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Post-operative anorectal manometry in children with Hirschsprung disease: a systematic review

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Short title: Anorectal manometry in children with Hirschsprung disease

Abbreviations: ARM: anorectal manometry; **DC**: descending colon; **EAS**: external anal sphincter; **FI**: fecal incontinence; **HAEC**: Hirschsprung associated enterocolitis; **HD**: Hirschsprung disease; **HRAM:** high-resolution anorectal manometry; **IAS**: internal anal sphincter; **LHSA:** laparoscopic heart-shaped anastomosis; **LR:** lower rectum; **LSP:** laparoscopy-assisted Soave procedure; **MDT**: modified Duhamel technique; **MR:** mid-rectum; **MTR**: modified transanal rectosigmoidectomy; **PRISMA**: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; **PROSPERO**: International Prospective Register of Systematic Reviews; **PSAPP**: posterior sagittal abdominoperineal pull-through; **QoL**: quality of life; **RS**: rectosigmoid; **S**: solid-state**; SP**: saline perfused**; SC**: sigmoid colon; **TAA**: transabdominal approach; **TC**: transverse colon; **TEPT:** transanal endorectal pull-through; **UR**: upper rectum; **WP**: water-perfused; **– :** not reported.

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ABSTRACT

Background: Hirschsprung disease is commonly encountered by pediatric surgeons. Despite advances in the surgical management, these children may experience symptoms of bowel dysfunction throughout adulthood. Anorectal manometry may be used to assess post-operative anorectal structure and function. This review aimed to consolidate and evaluate the literature pertaining to post-operative findings of anorectal manometry in children with Hirschsprung disease.

Purpose: (1) Synthesize the available data regarding anorectal motility patterns in children following repair of Hirschsprung disease. (2) Evaluate the reported anorectal manometry protocols.

Data Sources: We performed a systematic review of four databases: Embase, MEDLINE, the Cochrane Library, and PubMed.

Study Selection: This systematic review was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Studies reporting results of post-operative anorectal manometry in children with Hirschsprung disease were evaluated for inclusion.

Results: Twenty-three studies satisfied inclusion criteria, with a combined cohort of 939 patients. Post-operative anorectal manometry results were reported for 682 children. The majority of included studies were assessed as "poor quality". Disparate manometry protocols, heterogeneous cohorts, and lack of standardized outcome assessments introduced a risk of outcome reporting bias, limited the comparability of results, and impeded clinical translation of findings.

Conclusions: This systematic review demonstrated the lack of high-quality evidence underlying the current understanding of post-operative anorectal motility in children with HD. There was little consistency in reported manometry outcomes between studies. In future work, emphasis must be placed on the application of standardized manometry protocols, cohort reporting, and patient outcome assessments.

Keywords: manometry, Hirschsprung Disease, gastrointestinal motility, high-resolution manometry, anorectum.

INTRODUCTION

Hirschsprung disease (HD) is a surgical condition that affects approximately 1 in 5000 live births. It is characterized by a lack of ganglion cells in the distal bowel, with variable involvement proximally. Patients usually require an operation in the first months of life to prevent life-threatening complications of functional bowel obstruction. Operative principles are to resect the distal aganglionic segment and form a coloanal anastomosis, whilst preserving fecal continence [1].

There have been significant advances in the surgical approach to children with HD. First recognized by ancient Hindu surgeons [2], the condition was ultimately named after Harald

Hirschsprung, who presented two cases in 1886 [3]. However, it was not until 1948 that Swenson described the first successful surgical repair [3]. Although early surgical interventions offered a curative approach to management, children experienced significant post-operative morbidity [4]. Suboptimal outcomes led to the development of different surgical techniques, refining the operative approach to minimize iatrogenic sequelae and improve technical ease [4-6].

Despite advances in surgical management, a significant proportion of these children experience bowel dysfunction, including constipation and/or fecal incontinence. As anal sphincter function and coordination of the anorectum is important in maintaining continence, assessment of the functionality of these regions after surgery is important. Anorectal manometry is a well-established procedure that may be used to evaluate post-operative anorectal physiology [7]. In turn, it may potentially facilitate comparison of operative techniques.

As the anorectum is relatively accessible, manometry in this region has received considerable attention. However, there have been few attempts to consolidate anorectal manometry findings in children following surgical repair of HD. We sought to synthesize the available data in this cohort, to evaluate the current knowledge and highlight future directions for investigation.

METHODS

A primary search was conducted in Embase, MEDLINE, PubMed, and the Cochrane Library in November 2019 and repeated in March 2020. Results were restricted to human studies published after the 1st January 1980. This systematic review was conducted in compliance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [8]. The methodology was published prospectively on PROSPERO (CRD42020155806). The search strategy is summarized in Appendix 1.

Study selection

Following removal of duplicate articles, the title and abstract of identified studies were independently assessed for eligibility by two authors (H.E.B. and J.S.). Studies reporting a cohort, cross-sectional, case-control, or longitudinal methodology were selected for full-text review, as were clinical trials. Systematic reviews, meta-analyses, animal studies, conference abstracts, and case reports were excluded.

The inclusion criteria were: anorectal or colonic manometry in children following surgical correction of HD, children aged 0 – 18 years, and English language. This review focused on anorectal manometry findings. Studies that conducted pre-operative manometry only were excluded. Studies assessing mixed disease cohorts (HD and other conditions) and/or age groups were eligible for inclusion, provided the results from children with HD less than 18 years of age were reported separately in the final analysis.

Data extraction

Data were extracted independently by two authors (H.E.B. and J.S). With respect to cohort characteristics, extracted data points included: patient age (age at primary repair and age at time of manometry); sex; length of affected bowel; and post-operative bowel function assessment (instruments and outcomes). Manometry characteristics included: manometry type; parameters assessed; protocol; catheter type and sensor spacing; and motility outcomes, including symptom correlations.

Quality assessment

The quality of included non-randomized studies was assessed using the Newcastle-Ottawa Scale. The scale applies eight criteria in three groups - selection, comparability, and exposure - to assess the methodological quality of observational studies. The highest quality studies may be awarded a maximum total of nine [9].

RESULTS

Search results

A total of 603 records were identified after removal of duplicates. Fifty-three studies were reviewed in full. Twenty-three studies, assessing a total of 939 patients, were eligible. Search results and study selection are presented in Figure 1.

Included studies incorporated anorectal manometry to investigate different aspects of HD management. These included evaluation of (1) surgical repair techniques [10-24]; (2) post-operative anorectal physiology [12, 25, 26]; (3) non-operative strategies for bowel dysfunction management [19, 27, 28]; and (4) the role of different manometry techniques in post-operative care [18, 22, 29, 30].

These studies reported postoperative manometry results in 682 children with HD (range 3 months – 17 years). The median manometry cohort size was 19 children (range 3 – 80). Data were insufficient to calculate the combined cohort median age or sex ratio.

Operative repair type was provided for 500/682 (73.3%) children. Variants of the Soave procedure were the most frequently reported (277/500, 55.4%), with the transanal endorectal pull-through the most commonly reported approach (209/500, 41.8%). The length of aganglionosis was described for 226/682 (33.1%) children. Of these, the majority (180/226, 79.6%) had aganglionosis limited to the rectosigmoid. Cohort clinical characteristics are summarized in Table 1.

Quality assessment

Few studies demonstrated robust methodology. Only four of the 23 papers adequately addressed the criteria outlined in the Newcastle Ottawa Scale and were classified as "good quality" [11, 22, 24, 25]. The majority were classified as "poor quality", predominately due to limitations identified in the "comparability" category. Quality evaluations are presented in Supplementary Information 1.

Anorectal manometry

Equipment

A variety of manometry techniques were reported. Water or saline perfused catheters were utilized in 16 studies [10, 13, 15-18, 20-23, 25, 26, 28, 30-32]. High-resolution manometry was described by two [29, 30]. Three studies reported 3-D assessment: two used water-perfused catheters [23, 30], whilst Banasiuk *et al*. [29] utilized a 256 sensor solid-state catheter.

The number of sensors on the manometry catheters ranged from a single recorded outlet located on one [20, 21] or two catheters [26], to 256 sensors used for 3-D high-resolution manometry [29]. The majority utilized catheters with two - eight sensors [12, 13, 17, 18, 22, 23, 25, 30-32]; nine studies did not describe the catheter employed [10, 11, 14-16, 19, 24, 27, 28]. Notably, sensor spacing was described by only four studies (range 0.21 – 2cm) [17, 25, 29, 30]. Catheter diameter was reported by the minority, but demonstrated a wide range (outer diameter 8Fr [2.67mm] – 10.57mm) [17, 18, 21, 23, 29, 30, 32]. Catheter details are summarized in Table 2.

