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Laparoscopic assistance for primary transanal pull-through in Hirschsprung's disease: a systematic review and meta-analysis

David Thomson,[1] Benjamin Allin,[1] Anna-May Long,[1] Tim Bradnock,[2] Gregor Walker,[2] Marian Knight[1]

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[1]National Perinatal Epidemiology Unit, University of Oxford, Oxford, UK
[2]Department of Paediatric Surgery, Royal Hospital for Sick Children, Glasgow, UK

Correspondence to
Dr Marian Knight;
marian.knight@npeu.ox.ac.uk

ABSTRACT

Objective: To compare outcomes following totally transanal endorectal pull-through (TTERPT) versus pull-through with any form of laparoscopic assistance (LAPT) for infants with uncomplicated Hirschsprung's disease.

Design: Systematic review and meta-analysis.

Setting: Five hospitals with a paediatric surgical service.

Participants: 405 infants with uncomplicated Hirschsprung's disease.

Interventions: TTERPT versus LAPT.

Primary and secondary outcome measures: Primary outcomes: mortality, postoperative enterocolitis, faecal incontinence, constipation, unplanned laparotomy or stoma formation, and injury to abdominal viscera.

Secondary outcomes: Haemorrhage requiring transfusion of blood products, abscess formation, intestinal obstruction, intestinal ischaemia, enteric fistula formation, urinary incontinence or retention, impotency and duration of procedure.

Results: Five eligible studies comprising 405 patients were identified from 2107 studies. All studies were retrospective case series, with variability in outcome assessment quality and length of follow-up. Operative duration was 50.29 min shorter with TTERPT (95% CI 39.83 to 60.74, p<0.00001). There were no significant differences identified between TTERPT and LAPT for incidence of postoperative enterocolitis (OR=0.78, 95% CI 0.44 to 1.38, p=0.39), faecal incontinence (OR=0.44, 95% CI 0.09 to 2.20, p=0.32) or constipation (OR=0.84, 95% CI 0.32 to 2.17, p=0.71).

Conclusions: This meta-analysis did not find any evidence to suggest a higher rate of enterocolitis, incontinence or constipation following TTERPT compared with LAPT. Further long-term comparative studies and multicentre data pooling are needed to determine whether a purely transanal approach offers any advantages over a laparoscopically assisted approach to rectosigmoid Hirschsprung's disease.

Trial registration number: PROSPERO registry-CRD42013005698.

Strengths and limitations of this study

- We present evidence from five retrospective studies of 405 patients.
- This is the first study to systematically review the available literature comparing totally transanal endorectal pull-through procedures with laparoscopically assisted pull-through procedures.
- The only significant difference between procedures was a shorter operation time with totally transanal endorectal pull-through. Incidence of serious postoperative complications, including enterocolitis, faecal incontinence and chronic constipation, did not differ between the two procedures.
- The main limitations of this study include limited statistical power as we identified only five eligible studies, the generally low quality of the studies, heterogeneity with respect to outcome assessment, and limited long-term follow-up.
- This study identifies an urgent need for high-quality prospective studies and an absence of any data obtained using randomisation methods.

INTRODUCTION

Since the first description of Harald Hirschsprung's eponymous condition in 1889,[1] there has been ongoing debate regarding the optimal surgical approach. The choice of rectal dissection technique is controversial, although the three primary options remain full-thickness dissection with end-to-end anastomosis as described by Swenson in 1948,[2] and Duhamel's retrorectal anastomosis or Soave's extramucosal dissection which were developed later.[3 4] During the 1980s, one-stage (primary) procedures were proposed for uncomplicated cases, thereby avoiding the morbidity associated with stoma formation.[5] In 1995, Georgeson *et al*[6] described a minimally invasive approach using laparoscopy for colonic biopsies and mobilisation, followed by

transanal endorectal dissection of the rectum and coloanal anastomosis. Subsequently, laparoscopic Swenson and Duhamel-type procedures have been described.[7 8] In 1998, De La Torre *et al* reported the first entirely transanal primary endorectal pull-through without laparoscopic assistance.[9] The transanal Swenson-type procedure has been reported but no case-controlled data have been published; a purely transanal Duhamel is not feasible technically.[10]

