no significant difference in incontinence improvement rates between AC with and without BOP. The VUR resolution rate assessed in three studies ranged from 12.5 to 64%. Three studies showed a variation in bladder capacity from 52.8 to 70% of the expected bladder capacity pre-AC to 95.9 to 119%, post-AC. A fourth study showed a variation in bladder capacity from 87 ml pre-AC to 370 ml post-AC. Two studies showed a variation from 3.2 to 4.6 ml/cm H₂O pre-AC to 13.7 to 41.3 ml/cm H₂O post-AC in bladder compliance. The EFP in three studies varied from 37.2 to 47.6 cm H₂O pre-AC to 11 to 17.4 cm H₂O post-AC.

Conclusion After AC, urinary incontinence, bladder capacity, EFP, and bladder compliance improved in children and adolescents with NB.

Keywords Augmentation cystoplasty · Neurogenic bladder · Urinary incontinence · Urodynamics

Ak AC BC	g	CIC EBC EFP NB	Clean intermittent catheterization Expected bladder capacity End filling detrusor pressure Neurogenic bladder
\boxtimes	Flávia Cristina de Carvalho Mrad flaviacarvalhomrad@gmail.com	PRISMA PROSPERO	Preferred Reporting Items for Systematic Reviews and Meta-Analyses International Prospective Register of Sys-
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3	Urology Unit, Hospital Felicio Rocho, Belo Horizonte, Brazil Department of Urology, Universidade Estadual de Feira de Santana (UEFS), Feira de Santana, Brazil	UTIs VUR	Urinary tract infections Vesicoureteral reflux



Introduction

The lower urinary tract is responsible for the low-pressure filling and periodic voluntary emptying of the bladder in a coordinated manner [1, 2]. It involves the coordination of muscle contraction and relaxation of urinary sphincters controlled by the nervous system [1–5]. Damage to the nervous system can lead to neurogenic bladder (NB), causing abnormal bladder and/or sphincter functions [3–9]. NB is primarily caused by neural tube defects [4, 10–12] and is present in approximately 98% of all children and adolescents with myelomeningocele [13]. Other causes include sacral agenesis, imperforate anus, spinal cord injury, cerebral palsy, brain or spinal tumors, and pelvic surgery [3, 7].

NB accounts for about 25% of the most severe symptoms in pediatric urology [14]. Patients with NB may present urinary and fecal incontinence, severe constipation, urinary tract infections (UTIs), and vesicoureteral reflux (VUR), which can result in kidney scarring and kidney failure. Delayed diagnosis, frequent UTIs, thickened bladder wall, high post-void residual volume, and primary or secondary VUR further increase the risk of upper urinary tract deterioration. Additionally, urodynamic parameters such as reduced bladder capacity and compliance, high detrusor leak point pressure, or end filling detrusor pressure (EFP) (> 40 cm H₂O) are predictive factors of kidney damage [3–9, 14, 15].

There are two main approaches to managing neurogenic bladder in children and adolescents: proactive and expectant. The proactive approach involves early initiation of clean intermittent catheterization (CIC), close monitoring, liberal use of medications, and timely surgical interventions. The expectant approach is more conservative and only involves interventions when changes in the upper tract are detected during patient monitoring [4–6, 16]. Studies tend to favor proactive management [17]. There are second-line treatments such as beta-agonists and botulinum toxin A. However, despite maximal medical and extended intervention, some patients may require surgical intervention, including augmentation cystoplasty (AC) [4, 16, 18–20].

AC was first described in the late nineteenth century and refined by Goodwin in the 1950s [21]. This procedure involves using a portion of the ileum or colon to increase the capacity and compliance of the bladder, allowing urine to be stored at low pressures [18–22]. Additionally, AC may include creating a catheterizable conduit [23] using either the vermiform appendix or the small intestine [24]. This procedure can significantly improve the quality of life for patients with NB by reducing urinary incontinence, enhancing treatment adherence, and reducing the risk of upper urinary tract involvement [25]. However, it does carry risks due to long-term complications arising from functional differences between the urinary and intestinal epithelium [25–28].

Although AC has high patient satisfaction rates [29], results vary significantly in the medical literature. Therefore, this systematic review compares children's and adolescents' clinical and urodynamic parameters before and after performing AC.

Methods

The present systematic review was guided by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [30] and registered with the International Prospective Register of Systematic Reviews (PROSPERO) [31] under number CRD42023467367.

Eligibility criteria

The PICO structure (Problem or Population, Interventions, Comparison and Result) was used in the development of the search for an answer to the central question of this review: What are the main clinical and urodynamic changes after augmentation cystoplasty in children and adolescents with neurogenic bladder? This phase was developed by all authors as follows:

- P- Patients aged 3 to 19 years with a confirmed diagnosis of neurogenic bladder
- I- Augmentation cystoplasty
- C- Compare clinical and/or urodynamic parameters before and after augmentation cystoplasty surgeries
- O- Clinical and/or urodynamic outcomes (urinary continence, resolution of vesicoureteral reflux, median estimated bladder capacity, median bladder compliance, median detrusor end fill pressure).

Studies whose samples included children and adolescents with other underlying pathologies, such as metabolic and intestinal diseases and patients lost to follow-up before one year postoperatively, were excluded from this systematic review.

Search strategy and selection procedure

The electronic bibliographic databases MEDLINE (via PubMed), SCOPUS and Web of Science were searched until March 2024 by two authors (FCCM and MMAV). The research was carried out systematically and independently using the terms: ("Urinary Bladder Neurogenic" OR "Bladder Neurogenic") AND ("Cystoplasty" OR "Augmentation Cystoplasty"). Reference checking of selected articles was used to identify additional studies that were missed. Articles were selected in English, Spanish, French, Japanese,



German, Polish, Hebrew, Turkish, Dutch, Danish, Czech, Chinese, and Portuguese. Reviews, letters, case reports, notes, editorials, book chapters, conference papers, case series, and comments were excluded.

Once the search strategy was completed, all the identified studies were organized into an online library system. The two authors (FCCM and MMAV) removed any duplicate articles and independently selected the studies based on their titles and abstracts. Later, the full text of the selected articles was examined by three independent reviewers (FCCM, MMAV, and OAFR) using pre-defined eligibility criteria. Any discrepancies or eligibility issues were resolved through discussion until a final consensus was reached. The reasons for excluding articles are recorded in this review. A scan of the references of included studies was performed to identify any additional studies that may have been missed.

Data extraction

Four authors (DJOF, HNI, JOO, and PLLS) developed a data extraction form and used it to extract data from the studies included in this systematic review.

The data selected for extraction were: author name, study design, study population and country of origin, demographics and sample size, criteria for diagnosis (etiology) of NB, period of follow-up, surgical procedures, clinical and urodynamic parameters; outcomes before and after intervention: clinical outcomes (urinary incontinence, presence of VUR) and urodynamic outcomes (expected bladder capacity (EBC) (%); end filling detrusor pressure (EFP) (cm H₂O); bladder compliance (ml); success outcome measures: clinical (improved urinary incontinence and resolution of VUR) and urodynamic (bladder capacity greater than 50% predicted; EFP < 40 cm H₂O) and limitations.

The authors resolved any discrepancies in the extracted data through discussion and contacted the authors of the included studies to clarify any unclear information.

Assessment of the risk of bias in individual studies

The included studies were assessed for potential bias by three authors (DJOF, HNI, and JOO) using the Risk Of Bias In Non-Randomized Studies-of Intervention (ROBINS-I) assessment tool [32]. Afterward, the authors used the Risk-Of-Bias Visualization (ROBVIS) web application to visually present the bias assessment of the included articles [33].

The ROBINS-I tool has three domains, namely Preintervention, Intervention, and Post-intervention, which assess biases related to confounding, selection of study participants, classification of interventions, deviations from intended interventions, missing data, outcome measurement, and selection of reported outcome. The overall risk of bias and domain-level judgments in ROBINS-I were classified as low, moderate, serious, critical, or not available. We chose to use the ROBINS-I tool since all the studies included in this systematic review were non-randomized [32].

Results

Selection of included studies

The search terms ("Urinary Bladder Neurogenic" OR "Bladder Neurogenic") AND ("Cystoplasty" OR "Augmentation Cystoplasty") resulted in a total of 474 articles. Of these, 244 articles were found in MEDLINE (via PubMed), 197 in SCOPUS, and 33 on the Web of Science. After removing duplicates, reviews, editorials, and case reports, 263 studies remained. Out of the 263 studies identified, 95 were excluded after analyzing the title, and 127 were excluded after reading the abstract as they didn't meet the inclusion criteria. Therefore, only 41 studies were left to be screened by reading the full text. Of these studies, 35 were excluded for reasons such as patients over 19 years of age, patients without a confirmed diagnosis of NB, and incomplete description of urodynamic and/or clinical data, among other factors. Thus, only six articles [34-39] were included in this systematic review. Figure 1 summarizes the database search following the PRISMA guidelines [30].

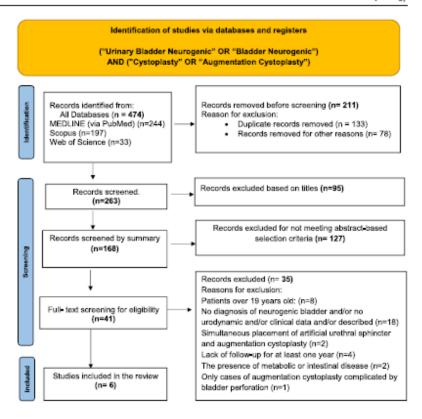
Characteristics of the included studies and participants

The review examined six studies [34–39] that included 212 children and adolescents with NB, primarily caused by neural tube defects, who underwent AC. In two studies, 73 individuals also underwent AC along with bladder outlet procedures (BOP) [36, 38]. Among the participants, 34.9% (74/212) underwent the procedure with the sigmoid segment, and 30.6% (65/212) underwent surgery with the ileum segment. The surgical technique used was not reported in 73 patients [36, 38].