Preparation and sedation

Several strategies for bowel preparation prior to anorectal manometry were reported. Enemas were utilized most frequently [18, 20, 25, 26, 30]. Enema composition included glycerin [20, 26], glycerinated physiological serum solution [18], and sodium phosphate [30]. Three studies did not routinely administer bowel preparation, whilst the remainder did not provide details regarding their approach [12, 22, 29]. Preparation details are summarized in Table 2.

The approach to procedural sedation was addressed in 11 studies. Of the four that reported use of procedural sedation, the sedative agents administered were chloral hydrate, ketamine chloride, and thiopental sodium [16, 17, 20, 26]. Seven studies did not use sedation to perform anorectal manometry [10-12, 18, 22, 29, 30]. The remainder did not describe their approach. Sedation regimens are summarized in Table 2.

Manometry outcomes

A variety of manometry parameters were reported. Evaluated parameters are provided in Table 3. Resting pressure (100%), rectoanal inhibitory reflex (RAIR) (69%), and squeeze pressure (44%) were the most frequently described. There was significant variation between studies with respect to parameters, terminology, and definitions. Due to the variation in methodology and outcomes, absolute values were not combined. Key findings and study limitations are summarized in Table 4.

Resting pressure

Resting pressure was the most commonly reported parameter, being described by all studies [10-32]. However, the location of measurement and calculation varied. Studies described resting pressure measurements in the rectum, anal canal [22, 25, 28, 31], anal sphincter [19, 27], or a combination [16, 20, 26, 32]; the majority did not define the site of measurement. Several articles reported maximal resting pressure alone [22, 28, 31]; others reported resting pressure and maximal pressure, with insufficient detail provided to determine whether the parameter reflected maximal resting pressure or squeeze pressure [19, 25]. One study reported resting and squeeze pressure as being measured in both cmH_2O and mmHg; however, the unit used for the results remains unclear [24]. The majority did not define the assessment protocol.

There was marked variation in absolute values. Resting pressure ranged from 10.1 ± 4.3 mmHg, reported by Nagasaki *et al*. [26] in children up to three years post-surgical repair, to 167 ± 36 mmHg, identified in children with obstructive symptoms [24]. Manometry results, including absolute values (standardized to mmHg), are summarized in Appendix 2.

Six studies explore the relationship between fecal incontinence and resting pressure, although none differentiated passive from urge incontinence. Of these six, three found an inverse correlation between resting pressure and fecal incontinence [13, 20, 26]. Conversely, three found no association [11, 18, 24]. Stensrud *et al*. [22] reported a relationship between fecal incontinence and internal anal sphincter (IAS) defects; however, not all defects were associated with a reduction in resting pressure.

Two studies identified a relationship between increased resting pressure and obstructive symptoms [20, 24]; this relationship was refuted by three [18, 31, 32]. Banasiuk *et al*. [29] reported a trend toward an increasing number of stools per day with decreasing resting pressure; however, this was not significantly correlated with symptoms.

An additional three, small studies evaluated the efficacy of nitrate pastes for non-operative management of obstructive symptoms [19, 27, 28]. All three described marked improvement in parent-reported symptoms, with an associated reduction in post-intervention resting pressure (35% - 59.1% reduction).

Rectoanal inhibitory reflex

Evaluation of the RAIR was reported by the majority [10, 13, 15, 16, 18, 20, 21, 23-26, 28, 29, 31, 32]. There was significant variability in study definitions, including terminology, quantitative criteria, and manometry protocols. Six studies reported the assessment protocol: two defined a positive RAIR as a decrease of ≥25% of mean resting pressure [24, 29], whilst Jiao *et al*. [17] required a decrease of ≥70%. Chung *et al*. [10] defined the RAIR as a reduction in sphincter pressure of ≥15mmHg, sustained for five seconds. Miele *et al*. [25] considered a 10mmHg reduction indicative of the RAIR.

The proportion of children with the RAIR identified post-operatively ranged from 0% [15, 16, 21, 25] to 87.5% [29]. Assessment was conducted between 9.2 and >48 months following primary repair. Four studies did not identify the RAIR in any participants, following a range of pull-through types: TEPT [15], Martin's operation [18], Soave [25], Duhamel [25], and posterior sagittal abdominoperineal pull-through (PSAPP) [21]. Post-operative duration of children without demonstrated RAIR ranged from 12 months to 32 months [15, 16, 21, 25].

Anal squeeze pressure

Ten studies assessed anal squeeze pressure [11, 13-15, 18, 22-24, 29, 30]. Study variations included maximal squeeze pressure, maximal segmental pressure during squeeze, squeeze pressure of high pressure zone, and pressure response to voluntary contraction. Active contractive pressure was reported by Huang *et al*., calculated as the difference between anal canal contractive pressure and resting pressure [15]. Post-operative squeeze pressures ranged from 45 mmHg (25.5 – 76.5 mmHg), in children with aganglionosis limited to the upper rectum following transanal repair [11], to 202.2 ± 71.2 mmHg, identified using HRAM [29]. Study definitions, norms, and absolute values are summarized in Appendix 2.

Post-operative outcome assessment

Five studies reported post-operative bowel function assessment using established measures. Measures included the Bowel Function Score (BFS), Rome III, Kelly, and Rintala continence scoring methods [10, 11, 15, 29, 30]. Ten studies used study-specific assessments [13, 16-18, 22-25, 28, 31]. The remainder either did not assess [12, 21] or did not report symptom assessment [14, 19, 20, 26, 27, 32].

There was additional variability in the criteria used to define symptoms. Few studies provided symptom definitions; however, there were inconsistencies in criteria reported. For example, constipation was defined as both “reduced bowel actions” and “bowels open less than every three days” [17, 18]. Post-operative bowel function assessments and outcomes are summarized in Table 5.

DISCUSSION

A significant proportion of children will experience bowel dysfunction following surgical repair of HD [33-35]. In an attempt to gain insight into the potential causes of post-operative constipation and/or fecal incontinence, anorectal manometry may be used to assess anorectal function. However, our systematic review has demonstrated widespread variability in manometry protocols, reporting, and clinical outcome assessment. Ultimately, our review highlights that a lack of standardization limits clinical translation of findings.

Impact of surgical approaches on manometry findings

Operative approaches to HD have evolved to minimize surgical trauma [4, 36]. Objective outcome comparison after technique modification is fundamental to improving surgical care. Anorectal manometry has been used to measure anorectal function after different surgical procedures [29, 37]. The most commonly assessed procedure was the transanal endorectal pull-through (TEPT) [38-40]. Despite several key advantages of this approach, two main limitations have been highlighted: a transanal approach may lead to stretching of the anal sphincters and/or damage the sensory mucosa involved in the continence mechanism, which lies proximal to the dentate line [41].

Anorectal manometry results from 209 children following transanal procedures were included in this review; however, findings were inconsistent. Following TEPT, three studies either identified normal resting pressures in the majority of assessed children (72.9% [10] and 75.6% [11]) or anal pressures that were unchanged by the procedure [23]. In the latter of these studies, the unchanged anal pressures, along with the absence of bowel dysfunction reported by the seven children assessed, led the authors to conclude that transanal procedures preserve sphincter complex function [23]. In contrast, while "normal" resting pressures were reported in two studies, a high proportion of those children reported fecal incontinence (57% [11]; 33% >twice per week [10]) and reduced Bowel Function Scores (mean BFS 16, range 7 – 20; normal ≥18) [10, 11], suggesting a poor correlation between "normal" anal resting pressure and fecal incontinence.

In children following transanal 1-stage Soave and Ikeda-Soper procedures, one study reported that anal squeeze pressure was the only parameter that differed significantly in comparison to baseline measures [15]. The authors postulated that this was due to sphincter stretching during transanal repair. However, the incidence of specific bowel dysfunction symptoms, and their relationship to repair type and manometry findings, were not reported, making the clinical relevance difficult to interpret [15]. Similarly comparing transanal and transabdominal approaches, Stensrud *et al*. used anal endosonography to suggest that IAS defects were more common after transanal approaches, and that defects were associated with fecal incontinence [22]. However, only large defects were associated with reduced anal resting pressure. While these data are of potential clinical significance, the authors noted that the study was not designed to compare surgical procedures.

Several studies demonstrated altered manometry findings in children following Duhamel repair. In comparison to TEPT, Banasiuk *et al*. identified a trend towards greater mean values of pressure asymmetry following Duhamel repair [29]. However, this was neither statistically significant nor correlated with functional outcomes. The authors concluded that both procedures affect the sphincter complex to a similar degree [29]. Tang *et al*. [30] reported marked anal pressure asymmetry in children following Duhamel repair, whilst only moderate asymmetry was identified following Soave procedures. However, the clinical significance of such findings remains undetermined.