The totally transanal endorectal pull-through (TTERPT) has gained rapid acceptance across many paediatric surgical units.[11] Purported benefits of this approach include utilisation of a single incision and the avoidance of abdominal wall scarring, with the potential for better cosmesis and reduced postoperative pain, a shorter operating time and the suitability of this technique for use in resource-poor settings which may lack equipment for laparoscopy.[11–13] Potential disadvantages regarding a totally transanal approach include the possible impact of prolonged dilation of the sphincter muscles on faecal continence,[14 15] the risk of colonic torsion and the inability to confirm the histological transition zone (TZ) prior to starting mobilisation of the colon as many surgeons would change their operative approach when faced with longer segment aganglionosis.[16]

In a recent survey of practice in the UK, the majority of responding surgeons who utilise an endorectal dissection employ laparoscopic surgery for biopsies or mobilisation.[16]

The aim of this study was to conduct a systematic review and meta-analysis to compare outcomes for infants with Hirschsprung's disease undergoing a TTERPT procedure with those undergoing a laparoscopically assisted transanal pull-through (LAPT).

METHODS

A study protocol outlining the search strategy, outcomes, and methods of data extraction and statistical analysis was designed and prospectively registered with the Prospero database (CRD42013005698).[17]

Search strategy

We searched all publications from 1 January 1998 to 1 January 2014 from EMBASE, MEDLINE and Cochrane library databases using the search strategy detailed in online supplementary appendix I. MeSH/EMTREE terms used were *Hirschsprung disease* and *laparoscopy*. Keyword searches included recto-sigmoid, Hirschsprung*, aganglionosis, colon* resection, pull*through, trans*anal, endo*anal, trans*abdominal, biops*, Soave*, Swenson* and Boley*. For the Cochrane library database, a broad search term 'Hirschsprung' was used to search title, abstract and keyword fields. No limits were applied to language or location of study. All articles with comparative study arms were eligible for inclusion.

Inclusion/exclusion criteria

Study inclusion and exclusion criteria are summarised in table 1.

Titles and abstracts of potentially relevant papers were screened by two independent authors (DT and BA). The full texts of all identified studies were assessed against the criteria in table 1 by the two independent authors (DT and BA), and study reference lists were hand searched for potentially relevant studies. Any discrepancies were resolved by consensus discussion with a third author (MK).

Data extraction

Data were extracted by the two independent authors (DT and BA) using a predesigned proforma. Data were collected regarding: age at gestation, diagnosis and surgery, level of anal dissection, length of mucosal cuff, length and location of aganglionosis, and any congenital abnormalities.

Primary outcomes were: mortality, postoperative enterocolitis, faecal incontinence, constipation, unplanned laparotomy or stoma formation, and injury to abdominal viscera.

Secondary outcomes were: haemorrhage requiring transfusion of blood products, abscess formation, intestinal obstruction, intestinal ischaemia, enteric fistula formation, urinary incontinence or retention, impotency and duration of procedure.

Quality assessment

Two independent authors (DT and BA) assessed study quality using the Newcastle-Ottawa Scale for case–control and cohort studies.[18]

Statistics

Continuous data were analysed using an inverse variance model to produce a mean difference. Dichotomous variables were analysed using a Mantel-Haenszel model to produce ORs. χ^2 Test for heterogeneity was used to assess agreement within studies. Random-effects models were used when there was significant variation in outcome assessment measures between studies or when there was evidence of significant heterogeneity; otherwise, fixed-effects models were used. All analyses were performed using Review Manager V.5.2 software.[19]

Table 1 Inclusion/exclusion criteria

Inclusion	Exclusion
Primary pull-through procedure as planned operation	Infants managed with stoma prior to decision for definitive surgery Infants planned for open or multistaged procedure Infants planned for Duhamel-type anastomosis
Biopsy-proven diagnosis of Hirschsprung's disease	No histological confirmation of diagnosis