The studies included 44.8% (95/212) male patients aged between 3 and 19 years. The average follow-up time presented in the studies varied from 1 to 19.3 years. Only one study was conducted prospectively, and all studies were presented in English except for one, which was carried out by Zaragoza-Torres et al. [37] and which was presented in Spanish. Table 1 provides detailed information about the studies and participant characteristics.



Fig. 1 Flowchart with the research methodology following PRISMA guidelines [30]



Main clinical findings of the included studies

In two studies [35, 39], researchers examined the effectiveness of AC without BOP for urinary incontinence in 26 and 22 patients, respectively. Medel et al. [35] presented findings from two groups: one consisting of 19 patients who experienced urinary incontinence before undergoing AC, and another comprising seven patients who were continent before undergoing AC. The improvement rate among the patients was 78.9% (15/19), and continence was maintained in the group that was continent before the procedure. Chang et al. [39] demonstrated an 76.5% (13/17) improvement in urinary incontinence. In a third study, Khoury et al. [36] divided the groups into AC without BOP (G1) and with BOP (G2) and found that the improvement rates for incontinence were 91.3% (21/23) and 80% (8/10), respectively, without statistical significance.

Three studies [35, 36, 39] showed data about the effectiveness of AC in the resolution of VUR. Medel et al. [35] showed eleven patients with sixteen units (30.7%) with VUR; all these patients were reimplanted concomitantly with the AC. VUR resolution was achieved in 81.2% of the units, with only three remaining refluxing units. Khoury

et al. [36] identified VUR in 16 patients undergoing AC without BOP, eight of whom were reimplanted during the AC, and eight underwent AC exclusively without ureteral reimplantation. The eight reimplanted patients and six of the non-reimplanted had resolution of the VUR. Two patients who had AC only had their VUR downgraded. In the AC with BOP group, there was no assessment of VUR. In the Chang et al. study [39], eighteen patients had VUR in 25 kidney units (81.8%). Of these, seventeen units received surgical or endoscopic treatment before or during the AC. VUR resolution was found in sixteen kidney units (64%) and downgraded in seven (28%). None of these studies presented separate results for the VUR resolution rate of reimplanted patients versus those who underwent AC exclusively.

Table 2 presents the main clinical findings of the studies included in this review.

Main urodynamic findings of the included studies

Four studies investigated variation in bladder capacity, focusing on expected bladder capacity (EBC) for age [34, 35, 37, 39]. Three of these studies evaluated mean bladder capacity before and after AC [35, 37, 39]. In Medel's study



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Table 1 Characteristics of the studies and demographic data of the samples

Studies	Study design	Sample n=212	Study population		Country of	Follow-up	NB etiology	Augmentation
			Male n (%)	Age (y) mean* or median** (range or IQR)	origin	in years and/ or mean* or median** (range or IRQ)	Neural tube defects n (%)	cystoplasty n (surgical tech- nique)
Arikan et al., 2000 [34]	Prospective	18	10 (55.5)	10.3* (5–17)	Turkey	3.42* (1.33- 5.83)	9 (50)	18 (Sigmoid colon)
Medel et al., 2002 [35]	Retrospective	26	12 (46)	12* (5–19)	Argentina	3.8* (1-10)	26 (100)	26 (Ileum)
Khoury et al., 2008 [36]	Retrospective	23 (G1= AC alone) 10 (G2= AC+BOP)	10 (43) 5(50)	7.7* (3–17) 9.8* (2–14)	Canada	7** (3–12) 5** (3–8)	23 (100) 10 (100)	20 (Ileum) 3 (Sigmoid colon) 10 (not reported)
Zaragoza- Torres et al., 2016 [37]	Cross- sectional descriptive	50	25 (50)	12** (6-16)	Mexico	>15	50 (100)	50 (Sigmoid colon)
Weaver et al., 2021 [38]	Retrospective	63 (G2=AC+BNP)	27 (44.3)	10.3** (IQR 6.2)	USA	5.73** (IRQ 6.55)	63 (100)	63 (not reported)
Chang et al., 2024 [39]	Retrospective	22	6 (27)	7.6* (3.2–12)	Taiwan	13.4* (7.5–19.3)	19 (86.5)	19 (Ileum) 3 (Sigmoid colon)

Data provided through contact with the authors

IQR; interquartile range, AC; augmentation cystoplasty, NB; neurogenic bladder, USA; United States of America, G1; group 1, BOP; bladder outlet procedure, G2; group 2, BNP; bladder neck procedure

Table 2 Main clinical findings of the included studies

	Sample included n	Urinary Incontinence n (%)		Vesicoureteral Reflux (VUR) n patients (%) n units (%)		
Surgery		Pre-AC	Post-AC	Pre-AC	Post-AC	
Arikan et al., 2000 [34]	18	-	3 (16.6)	4pts (22.2) 6 units (16.6)	not reported	
Medel et al., 2002 [35]	26	19 (73.1)	4 (15.4)	11pts (42.3) ^a 16 units (30.7)	3pts (11.5) 3units (5.8)	
Khoury et al., 2008 [36]	23 (G1 = AC alone) 10 (G2 = AC +BOP)	23 (100) 10(100)	2 (8.7) 2 (20)	16 pts (70) ^b 2 pts (20)	10pts (13) ^c not reported	
Zaragoza-Torres et al., 2016 [37]	50	-	-	-	-	
Weaver et al., 2021 [38]	63 (G2=AC+BNP)	-	-	24 pts (38.1)d	not reported	
Chang et al., 2024 [39]	22	17 (77.3)	4 (18.2)	18 pts (81.8) 25 units (56.8)*	not reported 9 units (9.1)**	

GI; group 1, BOP; bladder outlet procedure, G2; group 2, BNP; bladder neck procedure, VUR; vesicoureteral reflux, AC; augmentation cystoplasty



^{*17} units of VUR treated (15 with ureleral reimplantation and two with dextranomer hyaluronic acid copolymer) and eight units of VUR untreated

^{** 16} units of VUR resolved and eight units had their VUR grade reduced

^{*}All patients undergoing AC with ureteral reimplantation

^bEight patients with ureteral reimplantation and eight no ureteral reimplantation

^cAmong the patients who submitted to ureteral reimplantation: six resolved and two reduced the VUR grade

^dThree patients with ureteral reimplantation

[35] the mean bladder capacity was 70% and 119.9% of the EBC before and after the operation, respectively. Zaragoza-Torres et al. [37] reported the mean bladder capacity as 52.8% and 95.9% pre- and postoperatively, respectively, while Chang et al. [39] found it to be 53.2% and 110.6%. On the other hand, Arikan et al. [34] evaluated the variation in bladder capacity in ml, with an average bladder capacity of 87 mL before AC and 370 mL after AC.

Three studies have evaluated the variation in EFP measured in cystometric capacity [35, 37, 38]. Medel et al. [35] reported a mean pre-postoperative EFP of 47.6 cm $\rm H_2O$ and 14.8 cm $\rm H_2O$, Zaragoza-Torres et al. [37] showed a mean pre-postoperative EFP of 40.8 cm $\rm H_2O$ and 11 cm $\rm H_2O$, and Weaver et al. [38] reported a mean pre-postoperative EFP of 37.2 cm $\rm H_2O$ and 17.4 cm $\rm H_2O$, respectively.

Two studies [34, 37] presented data on the variation of compliance post-AC. In both studies, AC was performed only with sigmoid colon. The study by Arikan et al. [34] evaluated 18 patients, and the compliance variation was from 3.2 ml/cm $\rm H_2O$ pre-AC to 13.7 ml/cm $\rm H_2O$ post-AC. In the study by Zaragoza-Torres et al. [37] 50 patients were studied, and the compliance variation was from 4.6 ml/cm $\rm H_2O$ pre-AC to 41.3 ml/cm $\rm H_2O$ post-AC.

All the details regarding the urodynamic parameters mentioned in the studies included in this review are presented in Table 3.

Assessment of the risk of bias in individual studies

The studies included were analyzed for risk of bias using the ROBINS-I [32] tool, which was chosen based on the type of study design. The analysis presentation was presented visually using the ROBVIS [33] web application. According

to the analysis, all six included studies [34–39] presented a moderate overall risk of bias. Figure 2A and B provide a detailed analysis of the risk of bias for each study included in this review.

Discussion

In this systematic review, we evaluated the outcomes of AC for repairing bladder storage function damage caused by NB in children and adolescents. The parameters we analyzed included urinary incontinence, vesicoureteral reflux, as well as urodynamic findings such as bladder capacity, EFP, and bladder compliance.

Urinary continence is a multifaceted problem that involves medical, psychological, and social factors [40]. Even with medical treatment, 10–20% of children and adolescents with NB may require surgery due to persistent urinary incontinence [41–43]. Medel et al. [35] and Chang et al. [39] have had reasonable success rates of urinary incontinence after AC without BOP. According to these studies, 76.5 to 78.6% of patients showed improvement in urinary incontinence [35, 39]. The literature shows a more significant variation in the success rate for achieving urinary continence of 40–90% [7, 41–44], probably due to the complexity of the NB.