The study by Banasiuk *et al*. also identified recovery of the RAIR in a much higher proportion of children following TEPT (87.5%) when compared with Duhamel repair (33%) [29]. While the identified recovery of the RAIR following the Duhamel repair was comparable with another study, it is worth noting that there was no attempt to correlate the presence of the RAIR with stool frequency or symptoms [31]. Additionally, the TEPT cohort was younger (mean 27.9 versus 81.8 months) and assessed at a shorter post-operative duration (9.2 versus 40.8 months) [29]. As continence improves with age, this comparison of functional outcomes needs to be interpreted with caution.

Manometry outcomes and clinical correlates

As part of the continence mechanism, the pressure exerted by the IAS, external anal sphincter (EAS), and the puborectalis muscle should exceed pressure in the rectum [42]. The IAS contributes the majority of resting anal tone (pressure) [43]. Therefore, reduced tone may be associated with passive incontinence, whilst hypertonia may be associated with rectal evacuation disorders. In practice, interpretation may be challenging due to the variability of anorectal manometry findings in both healthy and symptomatic subjects [7]. Whilst several studies included in this review investigated correlations between anorectal manometry parameters and stooling, the findings were conflicting.

For those with fecal incontinence following HD surgery, two studies reported lower anal resting pressure [20, 26], while a third described an inverse relationship between anorectal pressures (resting, squeeze) and fecal incontinence [13]. Chung *et al*. [10] described a correlation between abnormal resting pressure and reduced functional scores, assessed using the BFS. Although Banasiuk *et al*. identified an inverse relationship between maximum and mean resting pressure and number of stools per day, these data were not correlated with fecal incontinence [29]. In contrast, other studies reported that anal resting pressure was not correlated with fecal incontinence [11, 18], while Zhang *et al*. [24] demonstrated similar resting pressures between asymptomatic children, children with fecal incontinence, and controls.

In children with rectal evacuation disorders (obstructive symptoms) and those with normal defecation following HD surgery, three studies found no significant anorectal manometry differences [18, 31, 32]. However, two of these studies did indicate that a proportion of the constipated children had colonic histological abnormalities [31, 32], suggesting that the constipation may have been unrelated to anorectal dysfunction [44]. In contrast, two studies demonstrated that constipation was associated with increased anal resting pressures [20, 24]. Additionally, in three small studies, improvement in obstructive symptoms was associated with a reduction in anal resting pressure [19, 27, 28]. However, the reported manometry pressures in these papers varied greatly and, as they did not provide catheter specifications, comparing these data to current or future studies is not possible. Notably, the studies did not quantify the reported symptoms.

Anorectal manometry is also used to assess the RAIR. Although this reflex is classically absent in children with HD, recovery of the RAIR has been demonstrated post-operatively [26]. It is also hypothesized that impairment of the reflex may contribute to bowel dysfunction [45]. In this review the proportion of the cohort with post-operative RAIR identified ranged from 0 – 87.5% [10, 13, 15, 16, 18, 20, 21, 23-26, 28, 29, 31, 32]. However, the clinical significance of the findings is difficult to determine. None of these studies reported a statistical assessment of correlation between the presence/absence of the RAIR and symptoms.

In addition, the criteria for defining the RAIR lack standardization. The North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) suggests a reduction of 5mmHg in IAS pressure to indicate a positive reflex, whilst a 15% reduction in resting pressure has also been proposed [37, 42]. Studies included in this review reported a range of criteria to assess the RAIR, including one that required a 70% decrease in resting pressure [17]. Changing the protocol to elicit the RAIR has been demonstrated to drastically alter the rate of identification [46]. Consequently, the reported presence or absence of the RAIR may have more to do with the criteria used to define it, rather than a genuine absence.

Motility correlates

One of the primary indications for anorectal manometry is to clarify the pathophysiology of post-operative symptoms [42]. In turn, manometry-symptom correlates may be compared with clinical and surgical characteristics, to identify risk factors for suboptimal outcomes and refine surgical care. This review highlighted that the described cohort characteristics and clinical outcome indicators lacked consistency. Few studies assessed bowel function using validated measures. This lack of standardized clinical assessment prevents identification of potential associations between surgical characteristics, post-operative symptoms, and manometry findings.

Outcome reporting heterogeneity has been identified as a key issue in the broader HD literature [33, 47]. Standardized outcomes for HD have been developed to improve consistency in this area, as have recommendations for pathology reporting [48, 49]. Minimum standards for reporting manometry cohort characteristics – tailored to children with HD – should be similarly adopted. This would improve both the comparability and clinical relevance of manometry findings.

Practice variability

The evolving technological landscape is reflected in the range of manometry methods identified. Studies reported here used an endotracheal tube cuff [12], low-resolution, water-perfused catheters [10, 13, 15-18, 20-23, 25, 26, 28, 30-32] and 3D manometry [23, 29, 30]. Surprisingly, few studies provided adequate catheter specifications. Given the impact of the catheter on absolute values, this is a significant issue when attempting to compare findings [44, 50]. Similar discrepancies were identified in preparation, criteria, and reported outcomes. Diverse assessment approaches are likely to have contributed to the observed variability in findings [43]. The issue of discordant anorectal manometry practice is not unique to this cohort. Recent studies have demonstrated remarkable discrepancies between motility centers [44]. The authors of that study identified an urgent need for consensus, leading to the publication of a standardized protocol for the recording and reporting of fundamental manometric measures [51].

LIMITATIONS AND CONCLUSION

This review was limited to children less than 18 years of age. Studies including pediatric manometry outcomes may have been excluded if findings were not separated by age. Whilst this offers the advantage of presenting only pediatric data, the included studies may not represent all available findings in children. Our review was limited to English language publications; findings may be subject to a language bias. Nevertheless, our review highlighted that included studies assessed heterogeneous cohorts, utilized disparate protocols, and displayed inconsistent reporting of manometry findings, introducing a substantial risk of outcome reporting bias. Key clinical characteristics, such as length of intestinal aganglionosis or time since repair, were also seldom provided. Using the Newcastle-Ottawa Scale, this lack of comparability was largely responsible for the "poor" classification given to the majority of included studies. Comparability between studies was further hindered by inconsistent post-operative outcome assessments.

Collectively, this review demonstrates that there is a need for standardization of post-operative anorectal manometry in children with Hirschsprung disease. Future studies should adhere to a standardized pediatric manometry protocol and reporting framework. Consensus statements have been developed to offer such guidance [51, 52]. This would enhance the comparability of studies and reduce the risk of outcome reporting bias.

Similarly, minimum standards for Hirschsprung disease cohort characteristics – tailored to children undergoing anorectal motility assessment – should be developed. Standardized clinical outcome indicators should be used to enable the identification of potential manometry-symptom correlates. This would also facilitate robust assessment of response to subsequent manometry-guided interventions.

Anorectal manometry may offer the opportunity to characterize the relationship between post-operative changes and symptoms in children with Hirschsprung disease. However, robust methodology is required to improve the quality and consistency of this work.

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Dr Trajanovska, Dr Safe, A/Prof. Dinning, and Prof. Hutson critically reviewed and revised the manuscript for intellectual content.

A/Prof. King conceptualized and supervised the execution of the systematic review.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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TABLES

Table 1: Clinical characteristics of included studies.

First author	Year	Cohort (Total (Male))		Study population summary	Age at time of manometry	Length of affected colon	Surgical repair type
		Total	*Manometry*				
Banasiuk [29]	2016	14 (12)	14 (12)	All children with HD repaired at a single center.	Mean: 51 months (range 14 – 168 months)	Ileum: 1 (7%) TC: 4 (29%) DC: 7 (50%) SC: 2 (14%)	TEPT: 8 (57%) Duhamel: 6 (43%)
Chung [10]	2015	37 (30)	37 (30)	Cooperative**, toilet-trained patients** aged >3 years who had undergone **primary TEPT** >1 year prior, without anorectal, neurological or intellectual comorbidities.	Median: 60 months (range 36 – 144 months)	TC: 4 (11%) DC: 5 (13%) RS: 28 (76%)	TEPT: 37 (100%) *Stoma prior: 6 (16%)*
Chung [11]	2018	45 (34)	45 (34)	Children aged >3 years with **short segment** HD (limited to rectosigmoid) post **TEPT**, without anorectal, neurological, or intellectual comorbidities.	Median: 52 months (range 36 – 172 months)	RS: 45 (100%) - DC: 8 (18%) - SC: 12 (12%) - UR: 14 (31%) - LR: 11 (24%).	TEPT: 45 (100%) *Stoma prior: 8 (18%)*
Demirbag [31]	2013	18 (14)	18 (14)	Children post three-stage **Duhamel** repair.	Not reported. *-Age at operation: 19 months (range 12 – 72 months).*	RS: 14 (78%) Long colonic: 3 (17%) Colonic atresia: 1 (6%)	Modified Duhamel three-stage repair: 18 (100%)
Frenckner [12]	1983	16 (11)	12 (-)	Children post **Soave-Boley** endorectal pull-through.	Mean: 4 years (range 1.25 – 9 years)	-	Soave-Boley: 16 (100%)