RESULTS

Literature search

A total of 2107 records were screened, of which 41 studies potentially met the eligibility criteria (figure 1). Thirty-one studies were excluded because there was no comparative study arm. Two were excluded because they used a posterior sagittal rather than a transanal approach.[20 21] One study was excluded because it used a laparoscopic Duhamel-type anastomosis[22] and one study because infants undergoing a staged procedure were pooled with primary procedure results.[23] Data were sought from the authors of two studies that pooled transabdominal and laparoscopic-assisted procedures.[24] Data were available and generously provided by the authors of one of these studies.[25] Four further retrospective observational studies were eligible for inclusion in the final review.[26–28]

Study characteristics

Four hundred and five patients were included in the meta-analysis; 159 underwent a LAPT and 248 underwent a TTERPT. Table 2 summarises the characteristics of included studies. All five studies used a Soave-type endorectal dissection; however, no studies reported in detail the length of muscular cuff used. No studies utilised a Swenson-type procedure. Three studies reported the site of the TZ. Huang *et al* report 11/29 (38%) short segment and 18/29 (62%) rectosigmoid TZ in the LAPT arm, and 14/44 (32%) short segment and 30/44 (68%) rectosigmoid TZ in the TTERPT arm. All cases reported by van de Ven *et al* had a rectosigmoid TZ. Kim *et al* reported a small number of left-sided (6/54) and mid-to-right TZs (1/54) in the LAPT arm, and 1/75 left-sided TZ in the TTERPT arm.

Study quality

Study quality was assessed using the Newcastle-Ottawa Scale for cohort studies.[18] Scores were low overall, with one study scoring 6/9, one scoring 5/9, one scoring 4/9 and two scoring 3/9. Methodological weaknesses common to all studies included inadequate selection of both operative groups because the exposure (ie, decision to operate via a laparoscopic-assisted or totally transanal technique) occurred before selection into the cohort study as all five were retrospective cohort studies. Description of demographic features of both cohorts varied greatly between studies as table 2 illustrates. Only one study utilised blinded outcome assessment[25] and only one study included a complete description of patients lost to follow-up.[29]

Duration of operation

Two studies reported data on duration of operation in 102 patients (52 TTERPT, 50 LAPT). Analysis using a fixed-effects model revealed a mean difference of 50.29 min shorter operative time with a totally transanal technique (95% CI 60.74 to 39.83, p<0.00001).