Some studies have attempted to differentiate between incontinent children who require BOP before or concomitant with AC and those for whom AC alone is sufficient to achieve dryness [40, 45, 46]. In Khoury's study [36], urinary incontinence improvement rates were compared between patients who underwent AC alone (91.3%) and those who underwent AC with BOP (80%). The study concluded that there was no statistical difference

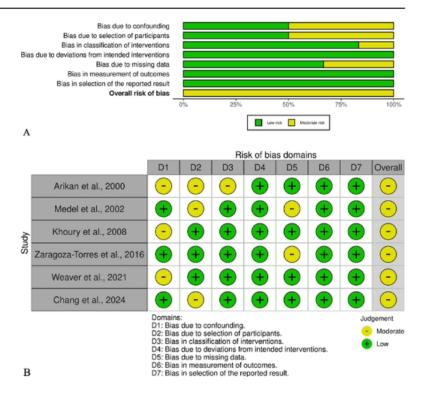
Table 3 Main urodynamic findings of the included studies

	Bladder capacity (BC) (range) mL mean* or median**		End filling detrusor pressure (EFP) in cmH ₂ O mean*±SD or median**(range)		Bladder compliance mL/cm H ₂ O	
	Pre-AC	Post-AC	Pre-AC	Post-AC	Pre-AC	Post-AC
Arikan et al., 2000 [34]	87±7	370±52		-	3.2±0.9	13.7±2.9
Medel et al., 2002 [35]	70* (% EBC) (22-140)	119.9* (% EBC) (54-180)	47.6* (3-97)	14.8* (2-40)	-	-
Khoury et al., 2008 [36]			-	-	-	-
Zaragoza-Torres et al., 2016 [37]	52.8 ± 20,1* (% EBC) 54** (11-100)	95.9±8,8* (% EBC) 100** (63-100)	40.8 ± 18.9* 40** (8-100)	11±8.9* 9** (2-47)	4.6 ± 3.2	41.3 ± 4.3
Weaver et al., 2021 [38]	44.1%** (10.5 - 102.6) (IQR 0,6)	-	37.2	17.4	-	-
Chang et al., 2024 [39]	53.2±27.4* (% EBC)	110.6 ± 22.4 (% EBC) No patient BC < 65% EBC	-	-	Reduced in 77.3% of the patients	29.1 ± 16.7

BC; bladder capacity, EBC; expected bladder capacity, EFP; end filling detrusor pressure, IQR; interquartile range



Fig. 2 A Risk of bias graph: review of authors' judgements about each risk of bias domain presented as percentages across all included studies based on the Risk Of Bias In Non-randomized Studies-of Interventions (ROBINS-I) [31, 32]. B Risk of bias summary: review of authors' judgements about each risk of bias domain presented for each of the included studies based on the Risk Of Bias In Non-randomized Studies-of Interventions (ROBINS-I) [31, 32]



in the rates of improvement in urinary incontinence between the two groups. Dave et al. [41] demonstrated an overall drying success rate of 78% in NB patients with urinary incontinence. Success rates were significantly higher in those who underwent AC with Mitrofanoff (90%) versus AC with BOP (66%). Additionally, there is also a 50% chance of needing additional surgery. According to Gonzalez and Sidi [40], bladder neck surgeries are unnecessary if one or both sphincters are competent, as concluded by their patients after performing cystography. Also, Cher and Allen [45], based on measures of urethral resistance pressures, concluded that when urethral resistance exceeds 25–30 cm H₂O, isolated ileocystoplasty would be sufficient for satisfactory urinary continence post-AC.

VUR can occur due to increased bladder pressure and anatomical changes in the ureter-bladder connection in patients with NB [46]. When these patients require AC for VUR, the decision to perform simultaneous ureteral reimplantation is uncertain due to the risk of persistent reflux and potential complications [47]. It is challenging to identify which patients would benefit from ureteral reimplantation. This review showed that three studies [35, 36, 39] found VUR in 45 patients. Treatment led to resolution rates of 64% to 100% and reduced VUR grade from 18.8 to 28%.

However, it needs to be clarified if ureteral reimplantation was necessary. Other studies provide essential information on the VUR approach. The studies did not distinguish between patients who had ureteral reimplantation with AC and those who had AC only. Therefore, it was unclear which patients would require reimplantation. Chiba et al. [47] found an 85% resolution of VUR and an 11% reduction in grade in 27 kidney units treated exclusively with AC. Zhang et al. [48] found that in 29 kidney units of patients with NB and VUR who underwent AC without reimplantation, 83% experienced resolution of VUR, while 10% showed a reduction in grade. Soygur et al. [46] found that VUR occurring at small volumes (average 29.6 ml) and low pressures (average 14.6 cm H₂O) benefit from simultaneous reimplantation with AC in patients with NB. Similarly, Wang et al. [49] conducted a study of 173 patients undergoing AC with or without ureteral reimplantation and concluded that the procedure should be performed for low-pressure VUR, high-grade VUR, and severe ureteral dilation and tortuosity, and ureterovesical junction obstruction.

The improvement in urodynamic patterns after AC in patients with NB is associated with improvement in clinic parameters mentioned in this review. The capacity of the bladder in children and adolescents varies with age. It can



be calculated using the formula [Age (years) × 30] + 30 [50]. Four studies in this review [34, 35, 37, 39] evaluated this variable and all showed a significant improvement in bladder capacity. Studer et al. [51] found that the follow-up study with a multidisciplinary team revealed that six months after AC, mean functional capacity increased as expected and tended to be maintained or improved further during subsequent follow-up. Increased bladder capacity enhanced urinary continence, and urotherapy proved essential for these patients. It's worth noting that we couldn't find any other studies demonstrating similar improvement in EBC after AC.

Three studies examined the efficacy of EFP [35, 37, 38], which measures detrusor pressure at maximum cystometric capacity. Considering the bladder's property of storing urine under low pressure, an increase in EFP is considered pathological. An increase of up to $10~\rm cm~H_2O$ is ideal [52]. An EFP greater than $40~\rm cm~H_2O$ is considered a risk for the upper urinary tract [53]. Chartier-Kastler et al. [54] found that maximal EFP decreased from $65.5 \pm 50.2~\rm cm~H_2O$ before surgery to $18.3 \pm 7.9~\rm cm~H_2O$ after augmentation enterocystoplasty in spinal cord injury patients. Similarly, Krebs et al. [55] observed a significant reduction in median maximum detrusor pressure from $38~\rm cm~H_2O$ before surgery to $15~\rm cm~H_2O$ after supratrigonal cystectomy and augmentation ileocystoplasty in patients with refractory neurogenic lower urinary tract dysfunction.

Considering age variations, determining a reference value for bladder compliance in children and adolescents is complex. It should be noted that detrusor pressure should not exceed 10 cm H2O in the EBC [52]. The loss of bladder accommodation capacity leads to clinical changes such as urinary incontinence and VUR and is the main reason for indicating surgical treatment for NB. Two studies analyzed in this review evaluated the improvement in bladder compliance and showed a significant enhancement in this urodynamic parameter after AC [34, 37]. These findings were consistent with other studies that showed improved bladder compliance after AC [56-58]. However, some authors disagree, presenting unsatisfactory results in improving this urodynamic parameter. This discrepancy may be attributed to the persistent contractile activity of the intestinal loop, which maintains cyclic elevations of bladder pressure [59].

It's important to note that this surgery carries risks, including long-term complications such as recurring UTIs, urinary stone formation, mucus production, vitamin B12 deficiency, metabolic imbalances, and electrolyte absorption. Bladder perforation and malignant lesions may also occur [35, 45-47]. Mortality rates range from 0 to 2.7%, with significant early morbidity rates [60, 61]. Approximately 7.6% of children and adolescents with spina bifida who undergo this procedure die on average 10.6 years

after the surgery, often due to non-urological infections rather than surgery-related complications or chronic kidney disease [62].

Although our review was comprehensive, it had some limitations. One of the major challenges was the small number of studies we could include, as well as the data heterogeneity. We found that some of the six studies we reviewed did not report essential non-urodynamic data analysis before or after AC. Even though postoperative urodynamics are routinely performed, we are concerned about the lack of standardization in assessing VUR resolution with and without ureteral reimplantation. The heterogeneity of the data prevented the performance of a meta-analysis, highlighting the need for more standardized studies to improve future research.

Conclusion

According to this review, we concluded that there was an improvement in urinary incontinence in children and adolescents with NB after AC. Furthermore, there was an improvement in bladder capacity, EFP, and bladder compliance among urodynamic parameters. Hence, more studies with improved designs are crucial to better evaluate the outcomes after an AC.

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Author's contributions All authors contributed to the study conception and design. The search in the database was carried out independently by FCCM and MMAV. After removing the duplicates, the remaining titles/abstracts were independently selected by two authors (FCCM and MMAV). The full text of the studies using predefined eligibility criteria was examined by three independent reviewers (FCCM, MMAV, and OAFR), and eligibility and discrepancies were resolved through discussion. DJOF, HNI, JOO and PLLS were responsible for extracting data from articles selected for inclusion. Risk-of-bias analysis of the eligible studies was performed by three authors (DJOF, HNI and JOO). The first draft of the manuscript was written by EML, FCCM, JBJ, MMA, OAFR and PLLS and all authors contributed to previous versions of the manuscript. All authors have read and agreed to the published version of the manuscript.

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Declarations

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4 MÉTODOS

4.1 Desenho do Estudo

Trata-se de um estudo de coorte retrospectivo, transversal e observacional de pacientes pediátricos e adolescentes consecutivos com BN refratária submetidos a CA entre fevereiro de 2009 e março de 2023 no Hospital das Clínicas da Universidade Federal de Minas Gerais (HC-UFMG). Os prontuários foram selecionados por meio de busca ativa, no Serviço de Documentação e Arquivo Médico após a anuência da Instituição e assinatura do Termo de Compromisso de Utilização dos Dados (TCUD) (APÊNDICE A).

4.2 Critérios de inclusão e exclusão

Crianças e adolescentes com BN refratária com idade até 19 anos de idade submetidos a CA no Hospital das Clínicas da Universidade Federal de Minas Gerais (HC- UFMG). Todos os pacientes elegíveis foram incluídos.

Foram excluídos do estudo os pacientes que apresentam com anomalias não neurogênicas do trato urinário inferior, vesicostomizados previamente, que perderam o seguimento em período inferior a um ano, ou aqueles que não aceitaram participar do estudo e não assinaram o Termo de Termo de Consentimento Livre e Esclarecido (TCLE) (APÊNDICE B) e/ou Termo de Assentimento Livre e Esclarecido (TALE) (APÊNDICE C e D).

4.3 Protocolo do Estudo

Os parâmetros avaliados neste estudo, antes e após a CA, com acompanhamento por pelo menos um ano, incluíram IU, RVU e dados urodinâmicos, como capacidade cistométrica máxima (CCM), Capacidade Vesical Esperada (CVE), complacência vesical e pressão detrusora ao final do enchimento.

A avaliação antes da CA seguiu um protocolo sistemático, que incluiu uma anamnese detalhada, apresentação clínica, exames laboratoriais seriados (gasometria, níveis séricos de creatinina, ureia, eletrólitos, urinálise, cultura de urina) e exames de imagem e radiológicos realizados em nossa instituição. Esses exames incluíram ultrassonografia renal e das vias urinárias, UCM e EUD.