First author	Year	Cohort (Total (Male))		Study population summary	Age at time of manometry	Length of affected colon	Surgical repair type
Gad El-Hak [13]	2010	52 (33)	52 (33)	Children post **Swenson** pull-through.	Not reported. - *Age at operation: 3.26 years (range 2 – 17 years).* - *Manometry performed pre-operatively, then 6 months + yearly post-operatively.*	-	Swenson: 52 (100%)
Hedlund [14]	1997	10 (9)	9 (-)	Children with short-segment HD, managed with **posterior sagittal resection** with coloanal anastomosis.	Mean: 5.1 years (range –) - *Age at operation: mean – (range 2 months – 7 years)*	SC: 3 (30%) - Proximal: 1 (10%) - Mid: 1 (10%) - Distal: 1 (10%) Rectum: 7 (70%) - UR: 5 (50%) - MR: 1 (10%) - LR: 1 (10%)	Posterior sagittal resection with coloanal anastomosis: 10 (100%)
Huang [15]	2008	147 (129)	64 (-)	Children post **Soave 1-stage transanal** endorectal pull-through or **Ikeda-Soper**	Cohort age at manometry: - - *Total cohort age at operation (Soave): mean 1.4 years (range 11d – 9 years).* - *Total cohort age at operation (Ikeda-Soper): mean 2.3 years (range 3 months – 10 years).* *Manometry conducted 6 and 12 months post-operatively.*	Manometry cohort: - **Total cohort:** - Max. UR[1]: 55 (37%) - Max. distal SC[2]: 92 (63%)	Soave: 108 (74%) - Transanal Soave: 44 (30%) - Laparotomy-assisted Soave: 35 (24%) - LSP: 29 (20%) Ikeda-Soper: 39 (26%) ***Manometry recipients***: 64/147 (44% total cohort) Transanal Soave: 35 (55%) Ikeda-Soper: 29 (45%)

[1] *Study definition*: **short segment** refers to aganglionosis that reaches the proximal or intermediate segment of the rectum, not exceeding 6 cm from the anus.
[2] *Study definition*: **common type** refers to aganglionosis that extends to the rectosigmoid region or the distal segment of the sigmoid colon, about 9cm from the anus.

First author	Year	Cohort (Total (Male))		Study population summary	Age at time of manometry	Length of affected colon	Surgical repair type
Iwai [16]	1987	5 (4)	5 (4)	Children with **total colonic aganglionosis** who underwent **Martin's operation**	Not reported. *- Cohort age at operation: 8 - 12 months of age* *ARM completed at 1, 3, 6 months and 1, 2, 3 years post op.*	Total colon: 2 (40%) Colon plus: - 5cm ileum: 1 (20%) - 25cm ileum: 1 (20%) - 45cm ileum: 1 (20%)	Martin's operation: 5 (100%)
Jiao [17]	2019	80 (58)	80 (58)	Post laparoscope-assisted Soave procedure or laparoscope-assisted **heart-shaped anastomosis.**	Not reported. *Age at operation:* *- LSP:: 18.97 +/- 27months* *- LHSA: 21.35 +/- 24.19 months*	Not reported. *Length of removed bowel:* *- Subtotal colectomy: 36 (45%)* *- Left colectomy: 44 (55%)*	LSP 44 (55%) LHSA: 36 (45%)
Martins [18]	2009	42 (36)	42 (36)	Children following repair of HD at a single center, with follow up anorectal manometry and profilometry.	Not reported. *Age at operation:* *- MDT mean 8.7 years (range 2 – 15 years)* *-MTR mean 5 years (range 1 – 9 years)* *First follow up manometry at 3 months.*	-	MDT: 23 (55%) MTR: 19 (45%)
Messina [19]	2007	3 (2)	3 (2)	**Persistent constipation** after Soave-Boley pull-through.	Mean 3.3 years (range 2 – 10)	-	Soave-Boley: 3 (100%)

First author	Year	Cohort (Total (Male))		Study population summary	Age at time of manometry	Length of affected colon	Surgical repair type
Miele [25]	2000	21 (-)	19 (-)	All patients with HD repaired at a single center > two years prior.	Mean 11.8 years (range 3.4 – 17 years)	RS: 13 (62%) TC: 5 (24% Dilatation to anus: 3 (14%) **Determined by narrowing on barium enema.*	Soave: 8 (38%) Duhamel: 9 (43%) Anorectal myectomy: 4 (19%)
Millar [27]	2002	4 (-)	4 (-)	Obstructive symptoms **post Soave** pull-through (including recurrent enterocolitis).	Mean 6.8 years (range 2 – 13)	-	Soave: 4 (100%) *Subsequent procedures: 2 (50%)* *- Rectal myectomy: 1 (25%)* *- Conversion to Duhamel: 1 (25%)*
Moore [32]	1994	178 (-)	43 (-)	Sixteen children with **obstructive symptoms** of unclear origin; 28 children with no post-operative symptoms.	Median age: -Obstructive symptoms: 5 years -Asymptomatic HD: 9 years	-	Swenson, Duhamel and Soave. Distribution of total and/or manometry cohort repair types not reported.
Nagasaki [26]	1980	57 (-)	53 (-)	Patients with HD treated at a single center.	Mean/median: not reported (range 3 months – 12 years)	-	Ikeda's Z-shaped anastomosis: 39/43 children assessed post-operatively (68%) Modified Duhamel: 8 (14%) Rectal myectomy: 6 (11%)
Nagasaki [20]	1989	46 (-)	46 (-)	Children post **Ikeda's Z-shaped anastomosis**	Not reported.	-	Ikeda's Z-shaped anastomosis: 46 (100%)

First author	Year	Cohort (Total (Male))		Study population summary	Age at time of manometry	Length of affected colon	Surgical repair type
Niedzielski [21]	1999	10 (7)	10 (7)	Post **PSAPP**	Not reported. *Age at operation:* *-10 – 18 months: 7 children* *- 2.5 – 5.5 years: 3 children*	Mean length of resected segment: 11.9cm (range 6 – 20 cm).	PSAPP: 10 (100%)
Stensrud [22]	2015	52 (42)	35 (-)	All children with follow-up manometry post HD repair at a single center.	Range: 3.4 - 16.6 years TEPT: median 6.4 years (range 3.4 - 14.3 years) TAA: median 11.2 years (range 4.4 - 16.6 years)	-	Total cohort: TEPT: 31 TAA: 21 *Preoperative stoma:* *-TEPT: 4 (13%)* *-TAA: 9 (43%)*
Tang [30]	2017	17 (9)	8 (4)	Children aged four years or more without neurological comorbidities attending bowel management clinic.	Eight years (range 6 – 10 years)	Rectosigmoid: 5 (63%) Ultra-short segment: 2 (25%) Long segment: 1 (12%) *Percentage of HD cohort.*	LSP: 5 (63%) Posterior myomectomy: 2 (25%) Duhamel: 1 (12%) *Percentage of HD cohort.*
Till [23]	2006	7 (-)	7 (-)	Post **TEPT** for HD limited to **rectosigmoid** without previous severe HAEC	Not reported. *Age at operation: 3.2 years (range 0.4 - 8.7 years).* *Re-assessed mean 14 months (range 3 – 21 months).*	Rectosigmoid: 7 (100%)	TEPT: 7
Tiryaki [28]	2005	18 (-)	18 (–[3])	**Obstructive symptoms** post repair following a trial of topical nitric oxide application	Mean age: 45 months (range not reported).	Symptomatic cohort: - RS: 4 (67%) - Long colonic: 2 (33%) Total cohort: -	Three-stage modified Duhamel repair: 18 (100%)

[3] Six children were symptomatic (five boys); 12 were asymptomatic (sub-cohort sex ratio not described).

First author	Year	Cohort (Total (Male))		Study population summary	Age at time of manometry	Length of affected colon	Surgical repair type
Zhang [24]	2007	58 (39)	58 (39)	Post **one-stage TEPT**	Not reported. *- Age at operation: 24.7 months* *- Duration of follow up: mean 15.8 months (range 6 – 24 months)*	Rectosigmoid: 58 (100%)	One-stage TEPT: 58 (100%)

ARM: anorectal manometry; **DC:** descending colon; **FI:** fecal incontinence**; HAEC:** Hirschsprung associated enterocolitis; **HD:** Hirschsprung disease; **LHSA:** laparoscopic heart-shaped anastomosis; **LR:** lower rectum; **LSP:** laparoscopy-assisted Soave procedure; **MDT**: modified Duhamel technique; **MR:** mid-rectum; **MTR**: modified transanal rectosigmoidectomy; **PSAPP**: posterior sagittal abdominoperineal pull-through; **QoL:** quality of life; **RS**: rectosigmoid; **SC**: sigmoid colon; **TAA**: transabdominal approach; **TC**: transverse colon; **TEPT:** transanal endorectal pull-through; **UR**: upper rectum **– :** not reported.