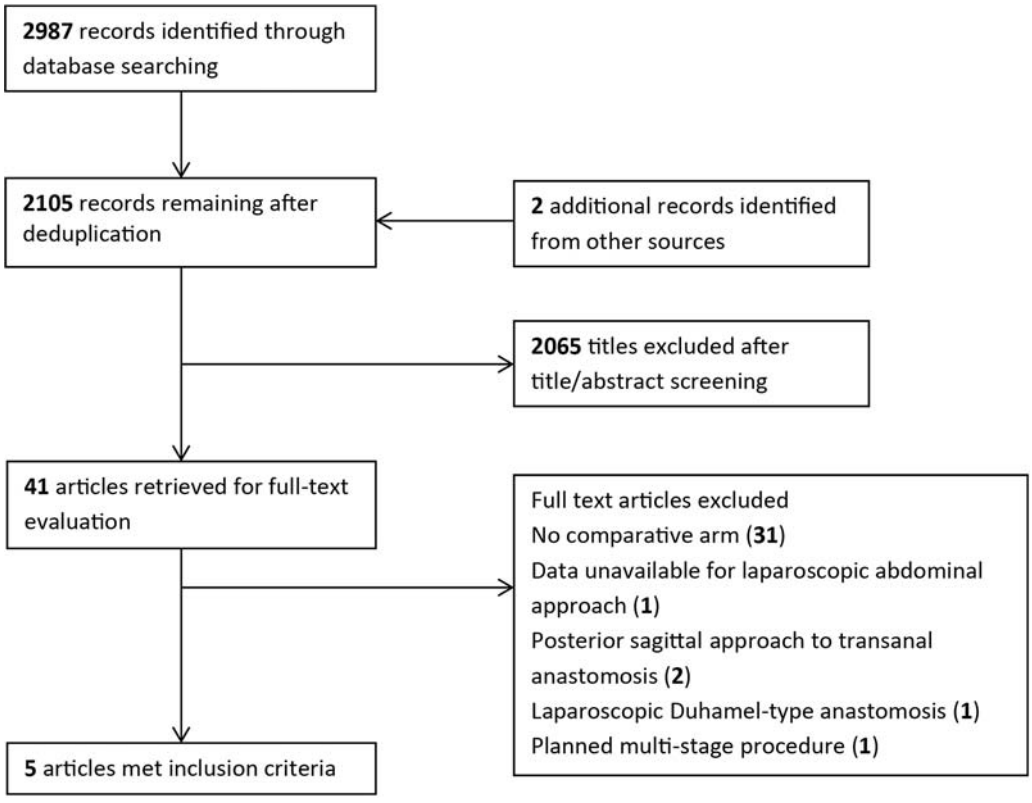

Figure 1 PRISMA flow chart summarising study selection process.

Table 2 Study characteristics

Study	Procedure (n)	Gender	Age at procedure (months)	Level of anal dissection	Location of disease segment	Congenital abnormalities	NOS score (/9)
Huang *et al*[26]	LAPT SO (29)	NA	NA	NA	Short(11) R-S (18)	NA	4
	TTERPT SO (44)				Short (14) R-S (30)		
Ishikawa *et al*[27]	LAPT (21) TTERPT (8)	NA	6.5±4.3 4.4±3.0	1 cm proximal to dentate line (both)	NA	NA	3
Kim *et al*[25]	LAPT (54)	M (43) F (11)	4.1±0.8	NA	Short or R-S (47) Left (6) M-R (1)	Down's (5) Heart (5) Other (5)	5
	TTERPT (75)	M (65) F (10)	5.1±1.0		Short or R-S (74) Left (1)	Down's (9) Heart (9) Other (7)	
Dahal *et al*[28]	LAPT (33)	M (27) F (6)	17±18.2	NA	NA	NA	3
	TTERPT (98)	M (85) F (13)	13±8				
van de Ven *et al*[29]	LAPT (22)	M (17) F (5)			R-S (22)	Down's (3)* Heart (0) Other (1)	6
	TTERPT (21)	M (17) F (5)			R-S (21)	Down's (2)* Heart (2) Other (1)	

*Down's and Waardenburg syndrome.
LAPT, transanal anastomosis with laparoscopic assistance; M-R, mid to right; NOS, Newcastle-Ottawa Scale; R-S, recto-sigmoid; SO, Soave; TTERPT, totally transanal endorectal pull-through; NA, not applicable.

Enterocolitis

Four studies reported data on incidence of postoperative enterocolitis in 268 patients (147 TTERPT, 121 LAPT). Analysis using a fixed-effects model revealed a non-significant OR of 0.78 for TTERPT versus LAPT (95% CI 0.44 to 1.38, p=0.39, figure 2).

Faecal incontinence

Three studies reported long-term data on incidence of faecal incontinence from 184 patients (102 TTERPT, 82 LAPT). Analysis using a random-effects model revealed an OR of 0.44 for TTERPT versus LAPT (95% CI 0.09 to 2.20, p=0.32, figure 3).

Constipation

Four studies reported long-term data on incidence of chronic constipation from 227 patients (123 TTERPT, 104 LAPT). Analysis using a random-effects model revealed an OR of 0.84 for TTERPT versus LAPT, with 29 instances recorded across four studies (95% CI 0.32 to 2.17, p=0.71, figure 4).