Qualquer perda de urina pela uretra foi considerada IU. Um diário miccional foi usado para avaliar a IU diurna entre os intervalos CIL quando aplicável, perda urinária durante o sono e melhora da IU após a CA. A melhora da IU foi avaliada usando os critérios da *International Children's Continence Society* (*ICCS*)¹. O sucesso inicial foi definido como nenhuma resposta (<50% de redução nos sintomas), resposta parcial (50% a 99% de redução nos sintomas) e resposta completa (IU ausente). Para o sucesso a longo prazo, a recidiva foi definida como mais de uma recorrência de IU por mês, e o sucesso contínuo foi definido como nenhuma recidiva dentro do 6° e 12° meses após a CA.

O RVU foi avaliado usando UCM e categorizado em graus I-V com base no sistema proposto pelo *Reflux Study Committee*². O RVU foi ainda categorizado como baixo grau (I-II) e alto grau (III-V) com base no grau de refluxo³. Uma melhora foi definida como qualquer redução no grau de RVU ou sua ausência.

Na análise dos dados urodinâmicos, CCM foi medida em ml. A CVE foi calculada usando a fórmula de Koff: $30 \times (idade \ em \ anos + 1)$ para crianças e adolescentes de quatro a 12 anos, enquanto é definido em 390 mL para pacientes mais velhos⁴. A CVE foi expressa como uma porcentagem. A baixa capacidade da bexiga é definida como menos de 65% da CVE, enquanto a capacidade média varia de 65% a 150%. A complacência da bexiga foi calculada como a mudança no volume (ΔV) dividida pela mudança na pressão do detrusor (Pdet), expressa em ml/cmH2O. A complacência é considerada alterada se estiver abaixo de 15 ml/cmH2O¹. A pressão detrusora ao final do enchimento mede a Pdet na CCM, aumentando idealmente em até $10 \ cmH2O^5$. Assim, os critérios para melhorar os parâmetros urodinâmicos incluem CVE > 65%, complacência da bexiga > $15 \ ml/cmH2O$ e pressão detrusora ao final do enchimento < $10 \ cmH2O$.

Os pacientes foram avaliados diariamente após a CA durante a hospitalização e tiveram consultas de acompanhamento no 1°, 3°, 6° e 12° meses após a alta. O diário vesical contendo os dados de IU foi revisado durante todas as consultas de acompanhamento após a CA. A ultrassonografia renal e das vias urinárias e a UCM foram realizadas no 3° mês após a CA, enquanto EUD foi realizado no 6° mês.

4.4 Técnica cirúrgica

A CA pela técnica de ileocistoplastia consiste na utilização de segmento de íleo distal para a ampliação do reservatório vesical. Um segmento de 20 a 25 cm do íleo terminal distando pelo menos 20 cm da válvula íleo cecal é ressecado com preservação de seu mesentério. O trânsito intestinal é reconstruído por anastomose dos segmentos intestinais. Este segmento de íleo isolado será detubulizado em sua borda anti-mesentérica. Em seguida este segmento aberto de íleo deverá ser reconfigurado em forma de "U", "N" ou "W" dependendo da preferência do cirurgião. Para a ampliação, a bexiga deverá ser aberta preferencialmente de forma sagital ampla, com cuidado para não lesar o trígono vesical. Este segmento detubulizado e reconfigurado de íleo será suturado com um ou dois planos de pontos contínuos de um fio de absorvível. Caso seja realizado concomitante um conduto cutâneo continente, este deverá ser implantado preferencialmente na parede vesical. Um tubo de cistostomia e sonda uretral deverão ser mantidos por pelo menos 15 dias⁶.

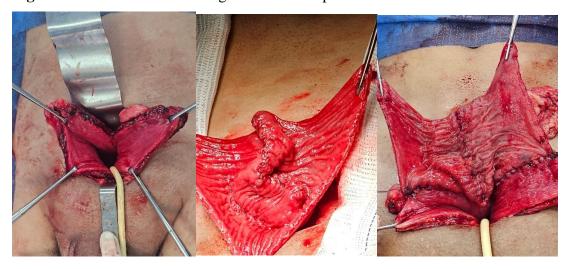


Figura 1 – Foto da técnica cirúrgica de ileocistoplastia

Fonte: Arquivo Pessoal do Autor

A cirurgia de apendicovesicostomia (cirurgia de Mitrofanoff) consiste na utilização do apêndice cecal implantado na bexiga com técnica antirrefluxo, garantindo um conduto cutâneo continente cateterizável e indolor para auxiliar os pacientes com necessidade de CIL. A apendicectomia é realizada junto à base do ceco, às vezes com ressecção de parte do ceco para

ampliar o comprimento do conduto. A vascularização do apêndice pela artéria apendicular e seu meso-apêndice deverão ser preservados. Uma das extremidades do apêndice é implantada na bexiga com técnica anti refluxo pela confecção de túnel submucoso de 4 a 5 cm. O apêndice pode ser implantado por técnica intra ou extra vesical acima do meato ureteral direito. A outra extremidade é exteriorizada na pele do abdome na região do umbigo ou na fossa ilíaca direita. O posicionamento do apêndice deve garantir uma posição retificada do conduto e mesoapêndice com seus vasos retificados e não tensionados. Uma sonda uretral número 10 ou 12 Fr deverá ser mantida durante duas semanas para garantir a cicatrização deste conduto. Após esse período o CIL é iniciado⁸.

Figura 2 – Foto da técnica cirúrgica de apendicovesicostomia cutânea continente (Mitrofanoff).



Fonte: Arquivo Pessoal do Autor

A cirurgia de ileovesicostomia continente (Yang-Monti) apresenta o mesmo princípio que a cirurgia de Mitrofanoff descrita acima. Porém o conduto é construído com segmento de íleo distal. Esta técnica é uma opção na ausência do apêndice cecal, nos casos que este não apresente comprimento adequado para a realização deste conduto ou quando o apêndice cecal for utilizado para a confecção de cecostomia continente para a realização de enema anterógrado (Cirurgia de Malone). Para a confecção deste conduto um segmento de 2,5 cm de íleo distal há pelo menos 20 cm da válvula íleo cecal deverá ser ressecado com preservação de seu mesentério. Este segmento deverá ser seccionado na transversal próximo à borda mesentérica.

Um segmento retangular formado será tubularizado longitudinalmente sob um molde de sonda uretral número 10 ou 12. Caso seja necessário um comprimento maior para este conduto podese realizar um duplo tubo de Yang-Monti⁹. A técnica de implante na bexiga e na pele da parede abdominal apresenta as mesmas características do Mitrofanoff descrita acima.

Figura 3 - Foto da técnica cirúrgica ileovesicotomia cutânea continente (Yang-Monti).



Fonte: Arquivo Pessoal do Autor

4.5 Análise estatística de dados

Para caracterização da amostra analisada foi feita uma análise descritiva das variáveis numéricas por meio de medidas de tendência central e variabilidade. As variáveis com distribuição normal foram apresentadas por meio de média e desvio-padrão, e aquelas com distribuição assimétrica foram apresentadas com mediana e demais quartis. Já para as variáveis categóricas foram feitas tabelas de distribuição de frequências, com apresentação de frequências absolutas e relativas.

Para testar a normalidade foi utilizado o teste de Shapiro-Wilk (Anexo 1).

Na comparação dos desfechos antes e após a intervenção foram utilizados os testes tpareado e Wilcoxon, para as variáveis numéricas com distribuição normal (complacência) e não-normal (CCM e % da CVE), respectivamente. Para as variáveis categóricas nominais (complacência alterada, CCM alterada e incontinência urinária) foi utilizado o teste de Mcnemar. Por fim, para a variável categórica ordinal refluxo (classificado em ausente, leve e grave) foi utilizado o teste de Homegenidade Marginal. É importante ressaltar que todos esses testes são apropriados para comparação do mesmo indivíduo em dois momentos do tempo e variam de acordo com o tipo de variável analisada.

Para todas as análises, um valor de p < 0.05 foi considerado estatisticamente significativo. A análise estatística foi realizada utilizando o IBM SPSS Statistics versão 21.0 (IBM Corp, Armonk, NY, EUA)

4.6 Aspectos Éticos

O Projeto de pesquisa foi aprovado pela Câmara departamental da Pediatria em 10 de maio de 2021 (Anexo 2) e pelo Comitê de Ética em Pesquisa (COEP) da Universidade Federal de Minas Gerais (CAAE- 48678721.6.0000.5149) em 29 de junho de 2021, sob Parecer número 4.874.121 (Anexo 3).

Os dados dos prontuários foram levantados após a anuência da Instituição e assinatura do Termo de Compromisso de Utilização dos Dados (TCUD). (Apêndice A)

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5 RESULTADOS E DISCUSSÃO

Os resultados e a discussão são apresentados sob a forma de artigo original.

5.1 Artigo Original

Clinical and urodynamic findings in children and adolescents with refractory neurogenic bladder undergoing augmentation cystoplasty

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Summary

Background

Neurological disorders, particularly neural tube defects like spina bifida, can lead to neurogenic bladder (NB) in children and adolescents. NB results in high-pressure bladder filling and poor emptying, which can cause complications such as urinary incontinence, recurrent infections, vesicoureteral reflux, and a higher risk of kidney damage. Initial treatments for NB may include clean intermittent catheterization, anticholinergic medications, or botulinum toxin A. Augmentation cystoplasty (AC) may be considered if these treatments prove ineffective. This

surgical procedure aims to create a low-pressure, high-capacity bladder using segments of the ileum or colon to improve bladder capacity and compliance.

Objective

This study aimed to evaluate urinary incontinence (UI), vesicoureteral reflux (VUR), and urodynamic parameters in patients' post-AC and compare these results to preoperative data.