Table 2: Summary of reported anorectal manometry specifications.

First author	Year	Catheter type	No. sensors	Sensor spacing	Preparation	Sedation / Anesthetic
Banasiuk [29]	2016	S *3D HRAM*	256	Longitudinal: 0.4cm Radial: 0.21cm	No routine preparation	No sedation
Chung [10]	2015	WP	-	-	-	No sedation
Chung [11]	2018	-	-	-	-	No sedation
Demirbag [31]	2013	WP	4	-	-	-
Frenckner [12]	1983	Air-filled balloons	2	-	No routine preparation	No sedation
Gad El-Hak [13]	2010	WP	8	-	-	-
Hedlund [14]	1997	Water-filled balloon	-	-	-	-
Huang [15]	2008	WP	-	-	-	-
Iwai [16]	1987	WP	-	-	-	Thiopental sodium (30mg/kg) per rectum
Jiao [17]	2019	WP	4	1cm	-	Chloral hydrate 6% (1mL/kg) orally
Martins [18]	2009	WP	4	-	Enema: 10% glycerinated physiological serum solution (10mL/kg)	No sedation
Messina [19]	2007	-	-	-	-	-
Miele [25]	2000	WP	2	2	Daily enemas for three days; usual laxatives withheld.	-
Millar [27]	2002	-	-	-	-	-
Moore [32]	1994	WP	2	-	-	-
Nagasaki [26]	1980	WP	Open tip (2)	-	Glycerin enema	5-7mg ketamine chloride, if required
Nagasaki [20]	1989	WP	Open tip	-	Glycerin enema	5-7mg ketamine chloride or 100mg/kg chloral hydrate, if required
Niedzielski [21]	1999	SP	Open tip	-	-	-
Stensrud [22]	2015	WP	8	-	No routine preparation	No sedation
Tang [30]	2017	WP: *3D HRAM*	24	1	Sodium phosphate rectal fleet enema	No sedation

					3mL/kg	
Till [23]	2006	WP: *3D Vector* [4]	4/8	-	-	-
Tiryaki [28]	2005	WP	-	-	-	-
Zhang [24]	2007	-	-	-	-	-

HD: Hirschsprung disease**; HRAM:** high-resolution anorectal manometry; **SP**: saline perfused; **S**: solid-state; **WP:** water perfused; **– :** not reported.

[4] Computerized vector manometry, the system provides a “3-dimensional graphic image of the sphincteric pressure profile along the functional anal canal” [23].

Table 3: Summary of anorectal manometry parameters reported by included studies, with comparable parameters grouped for comparison. Differences in terminology are indicated, with the study definition provided as a footnote.

First author	**Resting pressure**	**Squeeze pressure**	**Endurance squeeze**	**Anal canal length**	**High pressure zone (HPZ)**	**Sensation**	**Max. volume tolerated**	**RAIR**	**Cough**	**Bear down maneuver**	**Rectal compliance**	**Rectal contraction frequency (#/min)**	**Other**
Banasiuk [29]	●	●		●	●			●	●	●	●		Pressure asymmetry (rest, squeeze); ano-anal reflex
Chung [10]	●					●		●					
Chung [11]	●	●				●							
Demirbag [31]	●[5]							●					
Frenckner [12]	●						●[6]						
Gad El-Hak [13]	●	●		●		●		●					
Hedlund [14]	●	●											
Huang [15]	●	●			●	●		●					
Iwai [16]	●[7]				●			●			●		Anorectal pressure difference
Jiao [17]	●			●				●				●	

[5] Maximum anal resting pressure
[6] Rectal capacity: volume of balloon (mL) to elicit discomfort
[7] Anal and rectal pressures measured independently

First author	Resting pressure	Squeeze pressure	Endurance squeeze	Anal canal length	High pressure zone (HPZ)	Sensation	Max. volume tolerated	RAIR	Cough	Bear down maneuver	Rectal compliance	Rectal contraction frequency (#/min)	Other
Martins [18]	●	●	●[8]					●	●				Pressure with perianal stimulation; profilometry
Messina [19]	●[9]				●								
Miele [25]	●[10]							●			●		
Millar [27]	●[11]				●								Vector volume, total sphincter length
Moore [32]	●[12]				●	●	●	●			●	●	Anal canal pressure difference; anal sphincteric pressure barrier [13]
Nagasaki [26]	●[14]							●				●	
Nagasaki [20]	●[15]							●				●	
Niedzielski [21]	●							●					
Stensrud [22]	●[16]	●											

[8] Maintained voluntary contraction
[9] Median and maximum anal sphincter pressure: insufficient detail to determine if maximum pressure indicates squeeze pressure or maximum resting pressure.
[10] Resting and maximal anal pressure: insufficient detail to determine if maximum pressure indicates squeeze pressure or maximum resting pressure.
[11] Maximum anal sphincter pressure
[12] Resting rectal pressure and maximal anal canal pressure
[13] Anal sphincteric pressure barrier: area under the curve for HPZ in mm^2. Assesses the resistance of the sphincters and represents both the amount of pressure and the length over which it is exerted.
[14] Resting pressure in (1) rectum and (2) anal canal
[15] Resting pressure in (1) rectum and (2) anal canal
[16] Maximal anal resting pressure. Defined as the lowest point of the slow wave fluctuation curve.

First author	Resting pressure	Squeeze pressure	Endurance squeeze	Anal canal length	High pressure zone (HPZ)	Sensation	Max. volume tolerated	RAIR	Cough	Bear down maneuver	Rectal compliance	Rectal contraction frequency (#/min)	Other
Tang [30]	●	●											Asymmetry (resting, squeeze)[17]
Till [23]	●	●		●	●[18]			●					Maximal segmental pressure[19]; segmental/total asymmetric index; vector volume at rest
Tiryaki [28]	●[20]							●					
Zhang [24]	●	●						●					Vector volume, vector symmetry index
Assessment frequency	*23*	*10*	*1*	*4*	*7*	*5*	*2*	*15*	*2*	*1*	*4*	*4*	

[17] Inter-quadrant pressure asymmetry index (Δp) = (maximal pressure – minimal pressure) / maximal pressure X 100%. Denotes symmetry of pressure distribution of the anal canal (total symmetry: Δp = 0%; total asymmetry: Δp = 100%).
[18] High pressure zone: expressed as percentage of anal canal length.
[19] Maximal segmental pressure: peak of all pressure values from eight channels within the anal canal (calculated at rest or squeeze)
[20] Maximum anal resting pressure.

Table 4: Summary of key findings.

First author	Manometry population summary	RAIR *(% present)*	Summary of key manometry findings	Limitations
Banasiuk [29]	All children with HD repaired at a single center (n = 42).	TEPT: 87.5% D: 33%	• Higher pressures recorded than water-perfused methods • Maximum and mean RP moderately correlated with stool number: lower RP associated with greater number of stools. Not correlated with FI. • Mean values of pressure asymmetry more common after Duhamel repair; not correlated with FI or stool frequency. • Greater RAIR recovery post TEPT (87.5%) versus Duhamel (33%); no difference in RP between repair groups. • No significant differences in other manometric variables assessed.	TEPT group younger (27.8 vs 81.8 months) and assessed at shorter post-operative duration; few children with obstructive symptoms; lack of control values for 3D HRAM in children.
Chung [10]	Cooperative**, toilet-trained patients** aged >3 years who had undergone **primary TEPT** >1 year prior (n = 37).	16.2%	• 72.9% of patients had RP in normal range • Abnormal RP, stoma, and HAEC were risk factors for abnormal BFS • No significant risk factor for abnormal manometric results identified	Small cohort; characteristics of excluded patients not reported; manometry findings correlated to BFS only (not symptoms*)*.
Chung [11]	Children aged >3 years with **short segment** HD (limited to rectosigmoid) post **TEPT** (n = 45).	-	• 75.6% patients had RP in normal range • Rectosigmoidectomy group had significantly higher incidence of FI (50%) and significantly reduced BFS (14 vs 18, p = 0.04). • Patients with shorter aganglionic segment (UR, LR) had significantly higher BFS; trend towards higher proportion of this group having a normal RP (not statistically significant).	Small cohorts (n = 45, four sub-groups); multiple surgeons may contribute to variation in technique and definition of subgroups (length of muscle cuff, level of transection proximal to normal biopsy).
Demirbag [31]	Children post three-stage **Duhamel** repair (n = 18).	22.2%*	• No significant difference in RP or RAIR between patients with obstructive symptoms and asymptomatic children. • Anorectal manometry not sufficient to understand obstructive symptoms	Small cohort; limited manometric assessment; heterogeneous cohort, including high proportion with additional colonic pathology.