Mortality

Mortality was reported in two studies with no incidences.[26 29]

Other outcomes

Data suitable for meta-analysis were not available from the identified studies for the following outcomes: unplanned

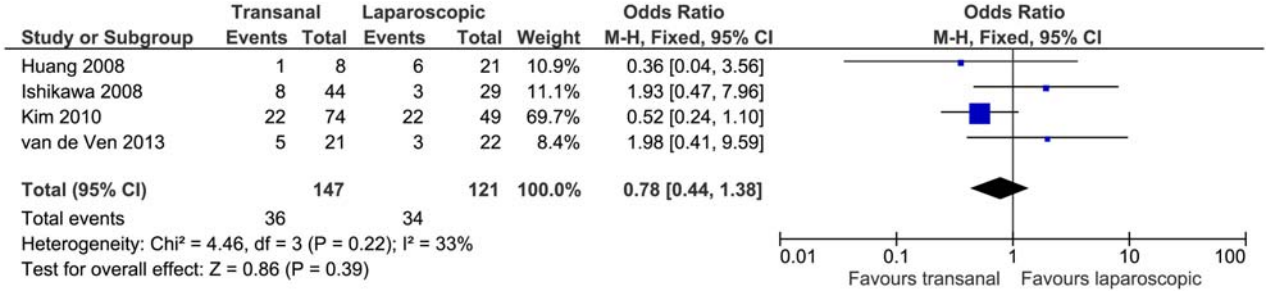

Figure 2 Forest plot to show enterocolitis rates among infants undergoing totally transanal endorectal pull-through or laparoscopically assisted transanal pull-through.

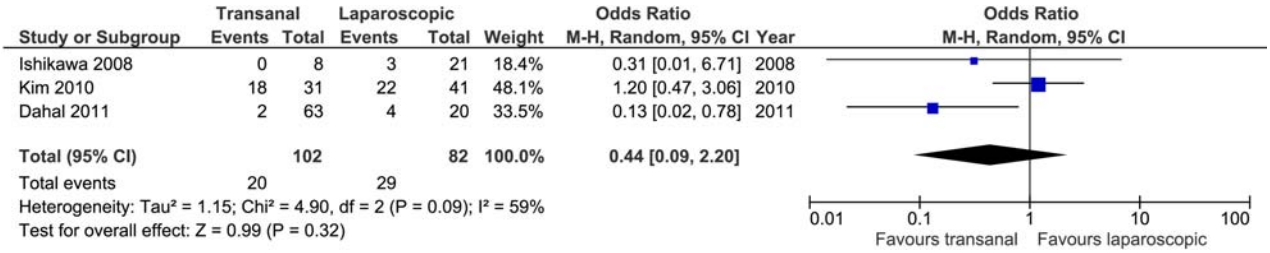

Figure 3 Forest plot to show faecal incontinence among infants undergoing totally transanal endorectal pull-through or laparoscopically assisted transanal pull-through.

laparotomy or stoma formation, injury to abdominal viscera, haemorrhage requiring transfusion of blood products, abscess formation, intestinal obstruction, intestinal ischaemia, enteric fistula formation, urinary incontinence or retention, impotency and sphincter achalasia.

DISCUSSION

Since the first reports in the late 1990s the transanal pull-through has become a popular procedure worldwide for Hirschsprung's disease management and the role of laparoscopy remains controversial.[12 35] This meta-analysis identified only five eligible studies comparing TTERPT to LAPT. In general, these studies were of low quality, featuring heterogeneity with respect to outcome assessment, limited adjustment for potential confounders and inadequate long-term follow-up. The only outcome assessed, where there was a significant difference, was duration of surgery, with two studies demonstrating a significantly shorter duration of operation time for TTERPT compared with LAPT. This may be due to avoidance of time spent accessing the abdomen with a laparoscopically assisted procedure and concords with results from studies comparing open abdominal procedures with transanal pull-through.[30] Unfortunately, these studies do not provide in-depth details of the reasons for the difference in operative time. As both studies included were retrospective observational studies and thus, likely to be subject to a degree of case selection, it is possible that cases with shorter, less-complicated disease segments were preferentially chosen for TTERPT.