Study design

The retrospective cohort study involved 42 consecutive patients with refractory NB who underwent AC alone between February 2009 and March 2023. The parameters evaluated in this study, pre- and post-AC, with follow for at least one year, included UI, VUR, and urodynamic data, such as maximum cystometric capacity, expected bladder capacity (EBC), bladder compliance, and end-filling detrusor pressure (EFP).

Results:

Of 22 eligible patients (50% male, median age 12 years), 77.3% underwent ileocystoplasty with Mitrofanoff. Pre-AC, UI was diagnosed in 81.8% of patients, with 83.3% achieving complete resolution post-AC (p<0.001). VUR was present in 31.8% of patients' pre-AC; post-AC, high-grade VUR resolved in 90.9 to 100% of the patients. (p=0.001). Median maximum cystometric capacity increased from 120 ml to 405 ml (p<0.001), and EBC normalized in 85.7% of patients (18/21) (p<0.001). Bladder compliance significantly improved from 6.4 ml/cmH2O to 38.3 ml/cmH2O (p<0.001), while median EFP decreased from 20.0 to 11.0 cmH2O (p<0.001).

Discussion

This study analyzed the preoperative and postoperative outcomes of children and adolescents with refractory NB who underwent ileocystoplasty. The findings revealed notable improvements in all assessed parameters, which are consistent with current literature. However, it is essential to acknowledge that the study does have some limitations, including its retrospective design and small sample size.

Conclusions

After AC, children and adolescents with refractory NB showed significant improvement in UI, VUR, maximum cystometric capacity, bladder compliance and EFP.

Keywords: augmentation cystoplasty; neurogenic bladder; urinary incontinence; vesicoureteral reflux. urodynamics.

Abbreviations

AC- Augmentation cystoplasty

CIC- Clean intermittent catheterization

EFP- End-filling detrusor pressure

EBC - Expected Bladder Capacity

ICCS-International Children's Continence Society (ICCS)

MCC- Maximum cystometric capacity

NB- Neurogenic bladder

Pdet- Detrusor pressure

RBUS- Renal and bladder ultrasound

UI- Urinary incontinence

UTIs- Urinary tract infections

UDS- Urodynamic study

VUR- Vesicoureteral reflux

VCUG- Voiding cystourethrography

Introduction

Neurological disorders can impact the function of the bladder and/or sphincter, leading to neurogenic bladder (NB). Neural tube defects, especially spina bifida, are the primary cause of NB in children and adolescents [1-3]. NB is characterized by the inability to fill under low pressure and periodic emptying, which can lead to complications such as urinary incontinence, recurrent urinary tract infections (UTIs), secondary vesicoureteral reflux (VUR), reduced bladder capacity and compliance, significantly high detrusor pressure, and increased risk of kidney damage [1-5]. The initial approach involves clean intermittent catheterization (CIC) and anticholinergic medication. If the first-line therapy fails, botulinum toxin A may be used, before considering augmentation cystoplasty (AC) [1-4].

AC is a surgical procedure used in adults and children with refractory NB. The main goal of AC is to create a bladder reservoir with low pressure and high capacity to preserve kidney function and improve urinary incontinence and quality of life for patients and families [1,2,5,6]. The standard procedures for bladder augmentation are ileocystoplasty and

colocystoplasty [5,7]. The ileum and colon are preferred due to their long segments and adequate distensibility [7]. In ileocystoplasty, a 20 to 30 cm segment of the terminal ileum, located at least 15 cm from the ileocecal valve, is removed. In colocystoplasty, the sigmoid colon is often used because of its vascularization and mobility, and a 15 to 20-cm segment of it is removed. These segments are reshaped into a patch based on the surgeon's preference after being detubularized. The bladder is then opened either sagittally or transversely. The detubularized ileal or colonic patch is then connected to the bladder with absorbable sutures [6]. Furthermore, AC may encompass the development of a catheterizable conduit utilizing either the vermiform appendix or the small intestine [8].

A recent systematic review conducted by our group showed improvements in urinary incontinence (UI), end-filling detrusor pressure (EFP), maximum cystometric capacity (MCC), expected bladder capacity (EBC), bladder compliance, and end-filling detrusor pressure (EFP), in children and adolescents with refractory NB undergoing AC [9]. However, the review included only a small number of studies, and the data were heterogeneous. Therefore, this study aimed to evaluate UI, VUR, and urodynamic parameters in patients after AC and compare these results to the preoperative data.

Methods

Ethical approval

The institution's Ethics Committee approved the study under protocol CAAE 48678721600005149 (position statement: 4,874,121). Legal guardians and participants aged 10 to 17 signed the informed consent and assent forms. After obtaining consent from the institution and signing the data use commitment form, the medical records were selected through an active search in the medical service and archives.

Study design and patients.

This retrospective cohort study involved 42 consecutive patients with refractory NB who underwent AC by the same surgeon at the same institution between February 2009 and March 2023. Of these 42 patients, seven with non-neurogenic lower urinary tract anomalies and 13 who had previously undergone vesicostomy were excluded from the study. Thus, 22 patients

aged between seven and 19 years with NB caused by neurogenic urinary tract anomalies, followed for at least one year after the procedure, were eligible for the study.

Study protocol

The parameters evaluated in this study, pre- and post-AC, with follow for at least one year, included UI, VUR, and urodynamic data, such as MCC, EBC, bladder compliance, and EFP.

The pre-AC assessment followed a systematic protocol, which included a detailed anamnesis, clinical presentation, serial laboratory tests (blood gas, serum levels of creatinine, urea, electrolytes, urinalysis, urine culture), and imaging and radiologic tests performed at our institution. These tests included renal and bladder ultrasound (RBUS), voiding cystourethrography (VCUG), and a urodynamic study (UDS).

Any loss of urine through the urethra was considered UI. A bladder diary assessed daytime UI between CIC intervals when applicable, urinary loss during sleep, and UI improvement post-AC. The improvement of UI was evaluated using the International Children's Continence Society (ICCS) criteria [10]. Initial success was defined as no response (<50% reduction in symptoms), partial response (50% to 99% reduction in symptoms), and complete response (absent UI). For long-term success, relapse was defined as more than one recurrence of UI per month, and continued success was defined as no relapses within the 6th, and 12th months post-AC.

VUR was assessed using VCUG and categorized into grades I-V based on the system proposed by the Reflux Study Committee [11]. Reflux was further categorized as low-grade (III) and high-grade (III-V) based on the reflux grade [12]. An improvement was defined as any reduction in the grade of VUR or its absence.

In the analysis of urodynamic data, MCC was measured in ml. EBC was calculated using the Koff formula: $30 \times (age in years + 1)$ for children and adolescents aged four to 12 years, while it is set at 390 mL for older patients [13]. The EBC was expressed as a percentage. Low bladder capacity is defined as less than 65% of the EBC, while average capacity ranges from 65% to 150%. Bladder compliance was calculated as the change in volume (ΔV) divided by the change in detrusor pressure (Pdet), expressed in ml/cmH2O. Compliance is considered altered if below 15 ml/cmH2O [10]. The EFP measures Pdet at maximum cystometric capacity,

ideally increasing by up to 10 cmH2O [14]. Thus, the criteria for improving urodynamic parameters include EBC > 65%, bladder compliance > 15 ml/cmH2O, and EFP < 10 cmH2O.

Patients were evaluated daily post-AC during hospitalization and had follow-up appointments in the 1st, 3rd, 6th, and 12th months after discharge. The bladder diary containing UI data was reviewed during all post-AC follow-up appointments. RBUS and VCUG were performed post-AC in the 3rd month and UDS in the 6th month.

Statistical analysis

A descriptive analysis of numerical variables was conducted to characterize the sample using central tendency and variability measures. The mean and standard deviation were calculated for normally distributed variables, while the median and quartiles were used for asymmetric ones. Frequency distribution tables displayed absolute and relative frequencies for categorical variables. Normality was tested with the Shapiro-Wilk test.

When comparing pre- and post-AC results, the paired t-test and the Wilcoxon test were used for numerical variables with normal distribution (bladder compliance) and non-normal distribution (MCC/EBC and EFP), respectively. The McNemar test was used for nominal categorical variables (altered bladder compliance, altered EBC, and UI). The Marginal Homogeneity test was used for the ordinal categorical variable VUR.

For all analyses, a *p*-value < 0.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS Statistics version 21.0 (IBM Corp, Armonk, NY, USA)

Results

Of the 22 eligible patients, 50% were male, and the median age was 12 years (range 9 to 16), at the time of AC. The NB etiology was spina bifida in 81.2% (18/22) of patients. In 77.3% (17/22) patients, the AC technique performed was ileocystoplasty with Mitrofanoff.

Pre-AC UI was diagnosed in 81.8% (18/22) of patients, with complete resolution in 83.3% (15/18) of these post-AC patients (p<0.001). (Table 1).

VUR was found in 31.8% (7/22) of patients (10 kidney units) pre-AC. None of them underwent ureteral reimplantation. In post-AC, left and right high-grade VUR (III-V) were

resolved in 90.9% of cases (p=0.01) and 100% (p=0.001) of the patients, respectively (Table 1 and Figures 1A/1B).

 $\label{local_total_total_total} \textbf{Table 1} - \textbf{Comparative analysis of urinary incontinence and vesicoureteral reflux pre-and post-Augmentation Cystoplasty}$

	Pre-AC	Post-AC	<i>p</i> - value	
	n (%)	n (%)		
UI				
Absent	4 (18.2)	19 (86.4)	<0.001 a	
Present	18 (81.8)	3 (13.6)		
Right VUR				
Absent	19 (86.4)	22 (100)	<0.001 b	
Low-grade	2 (9.1)	0 (0)		
High-grade	1 (4.5)	0 (0)		
Left VUR				
Absent	15 (68.2)	20 (90.9)	0.012^{b}	
Low-grade	1 (4.5)	2 (9.1)		
High-grade	6 (27.3)	0 (0)		

UI Urinary incontinence. AC Augmentation cystoplasty; VUR Vesicoureteral reflux.