* Reflex reported as present but abnormal

First author	Manometry population summary	RAIR *(% present)*	Summary of key manometry findings	Limitations
Frenckner [12]	Children post **Soave-Boley** endorectal pull-through (n = 12).	-	• Pre- and post-operative resting pressure comparable • Rectal sensation not damaged by endorectal pull-through	Small cohort; limited by manometry techniques available; limited surgical / pathological characteristics provided
Gad El-Hak [13]	Children post **Swenson** pull-through (n = 52).	11.54%	• Inverse relationship between anorectal pressures (RP and squeeze) in the continent and major incontinent groups. Incontinence may be due to weakened IAS. • Swenson technique unsatisfactory due to high rate of fecal incontinence; some manometry parameters (such as RAIR) may improve with time.	Assessment of correlation between obstructive symptoms and manometry findings not reported; limited surgical / pathological characteristics provided.
Hedlund [14]	Children with short-segment HD, post **posterior sagittal resection** with coloanal anastomosis (n = 9).	-	• No difference in RP and squeeze pressure in comparison to Swenson	Small cohort; limited manometry performed; novel surgical approach limits comparability.
Huang [15]	Children post **Soave 1-stage** transanal endorectal pull-through or **Ikeda-Soper** (n = 64).	0%	• Transanal procedure demonstrated significantly lower squeeze pressure. • However, other manometry parameters and bowel function comparable (Soave 1-stage transanal endorectal pull-through vs. Ikeda-Soper).	Manometry findings of transanal Soave compared with Ikeda-Soper (rather than the reported lap-assisted Soave groups); manometry findings compared with overall Kelly's score: incidence of specific symptoms and relationship to manometry not reported.
Iwai [16]	Children with **total colonic aganglionosis** post **Martin's operation** (n = 5).	0%	• Decreased RP 1 month post-operatively, normalized at 3 months.	Small cohort; limited symptom assessment; manometry not compared with symptoms.
Jiao [17]	Post laparoscope-assisted **Soave** procedure or laparoscope-assisted **heart-shaped anastomosis (LHSA)** (n = 80).	Not stated	• RP lower and anal canal length shorter post LHSA than LSP • Trend towards higher incidence of constipation and FI following LSP, however, not significantly so.	Reported symptom definitions lack specificity; manometry findings not compared with symptoms.

First author	Manometry population summary	RAIR *(% present)*	Summary of key manometry findings	Limitations
Martins [18]	Children **modified Duhamel** or **modified transanal rectosigmoidectomy**, with follow up anorectal manometry (n = 42).	No difference MDT:MTR. *Proportion not reported*	• Manometry parameters comparable between surgical techniques, suggesting transanal procedure did not disrupt sphincter mechanism • RP not correlated with presence or severity of FI	Significantly younger group post transanal procedure; limited outcome assessment; statistical correlation of manometry findings with symptoms conducted but not provided.
Messina [19]	**Persistent constipation** after Soave-Boley pull-through (n = 3).	-	• Decrease in RP (38.7%) following topical application of isosorbide dinitrate paste, associated with parent-reported improvement in persistent obstructive symptoms.	Small (n = 3); limited statistical analysis; patient symptoms poorly characterized pre- and post-intervention.
Miele [25]	All patients with HD repaired at a single center > two years prior (n = 19).	0%	• Manometry findings comparable to those in control children	Small cohort; potentially subject to non-response bias; symptoms not correlated with manometry findings.
Millar [27]	Obstructive symptoms **post Soave** pull-through (including recurrent enterocolitis) (n = 4).	-	• Decrease in RP (53%), sphincter length (22%), and high pressure zone length (25%) following topical application of isosorbide dinitrate paste, associated with parent-reported improvement in persistent obstructive symptoms.	Small (n = 4); limited statistical analysis; patient symptoms poorly characterized pre- and post-intervention.
Moore [32]	Sixteen children with **obstructive symptoms** of unclear origin; 28 children with no post-operative symptoms (n = 43).	14%	• Manometry findings not significantly different between children with obstructive symptoms post-operatively, asymptomatic age-matched group or controls; 14/16 symptomatic children had histological abnormality • No correlation identified between RAIR and function	Limited description of cohort characteristics; small proportion of patients with obstructive symptoms with subsequent biopsy being normal (2/16); subject to non-responder bias.
Nagasaki [26]	Patients with HD treated at a single center (n = 53).	77%	• Children with recurrence of RAIR had excellent continence; those without reported symptoms of bowel dysfunction. • Lower RP in children with FI	Symptom definitions not provided; limited statistical analysis of findings.
Nagasaki [20]	Children post **Ikeda's Z-shaped anastomosis** (n = 46).	80%	• Low RP in children with FI; elevated RP in children with constipation • Elevated or reduced RP responsible for post-operative constipation and fecal incontinence, respectively.	Symptom definitions not provided; limited cohort characteristics.

First author	Manometry population summary	RAIR *(% present)*	Summary of key manometry findings	Limitations
Niedzielski [21]	Post **PSAPP** (n = 10).	0%	• No significant difference between children post-PSAPP, post-Rehbein, or control children.	50% complication rate; no clear functional assessment; limited reporting of manometry findings.
Stensrud [22]	All children with follow-up manometry post HD repair at a single center (n = 35).	-	• Daily FI more likely to occur in children with IAS defects • Only the largest IAS defects were associated with reduced RP • IAS defects not correlated with lower RP, anal sphincter pressures not correlated with constipation or FI.	Designed to identify correlations between manometry and endosonography (not differences between procedures), TEPT group younger and had less pre-operative stomas than laparotomy assisted Soave group.
Tang [30]	Children aged four years or more without neurological comorbidities attending bowel management clinic (n = 8).	-	• Moderate anal pressure asymmetry in children post Soave; marked asymmetry in children post Duhamel and myomyectomy.	Small cohort (n = 8, 3 HD subgroups); heterogeneous surgical and pathological characteristics of HD; lack of normative 3D HRAM data in children.
Till [23]	Post **TEPT** for HD limited to **rectosigmoid** without previous severe HAEC (n = 7).	14.3%	• RP unchanged following TEPT compared with pre-operative values • Vector manometry findings comparable to controls • TEPT preserves functional integrity of the anorectal sphincter	Small cohort; all children asymptomatic; parent-reported outcomes.
Tiryaki [28]	**Obstructive symptoms** post repair following a trial of topical nitric oxide application (n = 18).	11%*	• Decrease in RP (35%) following topical application of glyceryl trinitrate ointment, associated with parent-reported improvement in persistent obstructive symptoms. • Manometric findings did not correlate with clinical symptoms; high RP in both symptomatic and asymptomatic children (no significant difference).	Small subgroup with obstructive symptoms (n = 6); recruitment and clinical characteristics of wider cohort not described; limited description of manometry protocol.
Zhang [24]	Post **one-stage TEPT** (n = 58).	8.6%	• RP significantly increased in children with constipation compared with asymptomatic children and controls	Parent-reported medical characteristics; symptom definitions not provided.

ARM: anorectal manometry; **BFS**: Bowel Function Score; **DC:** descending colon; **FI:** fecal incontinence; **HAEC:** Hirschsprung associated enterocolitis; **HD:** Hirschsprung disease; **HRAM:** high-resolution anorectal manometry; **IAS:** internal anal sphincter; **LHSA:** laparoscopic heart-shaped anastomosis; **LSP:** laparoscope-assisted Soave procedure; **MDT**: modified Duhamel technique; **MTR**: modified transanal rectosigmoidectomy; **PSAPP**: posterior sagittal abdominoperineal pull-through; **RAIR:** rectoanal inhibitory reflex; **RP:** resting pressure; **TAA**: transabdominal approach; **TEPT:** transanal endorectal pull-through; **– :** not reported.

Table 5: Reported post-operative bowel function: assessment measures and outcomes.