The other relevant outcomes assessed were the incidence of Hirschsprung's associated enterocolitis (HAEC), and functional gastrointestinal outcomes. We found no evidence to suggest any difference in rates of postoperative HAEC between TTERPT and LAPT procedures. Incidence of HAEC ranged from 10% to 45% across studies; this compares to a reported incidence of 5–35% from previous studies.[23 31] The variable rates of HAEC reported may relate to inconsistent definitions between studies. Kim *et al*[25] used a previously validated scoring system to assess severity and utilised a Delphi score to 'further secure uniformity' of the diagnosis of HAEC. Van de Ven *et al*[29] also used a Delphi score to diagnose HAEC. Neither Ishikawa *et al*[27] or Dahal *et al*[28] included definitions for the diagnosis of HAEC. We did not find evidence to suggest a difference in rates of faecal incontinence or constipation between TTERPT and LAPT groups. Of crucial importance in the assessment of incontinence and constipation is an adequate period of follow-up to allow assessment of children at an age when continence should be expected, and they have gained the necessary level of maturity and communication skills to report these outcomes. Follow-up durations were variable in the four studies that assessed these outcomes. Kim *et al*[25] restricted their analysis to infants over 3 years of age and Ishikawa *et al*[27] included only infants with three or more years of postoperative follow-up. Van de Ven *et al*[29] included all infants with follow-up longer than 3 months. Dahal *et al*[28] did not set a minimum follow-up period, with an age range from 6 to 171 months. In all studies, the methods used to assess faecal incontinence and constipation include an element of subjectivity. Kim *et al*[25] employed a previously published parental telephone interview survey of bowel function with investigators blinded to the patient's operative arm. Ishikawa *et al*[27] did not detail how follow-up data were obtained: constipation was defined as

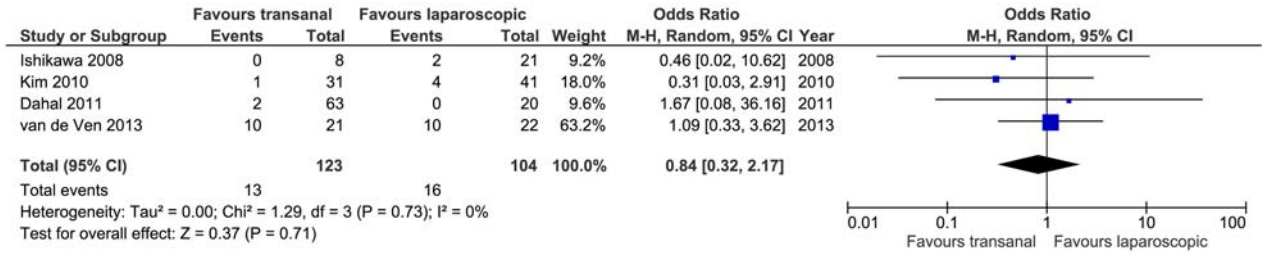

Figure 4 Forest plot to show constipation among infants undergoing totally transanal endorectal pull-through or laparoscopically assisted transanal pull-through.

requiring anorectal myectomy and soiling as "greater than once per week at three years post-surgery." Van de Ven *et al*[29] defined constipation as "need for laxatives, enemas and/or bowel irrigations longer than 3 months," but did not include data on faecal incontinence. Dahal *et al*[28] did not define their terms 'soiling' or 'constipation', or the methods used to collect follow-up data.