^a McNemar test; ^b Marginal Homogeneity test

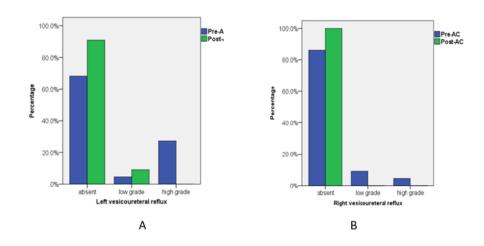


Figure 1. Left (A) and right (B) vesicoureteral reflux analyzed pre-and post-augmentation cystoplasty (AC)

The urodynamic findings are detailed in Table 2. The median MCC increased from 120 ml pre-AC to 405 ml post-AC (p<0.001). The EBC normalized in 85.7% (18/21) of patients' post-AC (p<0.001). There was a significant increase in bladder compliance from 6.4 ml/cmH2O pre-AC to 38.3 ml/cmH2O post-AC (p<0.001). The median values of the EFP decreased from 20.0 (13.8 -27.8) cmH2O pre-AC to 11 (9-12.6) cmH2O post-AC (p<0.001).

Table 2. Comparison of urodynamic data pre-and post-augmentation cystoplasty.

	1 1		
The discussion of the second	Pre-AC	Post-AC	
Urodinamic parameters	(n=22)	(n=22)	<i>p</i> -value
MCC (ml)			"
Median (P25 e P75)	120 (97.5 – 165)	405 (375 – 427.5)	<0.001°
% EBC			
Median (P25 - P75)	35 (25 – 50)	109.6 (99.4 – 127.4)	<0.001 °
Normal (66 a 149 EBC) n (%)	1 (4.5)	19 (86.4)	<0.001 b
Altered (\leq 65 ou \geq 150 EBC) n (%)	21 (95.5)	3 (13.6)	
Compliance ml/cmH2O			
$Mean \pm SD$	6.4 ± 2.1	38.3 ± 8.4	<0.001 ^a
Normal (≥15) n (%)	0 (0)	22 (100)	<0.001 ^b
Altered (<15) n (%)	22 (100)	0 (0)	
EFP cmH2O			
Median (P25 - P75)	20 (13.8 – 27.8)	11 (9 – 12.6)	<0.001°

AC Augmentation cistoplasty; MCC Maximum cystometric capacity; EBC Expected bladder capacity,

Discussion

This study compared the pre- and post-AC in 22 children and adolescents with refractory NB, primarily due to spina bifida. The parameters analyzed were UI, VUR, and urodynamic parameters (MCC/EBC, bladder compliance, and EFP) over at least one year post-AC. All patients underwent ileocystoplasty, associated with Mitrofanoff in 77.3% of cases, and there was an improvement in all evaluated parameters. These findings are consistent with a recent systematic review [9].

One of AC's goals is to achieve urinary continence [1,2,4,5,6]. The presence of UI in children and adolescents with NB is associated with reduced self-esteem, social interaction challenges, and vulnerability to bullying [15]. Non-surgical treatment may achieve urinary continence in 44% of cases [16]. In the analysis of this series, we observed a pre-AC UI rate of 81.8% (18/22) and complete resolution in 83.3% (15/18) of post-AC patients. Our findings were consistent with other studies that performed AC alone and observed improvement in UI in

SD standard deviation; EFP End -filling detrusor pressure

^a Paired t- test; b McNemar test; ^c Wilcoxon test

76.5% to 100% of patients [9,15,17-19]. The systematic review by Johnston et al. [16] presented slightly lower results (64%) for UI complete resolution of post-AC in these patients.

The treatment of VUR in NB patients, particularly those undergoing AC, remains debated. It's unclear which patients need ureteral reimplantation. Continued VUR in bacteriuric patients raises concerns about pyelonephritis [20], while complications from ureteral reimplantation [21] question the need for the procedure during AC. This study diagnosed VUR in 31.8% of patients, and resolution was achieved in 90.9% to 100% of high-grade VUR cases post-AC without ureteral reimplantation. Chiba et al. [22] and Zhang et al. [21] demonstrate results in agreement with our findings, showing resolution of VUR in 83 to 85% of pediatric patients with NB after AC, without ureteral reimplantation. Some authors suggest that NB patients with high-grade VUR and low-pressure VUR could benefit from AC concomitantly with ureteral reimplantation [20,23].

Our urodynamic findings showed improvements in all evaluated parameters. The increase in MCC/EBC was consistent with the findings of Chang et al. [24], who reported a rise in EBC from $53.2 \pm 27.4\%$ pre-AC to $110.6 \pm 22.4\%$ after AC. Likewise, Zaragoza et al. [25] observed an improvement in EBC from $52.8 \pm 20.1\%$ pre-AC to $95.9 \pm 8.8\%$ post-AC.

Although the term for this surgical reconstruction of the bladder suggests an increase in the reservoir's anatomical capacity, this urodynamic parameter is not the most critical factor influencing surgical outcomes. Instead, bladder filling pressure and compliance are the vital urodynamic factors for assessing bladder storage [18]. McGuire et al. [26] showed that detrusor pressure values > 40 cmH2O can lead to upper urinary tract injuries.

Our series demonstrated a 100% recovery of urodynamic data regarding bladder compliance and achieved an 85.7% success rate for EFP outcomes. Similar findings regarding these urodynamic outcomes have been identified in other studies. Zaragoza et al. [25] found a variation in compliance pre- and post-AC from 4.6 ± 3.2 to 41.3 ± 4.3 ml/cmH2O and a variation in EFP from 40.8 ± 18.9 to 11 ± 8.9 cmH2O. Chang et al. [24] reported that the detrusor pressure measured during cystometric capacity, referred to as EFP, showed a median value change from 21 (10 -55) cmH2O pre-AC to 11 (8 - 20) cmH2O post-AC in this series. In one of the most extensive published series on AC with long-term evaluation, Wang et al. [23] showed a variation in EFP from 38.0 ± 28.6 pre-AC to 14 ± 9.2 cmH2O post-AC. Sun et

al. [7] observed lower bladder pressure results, particularly for augmentations performed using bladder auto-augmentation and ureterocystoplasty techniques.

This study has limitations that should be acknowledged. First, it employs a retrospective design, which may impact the reliability of the findings. Additionally, the small sample size restricts the generalizability of the findings. It's worth noting that all surgeries included in this study were performed by the same surgeon at the same institution, and the same examiners conducted the follow-up exams. This consistency enhances the reliability of the data analysis.

Conclusions

AC effectively normalized urodynamic parameters in children and adolescents with refractory NB who did not respond to clinical treatments. Specifically, it improved MCC/EBC, bladder compliance, and EFP. These urodynamic enhancements positively impacted the resolution of UI and VUR. More extensive long-term prospective studies are needed to better evaluate outcomes after AC in these patients.

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We would like to express our heartfelt gratitude to the patients and their guardians who have been cared for in our pediatric urology service. Your willingness to allow us access to your data has been essential for us to carry out this study.

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Conflicts of Interest

The authors have no conflicts of interest to report.

Ethical approval

The institution's Ethics Committee approved the study under protocol CAAE 48678721600005149 (position statement: 4,874,121).

Titles and Legends of Tables

Table 1. Comparative analysis of urinary incontinence and vesicoureteral reflux pre-and post-augmentation cystoplasty.

UI Urinary incontinence; AC Augmentation cystoplasty; VUR Vesicoureteral reflux.

Table 2. Comparison of urodynamic data pre-and post-augmentation cystoplasty.

AC Augmentation cystoplasty; SD standard deviation; MCC maximum cystometric capacity; EBC Expected bladder capacity, EFP End-filling detrusor pressure

Titles and Legends of Figures.

Figure 1. Left (A) and right (B) vesicoureteral reflux analyzed pre-and post-augmentation cystoplasty (AC)

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^a McNemar test

^b Marginal homogeneity test

^a Paired t-test

^b McNemar test

^c Wilcoxon test

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6 CONSIDERAÇÕES FINAIS E PERSPECTIVAS FUTURAS

A CA tem se mostrado uma intervenção valiosa no manejo da BN em crianças e adolescentes, proporcionando benefícios significativos em diversos aspectos. Através da análise dos dados urodinâmicos, observou-se uma melhora considerável na capacidade funcional da bexiga, com aumento da capacidade de armazenamento e redução das pressões intravesicais. Esses aprimoramentos são cruciais para minimizar o risco de complicações renais e infecções urinárias, frequentemente associadas a condições de BN.

Além dos parâmetros urodinâmicos, a CA também impacta positivamente a qualidade de vida dos pacientes. Muitas crianças relataram uma diminuição da ansiedade e do estigma associado a continência urinária, resultando em uma maior confiança nas atividades diárias e sociais. O tratamento não só melhora a função vesical, mas também promove um desenvolvimento psicossocial mais saudável.

No entanto, é importante considerar os possíveis riscos e complicações associados à cirurgia. Entre as complicações mais comuns estão infecções urinárias, formação de cálculos, e distúrbios metabólicos que podem surgir após o procedimento. Além disso, a possibilidade de desenvolvimento de complicações a longo prazo, com a necessidade de reintervenções cirúrgicas, deve ser cuidadosamente avaliada. É fundamental que os profissionais de saúde realizem uma avaliação criteriosa dos pacientes, discutindo esses riscos e mantendo um acompanhamento rigoroso pós-operatório.

Portanto, a CA deve ser considerada uma abordagem eficaz e segura no tratamento da bexiga neurogênica, com benefícios que vão além da mera correção funcional, abrangendo melhorias significativas na qualidade de vida das crianças afetadas.

Com o intuito de garantir homogeneidade da avaliação dos dados desta dissertação foi necessário a exclusão de vários pacientes desta coorte. Sendo assim ficamos com apenas vinte e duas crianças e adolescentes de uma amostra inicial de quarenta e dois. O serviço de urologia pediátrica do Hospital das Clínicas da UFMG mantém o tratamento da maioria destes pacientes e tem admitido vários outros. Mantemos a rotina de registrar os dados destes após autorização de seus familiares e temos o intuito de apresentar uma casuística maior e com um tempo de seguimento mais longo podendo assim abordar melhor as possíveis complicações.