First author	Year	Assessment	Post-operative bowel function
Banasiuk [29]	2016	**Rome III** (constipation and fecal incontinence)	Constipation: 1/14 (7%); soiling: 6/14 (43%). Stools per day: TEPT 3.3 vs. Duhamel 2.8. Soiling comparable between procedures.
Chung [10]	2015	**Bowel Function Score (BFS)**	Constipation: 6/37 (16%); soiling: 21/37 (57%), >3 times per week 4/37 (11%) Enterocolitis 10/37 (27%); recurrent 6/37 (16%). Median BFS: 16 (range: 7-20); 26/37 BFS >18 (70%)
Chung [11]	2018	**Bowel Function Score (BFS)**	Constipation 18%; soiling >2/week: 33.3%. Median BFS: 16 (range: 7-20). By extent of HD: DC: 13; SC: 15; UR: 17; LR: 17).
Demirbag [31]	2013	**Questionnaire**: stool frequency, consistency, continence	Obstructive symptoms (constipation / enterocolitis): 7/18 (40%).
Frenckner [12]	1983	-	-
Gad El-Hak [13]	2010	**Miller's Score** (continent, minor/major fecal incontinence)	Post repair (2y): constipation 5/52 (10%); continent (96%), major incontinence 2/52 (4%).
Hedlund [14]	1997	-	Constipation: 1/10 (10%); normal function: 4/10 (40%); constipation + FI: 2/10 (20%).
Huang [15]	2008	**Kelly's Score**	**Transanal Soave**: 5.1±0.5; **Ikeda-Soper**: 5.2±0.6
Iwai [16]	1987	Stool frequency and consistency	5 - 12 stools per day (1 - 3 months post-repair)
Jiao [17]	2019	HAEC; constipation ("reduced bowel actions"); fecal incontinence ("involuntary between voluntary bowel actions").	**Laparoscope-assisted Soave procedure** (44). HAEC: 20.45%; constipation 28%; fecal incontinence 25%. **Laparoscopic heart-shaped anastomosis** (36). HAEC: 14%; constipation: 11%; fecal incontinence 14%.
Martins [18]	2009	Constipation (bowels open < every 3 days); fecal incontinence evaluated using Martins criteria	***Modified Duhamel***: constipation 35%, continent 74%; partially continent 39%, incontinent 0%. ***Modified transanal rectosigmoidectomy***: constipation 5%; continent 61%; partially continent 26%; incontinent 0%.
Messina [19]	2007	-	Persistent constipation
Miele [25]	2000	**Questionnaire**: soiling, fecal impaction, vomiting, diarrhea, abdominal pain/distension, anorexia, laxative, stool frequency.	
Millar [27]	2002	-	Persistent obstructive symptoms: 4/4 (100%); recurrent enterocolitis: 3/4 (75%)

Moore [32]	1994	-	Fecal incontinence 8/115 (7%); obstructive symptoms 16/107 (15%)
Nagasaki [26]	1980	-	Constipation 8/53 (15%); fecal incontinence 11/53 (21%)
Nagasaki [20]	1989	-	Constipation 6/46 (13%); fecal incontinence 11/46 (24%)
Niedzielski [21]	1999	-	All continent; all stool second daily at minimum
Stensrud [22]	2015	**Krickenback criteria**	Constipation: 13/52 (25%); fecal incontinence: weekly 28/52 (54%), daily 19/52 (37%). Fecal incontinence occurred in 63% with IAS defect; intact IAS 45%
Tang [30]	2017	**Rintala Score**	Mean 17.75 (range 15 – 19).
Till [23]	2006	**Parent report:** stooling patterns, fecal incontinence	No parent-reported complains of constipation or fecal incontinence.
Tiryaki [28]	2005	**Questionnaire**: fecal incontinence, frequency/awareness of defecation, treatment, symptoms.	Symptomatic cohort: 6/18 (33%). Constipation: 3/6 (50%); enterocolitis: 3/6 (50%)
Zhang [24]	2007	**Questionnaire**: HAEC, stool characteristics, constipation, soiling, treatments.	Constipation: 5/58 (9%); fecal incontinence: 9/58 (16%); enterocolitis: 3/58 (5%). Mean 2.2 ± 2.0 stools per day; 4/58 (7%) children had 8-10 stools per day.

FIGURE AND TABLES CAPTION LIST

Figure 1: Study selection flow diagram.

Table 1: Clinical characteristics of included studies.

Table 2: Summary of reported anorectal manometry specifications.

Table 3: Summary of anorectal manometry parameters reported by included studies, with comparable parameters grouped for comparison. Differences in terminology are indicated, with the study definition provided as a footnote.

Table 4: Summary of key findings.

Table 5: Reported post-operative bowel function: assessment measures and outcomes.

APPENDIX 1

Table 6 Sample search strategy: MEDLINE

1. hirschsprung disease/
2. (hirschsprung* or ((megacolon or mega-colon or rectosigmoid or recto-sigmoid or colonic or intestine) adj2 (congenital or aganglionic or aganglionosis or idiopathic or congenitum))).tw,kf.
3. manometry/
4. manometr*.tw,kf.
5. (1 or 2) and (3 or 4)
6. exp animals/ not human*.sh.
7. 5 not 6
8. limit 7 to yr="1980 -Current"

Table 7 Sample search strategy: Embase

1. Hirschsprung disease/
2. (hirschsprung* or ((megacolon or mega-colon or rectosigmoid or recto-sigmoid or colonic or intestine) adj2 (congenital or aganglionic or aganglionosis or idiopathic or congenitum))).tw,kw,dq.
3. manometry/
4. manometr*.tw,kw,dq.
5. (1 or 2) and (3 or 4)
6. exp animal/ not human*.sh.
7. 5 not 6
8. limit 7 to yr="1980 -Current"

APPENDIX 2

Table 9: Summary of consistently reported manometry parameters: parameter definitions, resting pressure, squeeze pressure, and rectoanal inhibitory reflex. Units of pressure standardized to mmHg.

First author	Resting pressure	Squeeze pressure	RAIR	Resting pressure (mmHg)	Squeeze pressure (mmHg)	RAIR (% present)
Banasiuk [29]	**Maximum and mean sphincter resting pressure.** Assessment not further defined. Operative approaches compared. No comparison with norms reported.	**Maximum squeeze sphincter pressure.** Squeeze: 10 – 20s. Operative approaches compared. No comparison with norms reported.	>**25%** decrease in mean resting pressure of anal canal. Balloon distended in 10mL increments (0-60mL).	**Mean**: TEPT 60.6 (SD 18.1) Duhamel 71 (SD 13.5) **Maximum**: TEPT 83.9 (SD 30.8) Duhamel 93.9 (SD 15.4)	**TEPT**: 202.2 (SD 71.2) **Duhamel**: 194 (SD 40.5)	**TEPT**: 87.5% **Duhamel**: 33%
Chung [10]	**Sphincteric resting pressure.** Normal: 30 – 60 mmHg Norms derived from two previous studies	-	Reduction in sphincter pressure of >**15mmHg for 5s** when balloon was inflated.	**Mean:** 44 (SD 14.4) **Median**: 45 (14-79) **Normal range (cohort)**: 72.9% High: 5.4%; Low: 21.6%	-	16.2%
Chung [11]	**Sphincteric resting pressure.** Normal: 30 – 60 mmHg Norms derived from two previous studies	**Sphincteric squeezing pressure**. Normal: 50 – 120mmHg. Norms derived from two previous studies and six age-matched controls	-	**DC**: 25 (10 – 53.5), 62.5% **SC:** 43 (26.5 – 58), 75% **UR:** 38 (15.5 – 46.5), 85.7% **LR:** 29 (11 – 41.5), 72.3% Normal range (**cohort**): 75.6% Median (range), % normal range	**DC**: 55 (18.5 – 80) **SC:** 68 (23 – 92.5) **UR:** 45 (25.5 – 76.5) **LR:** 62 (20 – 94.5)	-

First author	Resting pressure	Squeeze pressure	RAIR	Resting pressure (mmHg)	Squeeze pressure (mmHg)	RAIR (% present)
Demirbag [31]	**Maximal anal resting pressure.** Assessment not further defined. Asymptomatic and obstructive patients compared. No comparison with norms reported.	-	Not stated.	**Obstructive**: 40.5 (SD 8.1) **Asymptomatic**: 36 (SD 8.8)	-	22.2%[1]
Frenckner [12]	**Anal pressure** recorded at the level of the internal sphincter. Assessment not further defined. No comparison with norms reported.	-	-	**Pre-operative**: 59 (SD 25) **Post-operative**: 63 (SD 16)	-	-
Gad El-Hak [13]	**Resting anal pressure**, which is the function of the IAS supplemented by the EAS.	**Squeeze pressure,** which is the function of the voluntary control pathways and EAS.	Not stated.	**Pre-operative**: 61.3 (SD 16.3) **Post-operative**: Continent**:** 58.1 (SD 15.1) Minor incontinence**:** 49.1 (SD 15.1) Major incontinence: 37.1 (SD 12.1)	**Pre-operative**: 112.5 (SD 32.9) **Post-operative:** Continent**:** 107.7 (28.1) Minor incontinence**:** 101.4 (SD 14.1) Major incontinence: 62.5 (17.5)	11.54%
Hedlund [14]	**Anal resting pressure.** Assessment not further defined. Results compared with children post modified Swenson pull-through and normal controls.	**Anal squeeze pressure.** Assessment not further defined. Results compared with children post modified Swenson pull-through.	-	**Controls** (-): 65.3 (SD -) **Swenson** (15): 62.3 (10.5) **PSR** (9): 63 (SD 13.5)	**Controls** (-): 144.8 (SD -) **Swenson** (9): 156.0 (SD 36) **PSR** (6): 171.8 (SD 66.8)	-