The heterogeneity in outcome assessment methods and follow-up durations across these four studies must mandate caution in the interpretation of the finding that there was no evidence of a difference in faecal incontinence or constipation between the two surgical techniques. Of note is the fact that Kim *et al*[25] found that differences in stool frequency between transanal pull-through and transabdominal procedures have converged by age 7 years. There is some evidence that bowel function following definitive surgery for Hirschsprung's disease continues to improve until adolescence.[32] These findings reinforce our belief that longer durations of follow-up are vital to discover if apparent advantages of certain techniques persist as children develop. Since all the included studies were observational, there remains the possibility of uncontrolled confounding between the two treatment groups and thus, there are concerns regarding the comparability of both operative arms. All five studies were retrospective, with treatment selection occurring prior to inclusion in the study. Van de Ven *et al* reported on two units in which each performed one technique exclusively. While this reduces the risk of selection bias because patients are selected on a geographical basis rather than procedure technique, it introduces risks of confounding biases between sites.[29] Four studies reported on a timeframe during which unit practice had altered, generally shifting towards greater utilisation of TTERPT. It is possible that improvements in non-operative areas, such as nursing care and preoperative diagnosis, may have had an effect on outcomes. In addition, Dahal *et al*[28] acknowledge that the decision to utilise TTERPT or LAPT depended on results of barium enema, with longer segment disease more likely to be treated with a LAPT procedure. Reliance on a contrast enema to select patients for TTERPT introduces another potential difficulty for the surgeon, as recent reports suggest that 10–31% of infants have no radiologically identifiable TZ and a further 8–38% of reported TZs are discordant with the confirmed pathological length of aganglionosis.[33] These difficulties may result in a surgeon inadvertently attempting to perform a totally transanal operation for an infant with long segment Hirschsprung's disease, in whom the procedure may be unsuitable due to the need for extensive colonic mobilisation. In addition, a staged approach with retro-rectal dissection ('Long-Duhamel' technique) may be preferred if the aganglionosis involves a large proportion of the colon.[11 34]

Several important outcome measures could not be assessed in this meta-analysis. One putative advantage of totally transanal approaches is the avoidance of intestinal adhesions leading to bowel obstruction. None of the studies reported any incidence of bowel obstruction but adhesions are a potentially lifelong complication that may take many years to manifest clinically. Rates of conversion from TTERPT to laparoscopy or laparotomy were not clearly reported across studies. Dahal *et al* included four patients where the planned TTERPT was converted to a laparoscopic procedure because of failure of colonic mobilisation; however, it is not clear whether these patients were analysed by intention to treat. Van de Ven *et al*[29] report three cases where laparotomy was needed to treat colonic torsion following a TTERPT. Finally, other minimally invasive intra-abdominal techniques, such as umbilical incisions and minilaparotomies, were not assessed because these are outside the scope of this review.

Despite acknowledgement that more complicated and extensive disease segments require some form of intra-abdominal approach, including laparoscopy, minilaparotomy, umbilical incision or formal laparotomy,[11 12] there is currently a lack of guidance to determine when it is unsafe to attempt a TTERPT. Therefore, it is vital that a number of measures are undertaken by the research community to improve the information available on the value of this approach. First, long-term follow-up studies are needed to fully understand the impact of TTERPT and LAPT techniques on bowel, urinary and sexual functions, including assessment of patient's satisfaction and late complications, such as intestinal obstruction secondary to adhesions. Despite widespread enthusiasm for newer procedures, it is important to note that virtually all data on bowel function in adulthood in patients with Hirschsprung's disease come from those operated on with a transabdominal Duhamel technique.[32] Second, intention-to-treat analysis and reporting of comparative studies is vital, particularly in relation to the need to perform a laparotomy in a planned totally transanal procedure due to an unidentified long segment or total colonic aganglionosis. It is essential that authors accurately report such events, so that the true incidence of these occurrences can be gauged.

The issues we have raised regarding choice of operation would be best resolved by randomisation within a clinical trial of TTERPT versus LAPT approaches in patients with aganglionosis confined to the rectum and sigmoid colon on radiological assessment. However, this is unlikely to be feasible in a rare condition where individual clinician equipoise may be lacking. An alternative approach would be to conduct an expertise-based randomised controlled trial. In addition, multicentre data pooling, as exemplified by the BAPS-CASS programme in the UK,[36] is needed to investigate long-term complications and effectively power evidence-based guidelines to identify patient groups in whom laparoscopic or other intra-abdominal assistance should be utilised.

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Contributors DT designed the study, performed the literature search, data extraction and data analysis, and drafted the manuscript. BA performed data extraction and analysis. BA, A-ML and MK conceived and helped to design the study and reviewed the manuscript for important intellectual content. TB and GW assisted with study design and reviewed the manuscript for important intellectual content. MK is the guarantor of the study.

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