7 APÊNDICES

7.1 Apêndice A – Termo de Compromisso de Utilização de Dados

Termo de Compromisso de Utilização de Dados (TCUD)

1. Identificação dos membros do grupo de pesquisa

Nome completo (sem abreviação)	RG	Assinatura
Flavia Cristina de Carvalho Mrad	773.107.726-87	Dem and:
Mônica Maria de Almeida Vasconcelos	23038144304	asconce I
Otávio Augusto Fonseca Reis	044.151.576.29	plansecapies

2. Identificação da pesquisa

- a) Título do Projeto: "Avaliação de fatores de risco associados à cistoplastia de aumento em crianças e adolescentes com disfunção do trato urinário inferior."
- b) Departamento/Faculdade/Curso: Faculdade de Medicina /Departamento de Pediatria
- c) Pesquisador Responsável: Flávia Cristina de Carvalho Mrad

São dados a serem coletados somente após aprovação do projeto de pesquisa pelo Comitê de Ética da Universidade Federal de Minas Gerais (CEP-UFMG) e registrados no período fevereiro de 2007 e março de 2020

Os dados obtidos na pesquisa somente serão utilizados para o projeto vinculado. Para dúvidas de aspecto ético, pode ser contactado o Comitê de Ética em Pesquisa da UFMG (CEP/UFMG): Av. Antônio Carlos, 6627, Pampulha - Belo Horizonte - MG - CEP 31270-901 Unidade Administrativa II - 2° Andar - Sala: 2005 Telefone: (031) 3409-4592 - E-mail: coep@prpq.ufmg.br .

3. Declaração dos pesquisadores

Os pesquisadores envolvidos no projeto se comprometem a manter a confidencialidade sobre os dados coletados nos arquivos no serviço de nefrologia pediátrica do Hospital das Clínicas, bem como a privacidade de seus conteúdos, como preconizam a Resolução 466/12, e suas complementares, do Conselho Nacional de Saúde. Declaramos entender que a integridade das informações e a garantia da confidencialidade dos dados e a privacidade dos indivíduos que terão suas informações acessadas estão sob nossa responsabilidade. Também declaramos que não repassaremos os dados coletados ou o banco de dados em sua íntegra, ou parte dele, a pessoas não envolvidas na equipe da pesquisa.

Os dados obtidos na pesquisa somente serão utilizados para este projeto. Todo e qualquer outro uso que venha a ser planejado, será objeto de novo projeto de pesquisa, que será submetido à apreciação do CEP UFMG. Devido à impossibilidade de obtenção do Termo de Consentimento Livre e Esclarecido de todos os sujeitos, assinaremos esse Termo de Consentimento de Uso de Banco de Dados, para a salvaguarda dos direitos dos participantes.

Belo Horizonte, 26 de abril de 2021

Nome completo (sem abreviação)	RG	Assinatura
Flavia Cristina de Carvalho Mrad	773.107.726-87	Deman:
Mônica Maria de Almeida Vasconcelos	230.381.443-04	assence I
Otavio Augusto Fonseca Reis	044.151.576-29	Mousecapies

4. Autorização da Instituição

Declaramos para os devidos fins, que cederemos aos pesquisadores apresentados neste termo, o acesso aos dados solicitados para serem utilizados nesta pesquisa.

Esta autorização está condicionada ao cumprimento da pesquisadora aos requisitos da Resolução 466/12 e suas complementares, comprometendo-se a mesmo a utilizar os dados dos participantes da pesquisa, exclusivamente para os fins científicos, mantendo o sigilo e garantindo a não utilização das informações em prejuízo das pessoas e/ou das comunidades.

Antes de iniciar a coleta de dados pesquisador/a deverá apresentar o Parecer Consubstanciado devidamente aprovado, emitido por Comitê de Ética em Pesquisa Envolvendo Seres Humanos, credenciado ao Sistema CEP/CONEP.

Nome legível/assinatura e carimbo do responsável pela anuência da Instituição

Belo Horizonte, 26 de Abril de 2021

7.2 Apêndice B – Termo de Consentimento Livre e Esclarecido

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

O seu (a) filho (a) está sendo convidado (a) como voluntário (a) a participar da pesquisa "Fatores preditivos de desfecho em crianças e adolescentes com bexiga neurogênica e disfunções vesicais por outras etiologias submetidos á cistoplastia de aumento." Esse estudo iremos analisar todos os resultados de exames de antes e depois da cirurgia realizada na bexiga. Assim, tentaremos buscar formas de melhorar a indicação e os resultados da cirurgia da bexiga, o que poderá ajudar nos cuidados e na qualidade de vida do seu (a) filho (a). Solicitamos a sua autorização para usar os dados dos atendimentos e dos exames de imagem que seu (a) filho (a) fizeram durante o acompanhamento no Ambulatório de Urologia e Urologia Pediátrica do Hospital das Clínicas e estão anotados nos prontuários. Não haverá nenhum novo exame ou nova cirurgia.

Como riscos da pesquisa reconhecemos que os dados do seu (a) filho (a) poderia ser visto por outros profissionais e o seu prontuário danificado. Tentaremos reduzir esses riscos, da seguinte forma: o prontuário do seu (a) filho (a) somente será avaliado pelos pesquisadores envolvidos no estudo, cuidaremos da integridade do mesmo e não haverá a divulgação do nome do seu (a) filho (a).

Para participar deste estudo o Sr. (a) não terá custos e receberá qualquer vantagem financeira. Apesar disso, caso sejam identificados e comprovados danos provenientes desse estudo, o Sr. (a) tem assegurado o direito à indenização. O Sr. (a) terá o esclarecimento sobre o estudo em qualquer aspecto que desejar e estará livre para participar ou recusar-se a participar e a qualquer tempo e sem quaisquer prejuízos, valendo a desistência a partir da data de formalização desta. A sua participação é voluntária, e a recusa em participar não acarretará qualquer penalidade ou modificação na forma em que o Sr. (a) é atendido (a) pelo pesquisador, que tratará a sua identidade com padrões profissionais de sigilo. Os resultados obtidos pela pesquisa estarão à sua disposição quando finalizada. Seu nome ou qualquer outro item que indique sua participação não será liberado sem a sua permissão. O (a) Sr. (a) não será identificado (a) em nenhuma publicação que possa resultar.

Este termo de consentimento encontra-se impresso em duas vias originais, sendo que uma será arquivada pelo pesquisador responsável, na secretaria do Ambulatório no qual será realizada a pesquisa e a outra será fornecida ao Sr. (a). Os dados e instrumentos utilizados na pesquisa ficarão arquivados com o pesquisador responsável por um período de 5 (cinco) anos, na sala da unidade de nefrologia pediátrica no sexto andar do Hospital das Clínicas, e após esse tempo serão armazenados em nuvem (armazenamento virtual). Os pesquisadores tratarão a sua identidade com padrões profissionais de sigilo, atendendo a legislação brasileira (Resoluções Nº 466/12; 441/11 e a Portaria 2.201 do Conselho Nacional de Saúde e suas complementares), utilizando as informações somente para fins acadêmicos e científicos.

Eu,	, responsável pelo p	aciente
	documento de Identidade	fui
informado (a) d	os objetivos, métodos, riscos e benefícios da pesquisa "Avaliação	o de fatores
de risco associa	dos a cistoplastia de aumento em crianças e adolescentes com dis	sfunção do
trato urinário in	ferior. " "de maneira clara e detalhada e esclareci minhas dúvida	s. Sei que a

qualquer momento poderei solicitar novas informações e modificar minha decisão de participar se assim o desejar.

Rubrica	do pes	quisac	lor: _	 	
Rubrica	do pa	rticipa	ınte:_	 	

Declaro que concordo em participar desta pesquisa. Recebi uma via original deste termo de consentimento livre e esclarecido assinado por mim e pelo pesquisador, que me deu a oportunidade de ler e esclarecer todas as minhas dúvidas.

Nome completo do responsável pelo participante Data

Assinatura do responsável pelo participante

Pesquisador Coordenador da Pesquisa: Flávia Cristina de Carvalho Mrad

Endereço: Av. Professor Alfredo Balena número 190- Bairro Santa Efigênia

CEP: 30130-100 / Belo Horizonte - MG

Telefones: (31) 3409-9772

E-mail: pedfm@medicina.ufmg.br

Assinatura do pesquisador responsável

Pesquisador Participante: Otávio Augusto Fonseca Reis

Endereço: Av. Professor Alfredo Balena número 190- Bairro Santa Efigênia

CEP: 30130-100 / Belo Horizonte – MG

Telefones: (31) 3409-9772

E-mail: pedfm@medicina.ufmg.br

Assinatura do pesquisador responsável

Data

Data

Pesquisador Participante: Mônica Maria de Almeida Vasconcelos

Endereço: Av. Professor Alfredo Balena número 190- Bairro Santa Efigênia

CEP: 30130-100 / Belo Horizonte – MG

Telefones: (31) 3409-9772

E-mail: pedfm@medicina.ufmg.br

Assinatura do pesquisador participante Data

Em caso de dúvidas, com respeito aos aspectos éticos desta pesquisa, você poderá consultar:

COEP-UFMG - Comissão de Ética em Pesquisa da UFMG

Av. Antônio Carlos, 6627. Unidade Administrativa II - 2° andar - Sala 2005. Campus Pampulha. Belo Horizonte, MG – Brasil. CEP: 31270-901. E-mail: coep@prpq.ufmg.br. Tel: 34094592.