[1] Reflex reported as present but abnormal

First author	Resting pressure	Squeeze pressure	RAIR	Resting pressure (mmHg)	Squeeze pressure (mmHg)	RAIR (% present)
Huang [15]	**Resting anal canal pressure.** Assessment not further defined. Results of operative approaches compared. No comparison with norms not reported.	**Active contractive pressure:** difference between anal canal contractive pressure and the resting anal canal pressure. Results of operative approaches compared. Comparison with norms not reported.	Not stated.	**Transanal**: 51.7 (SD 4.2) **Ikeda-Soper**: 52.1 (SD 3.6)	Active contractive pressure **Transanal**: 52.3 (SD 15.6) **Ikeda-Soper:** 55.7 (SD 15.4)	0%
Iwai [16]	**Rectal and anal pressures** reported. Assessment not further defined. No comparison with norms reported.	-	Not stated.	**Preoperative:** 45 **Postoperative**: 1 month: 18.6 3 months: 24.1 (Mean; SD not reported).	-	0%
Jiao [17]	**Anal resting pressure**. Assessment not further defined. No comparison with norms reported.	-	-Pressure decrease of **>70%** -in response to 10-30mL increase in stimulation volume; -negative after three attempts at stimulation	**Pre-operative:** LHSA: 67.8 (SD 14.2) LSP: 66.8 (SD 12.7) **Post-operative:** LHSA: 60.64 (SD 9.33) LSP: 68.84 (SD 11.8)	-	Assessment reported; **outcome not stated.**
Martins [18]	**Resting pressure of the zone of greatest pressure in the anal canal**. No comparison with norms reported.	**Pressure response to voluntary contraction** in the zone of greatest pressure in the anal canal.	Not stated	**Duhamel**: 53.44 **TEPT**: 60.67 (Mean; SD not reported).	**Duhamel**: 94.50 **TEPT**: 95.47 (Mean; SD not reported).	TEPT + Duhamel equivalent. **Proportion not reported**

First author	Resting pressure	Squeeze pressure	RAIR	Resting pressure (mmHg)	Squeeze pressure (mmHg)	RAIR (% present)
Messina [19]	**Median and maximum anal sphincter pressure** reported. Assessment not defined. No comparison with norms reported.	-	-	**Pre-treatment**: median 115.6 (102 – 130); maximum 160 (145-175) **Post-treatment:** reduction of 59.1% median pressure, 34.1% maximum pressure.	-	-
Miele [25]	**Anal resting pressure** determined by pull-through technique: pressures recorded after catheter withdrawn in 1cm increments, maximum pressure sustained for 10s recorded. Compared with 11 controls.	-	Two assessments: (1) Highest percentage relaxation after distension with 30 and 60mL air (2) Lowest volume in mL to elicit reflex of **>10mmHg**	**Maximal anal pressure** **Controls**: 110.0 (SD 15.3) **Cohort**: 122.7 (SD 13.6) **Resting anal pressure** **Controls**: 68.5 (SD 21.3) **Cohort**: 75.9 (SD 15.5)	-	0%
Millar [27]	**Maximal anal sphincter pressure**. No comparison with norms reported.	-	-	**Pre-treatment**: 165 (96 – 250) **Post-treatment**: reduction of median 88.6 (46-90)	-	-
Moore [32]	**Resting rectal pressure and maximal anal canal pressure**. Results compared with 20 children with constipation and 10 normal controls.	-	Not stated	Median maximal anal canal pressures: **Controls**: 31.8 Constipation: 27.7 **Hirschsprung disease:** Obstructive symptoms: 21.6 No obstructive symptoms: 26.3	-	14%

First author	Resting pressure	Squeeze pressure	RAIR	Resting pressure (mmHg)	Squeeze pressure (mmHg)	RAIR (% present)
Nagasaki [26]	**Rectal and anal canal pressure**. Assessment not further defined. Results compared with 30 control children.	-	Not stated	Anal canal pressure: **Controls**: 10.1 ± 4.1 **Cohort:** **Pre-op**: 13.8 ± 3.7 **1 month post-op:** 13.4 ± 4.6 **1-3y post op**: 10.1 ± 4.3	-	77%
Nagasaki [20]	**Rectal and anal canal pressure**. Assessment not further defined. Results compared with 61 control children.	-	Not stated	Anal canal pressure: **Controls**: 21.2 ± 10.9 **Cohort:** **Pre-op**: 23.2 ± 9.7 **1 month post-op:** 16.3 ± 7.9 **2-3y post op**: 15.5 ± 5.9	-	80%
Niedzielski [21]	**Anal resting pressure**. Assessment not further defined. Results compared with 12 children post Rehbein and 30 controls.	-	Three measurements with inflation of balloon to 50mL.	**PSAPP**: 11.7 (SD 1.03) **Rehbein**: 11.8 (SD 1.03) **Controls**: 12.1 (SD 1.03)	-	0%
Stensrud [22]	**Anal resting pressure**: lowest point of the slow wave fluctuation curve. Findings of operative approaches compared; no reported comparison with norms.	**Squeeze pressure:** maximum peak pressure of three voluntary squeeze events.	-	**Cohort**: 40 (15 - 120) **Transanal**: 40 (15-75) **Transabdominal**: 48 (30-120)	**Cohort**: 131 (60-250) **Transanal**: 115 (60-250) **Transabdominal**: 180 (100-250)	-

First author	Resting pressure	Squeeze pressure	RAIR	Resting pressure (mmHg)	Squeeze pressure (mmHg)	RAIR (% present)
Tang [30]	**Resting pressure of high pressure zone**; reported as maximum/minimum. No reported comparison with norms.	**Squeeze pressure of high pressure zone**; reported as maximum/minimum. No reported comparison with norms.	-	Summary statistics not provided. **Maximal resting pressure range**: 53 - 113	Summary statistics not provided. **Maximal squeeze pressure range**: 103 – 302.	-
Till [23]	**Anal sphincter pressure at rest (ASPR)**: mean over 1 minute **Maximal segmental pressure (MSP)**: peak of all pressure values from eight channels in anal canal. Pre- and post-operative values compared.	**Maximal segmental pressure (MSP)**: peak of all pressure values from eight channels in anal canal during squeeze. Pre- and post-operative values compared.	Not stated	**ASPR** (4 channel): 49.2 **MSP at rest** (8 channel): 121 (SD 45.43)	**MSP squeeze** (8 channel): 178.75 (SD 45.13)	14.3%
Tiryaki [28]	**Maximum anal sphincter pressure**. Norms not reported.	-	Not stated	**Pre-treatment**: 45 (36 – 52) **Post-treatment**: reduction of 13.9 – 17.7 (35%)	-	11%**Error! Bookmark not defined.**
Zhang [24]	**Maximal resting pressure**. Compared to 33 age and sex-matched control children.	**Maximal squeezing pressure**. Assessment not further defined. Compared to 33 age and sex-matched control children.	-Reduction >25% resting pressure -Balloon: 50mL -On three consecutive measurements	**Cohort**: 157 ± 47 **Controls**: 152 ± 33 **Constipation**: 167 ± 36 **Fecal incontinence**: 151 ± 107 [2]	**Cohort**: 200 ± 65 **Controls**: 190 ± 38 **Constipation**: 211 ± 36 **Fecal incontinence**: 198 ± 102	8.6%

ARM: anorectal manometry; **DC:** descending colon; **HD:** Hirschsprung disease; **HAEC:** Hirschsprung associated enterocolitis; **FI:** fecal incontinence; **LHSA:** laparoscopic heart-shaped anastomosis; **LSP:** laparoscope-assisted Soave procedure; **MDT**: modified Duhamel technique; **MTR**: modified transanal rectosigmoidectomy; **PSAPP**: posterior sagittal abdominoperineal pull-through; **QoL:** quality of life; **RS**: rectosigmoid; **SC**: sigmoid colon; **TAA**: transabdominal approach; **TC**: transverse colon; **TEPT:** transanal

[2] Units unclear: separately reported as both cmH_2O and mmHg

endorectal pull-through; **– :** not reported.