7.3 Apêndice C – Termo de Assentimento Livre e Esclarecido

TERMO DE ASSENTIMENTO LIVRE E ESCLARECIDO

Você está sendo convidado (a), como voluntário (a), a participar da pesquisa "Fatores preditivos de desfecho em crianças e adolescentes com bexiga neurogênica e disfunções vesicais por outras etiologias submetidos á cistoplastia de aumento." Seus pais permitiram que você participe. Nesse estudo iremos analisar todos os resultados de exames de antes e depois da cirurgia realizada na bexiga. Assim, tentaremos buscar formas de melhorar os cuidados com a sua cirurgia para que você consiga conviver cada vez melhor com ela e ter uma vida bem independente. Para isso, gostaríamos de saber se você autoriza usarmos os dados que conversamos nas consultas e os exames que você fez. Não haverá nenhum novo exame ou nova cirurgia. Tudo isso está anotado no seu prontuário. Os riscos que pode ocorrer é que outros profissionais vejam seu prontuário e que ele seja danificado. Mas tentaremos evitar isso, pois, somente os pesquisadores envolvidos nesse estudo poderão acessar o seu prontuário, ninguém saberá que você está participando da pesquisa, não falaremos a outras pessoas, nem daremos a estranhos as informações que constam nele e tomaremos cuidado para não danificar. Os resultados da pesquisa vão ser publicados, mas sem identificar as crianças e adolescentes que participaram da pesquisa. Seus pais não gastarão e nem receberão dinheiro para que você participe desse estudo. E você pode falar que não querer mais participar a qualquer momento. Ninguém ficará triste ou chateado com você. Quando terminarmos a pesquisa divulgaremos os resultados. Os dados e instrumentos utilizados na pesquisa ficarão arquivados com o pesquisador responsável por um período de 5 (cinco) anos, na sala da unidade de nefrologia pediátrica no sexto andar do Hospital das Clínicas, e após esse tempo serão armazenados em nuvem (armazenamento virtual). Se você tiver alguma dúvida, você pode nos perguntar. Nós escrevemos os telefones na parte de cima desse texto.
Eu,
Nome completo do participante Data

Assinatura do participante

Pesquisador Coordenador da Pesquisa: Flávia Cristina de Carvalho Mrad

Endereço: Av. Professor Alfredo Balena número 190- Bairro Santa Efigênia

CEP: 30130-100 / Belo Horizonte - MG

Telefones: (31) 3409-9772

E-mail: pedfm@medicina.ufmg.br

Assinatura do pesquisador responsável Data

Pesquisador Participante: Otávio Augusto Fonseca Reis

Endereço: Av. Professor Alfredo Balena número 190- Bairro Santa Efigênia

CEP: 30130-100 / Belo Horizonte – MG Telefones: (31) 3409-9772/ (31) 3307-9445

E-mail: pedfm@medicina.ufmg.br

Assinatura do pesquisador responsável Data

Pesquisador Participante: Mônica Maria de Almeida Vasconcelos

Endereço: Av. Professor Alfredo Balena número 190- Bairro Santa Efigênia

CEP: 30130-100 / Belo Horizonte – MG Telefones: (31) 3409-9772/ (31) 3307-9445

E-mail: pedfm@medicina.ufmg.br

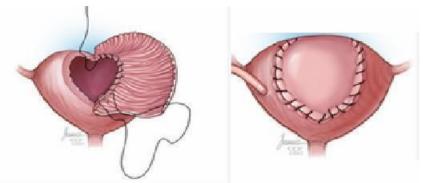
Assinatura do pesquisador participante

Data

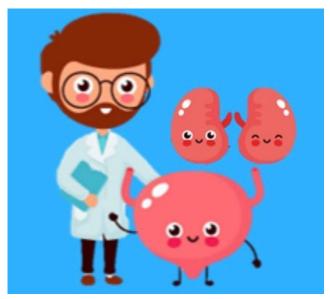
7.4 Apêndice D – Termo de Assentimento Livre e Esclarecido Ilustrado

TERMO DE ASSENTIMENTO LIVRE E ESCLARECIDO ILUSTRADO

Queremos convidar você para nos ajudar a fazer um trabalho chamado "Avaliação de fatores de risco associados a cistoplastia de aumento em crianças e adolescentes com disfunção do trato urinário inferior." Cistoplastia de aumento é a cirurgia que você fez na bexiga (onde o xixi fica guardado) e por onde seus pais ou você passa a sonda para tirar o xixi. O desenho aqui embaixo mostra a cirurgia que você fez.



Conversamos com seus pais e eles disseram que você poderia nos ajudar nesse trabalho, se quiser. Nessa pesquisa, nós iremos ver como a cirurgia feita na sua bexiga melhorou sua vida, e depois tentaremos buscar maneiras de você ter uma vida mais legal e sem precisar muito da ajuda dos seus pais para tirar o xixi da sua bexiga.



A sua ajuda no nosso trabalho seria você deixar que nós usássemos o que a gente conversa quando você vem nas consultas e aqueles exames que você já fez e estão anotados no seu prontuário (aquele lugar que você vê a gente escrevendo nas suas consultas), mas não vamos ter que fazer nenhum novo exame ou cirurgia. Tomaremos muito cuidado para não estragar seu prontuário e, apenas seus pais saberão que você está nos ajudando no trabalho, então fique tranquilo pois não falaremos o que está escrito no seu prontuário para pessoas estranhas.





Quando o trabalho ficar pronto, outras pessoas poderão ler, mas seu nome não sairá em nenhum lugar. Seus pais não gastarão e nem receberão dinheiro para que você nos ajude com esse trabalho.

Você pode falar que não quer mais participar do trabalho a qualquer momento. Ninguém ficará triste ou chateado com você.

Se não entender alguma coisa e só nos perguntar. Nós escrevemos os telefones no final desta folha para que seus pais possam nos ligar caso precisem. Ficaremos muito felizes em explicar o que você não entendeu.

Nome completo do participante Data

Assinatura do participante

Pesquisador Coordenador da Pesquisa: Flávia Cristina de Carvalho Mrad

Endereço: Av. Professor Alfredo Balena número 190- Bairro Santa Efigênia CEP:

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Telefones: (31) 3409-9772/ (31) 3307-9445

E-mail: pedfm@medicina.ufmg.br

Assinatura do pesquisador participante Data

8 ANEXOS

Anexo 1 - Teste Estatistica: Shapiro Wilki

	Shapiro-Wilk			
	Estatística	gl	Sig.	
CCM pré	.911	22	.050	
% capacidade esperada pré	.918	22	.068	
Complacencia pré	.935	22	.153	
Pdet CCM PRE OP	.852	22	.004	
CCM pós	.856	22	.004	
% capacidade esperada pós	.855	22	.004	
Complacencia pós	.950	22	.315	
Pdet CCM POS OP	.841	22	.002	

	Shapiro-Wilk			
	Estatística	gl	Valor-p	
CCM pre	.889	24	.012	
% capacidade esperada pre	.913	24	.040	
Complacencia pre	.957	24	.379	

	Shapiro-Wilk			
	Estatística	gl	Valor-p	
CCM pós	.916	35	.011	
% capacidade esperada pós	.902	35	.004	
Complacencia pós	.950	35	.115	

Anexo 2 – Parecer Departamento de Pediatria



UNIVERSIDADE FEDERAL DE MINAS GERAIS

Faculdade de Medicina Departamento de Pediatria

PARECER Nº

82/2021

PROCESSO Nº

23072

.244878/2020-69 ASSUNTO:

Parec

er 840 2021

Título do Projeto de Pesquisa:

Fatores preditivos de desfecho em crianças e adolescentes com bexiga neurogênica e disfunções vesicais por outras etiologias submetidos à cistoplastia de aumento.

Equipe de trabalho:

Profa Flávia Cristina de Carvalho Mrad (pesquisador principal), Profa Eleonora Moreira LIma, Profa Mônica Maria de Almeida Vasconcelos, Prof José Murillo de Bastos Netto, Dr Otávio Augusto Fonseca Reis, Dr José de Bessa Junior

Mérito:

Trata-se de um estudo retrospectivo, descritivo e analítico de uma coorte (análise de prontuários) de pacientes com anomalias de origem neurológica, funcionais ou anatômicas do trato urinárioinferior que apesar de tratamento clínico otimizado tiveram indicação de cistoplastia de ampliação vesical, realizadas por um mesmo cirurgião, no Hospital das Clínicas da Universidade Federalde Minas Gerais e no Hospital Felício Rocho, entre fevereiro de 2007 e março de 2020. Serão inicialmente avaliados 39 (trinta e nove) prontuários do Hospital das Clínicas da UFMG e 11 (onze) prontuários do Hospital Felício Rocho em relação a variáveis clínicas, laboratoriais e exames de imagem antes e após o procedimento cirúrgico. O objetivo principal desse estudo é avaliar os resultados e fatores preditivos associados a cistoplastia de aumento em crianças e adolescentes com bexiga neurogênica e disfunções vesicais por outras etiologias. O projeto pretende contribuir para o entendimento e possível prevenção de complicações associadas ao procedimento cirúrgico em questão. Os mínimos riscos decorrentes da pesquisa são claramente apresentados pelos pesquisadores, bem como os cuidados com os participantes. Os termos de consentimento/assentimento livre e esclarecidos estão com linguagem clara e atendem aos requisitos éticos.

Voto:

SMJ, sou pela APROVAÇÃO DO PROJETO.

Belo Horizonte, 10 de maio de 2021.

Profa. Laura Maria de Lima Belizario Facury Lasmar Chefe do

Departamento de Pediatria - FM - UFMG



Documento assinado eletronicamente por **Laura Maria de Lima Belizario Facury Lasmar, Chefe de departamento**, em 10/05/2021, às 14:59, conforme horário oficial de Brasília, com fundamento no art. 5º do Decreto nº 10.543, de 13 de novembro de 2020.



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Referência: Processo nº 23072.244878/2020-69

SEI nº 0716011

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Anexo 3 - Parecer Comite de Ética em Seres Humanos - COEP/UFMG







PARECER

Belo Horizonte, 17 de junho de 2021.

Declaramos para fins de comprovação no Comitê de Ética em Seres Humanos – COEP/UFMG que o projeto de pesquisa intitulado: "Fatores preditivos de desfecho em crianças e adolescentes com bexiga neurogênica e disfunções vesicais por outras etiologias submetidos à cistoplastia de aumento", de responsabilidade do Prof.º Flávia Cristina de Carvalho Mrad foi avaliado por essa Gerência e consideramos de suma relevância e de interesse para à instituição.

Atenciosamente, Mislene Galdino Diffue, Mislene Galdino Mislene Analista Administrativo Analista Administrativo

Mislene Galdino Diniz

Secretária da GEP.HC-UFMG/Ebserh