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A comparison between primary endorectal pull-through and staged procedures for patients with Hirschsprung's disease

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KEYWORDS

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ABSTRACT

Background: Primary endorectal pull-through is becoming a standard of care across the globe. This study was done to compare the outcome of patients with Hirschsprung's disease (HD) who underwent primary endorectal pull-through with patients who were treated with a staged approach.

Methods: A retrospective data review was done of all patients diagnosed with Hirschsprung's disease (HD) at Tygerberg Children's Hospital, a tertiary hospital in Cape Town, during an 11-year period (2007 – 2018). The patients were divided into 2 groups: the primary Endorectal pull-through (ERP) group and the staged group and the two groups were compared.

Results: Eighty patients with histologically confirmed Hirschsprung's disease (HD) were seen at our institution during the study period (2007 – 2018). Four patients did not meet the inclusion criteria and were excluded. Of the remaining seventy-six who were included, forty-six patients (60.5%) had a primary endorectal-pull through (Primary group) and thirty patients (39.5%) had staged procedures (Staged group) with a stoma before the final ERP. The peri-operative complications were subdivided into major and minor complications. Minor perioperative complications in the primary group were less (13%) compared to the staged group (33%) with a p-value of 0.017, making the difference statistically significant. Anastomotic strictures were the most common complication in both groups with abdominal wound infection being more common in the staged group. The late complications were similar in both groups with a p-value of 0.43. Constipation was the most common complication in both groups, followed by soiling.

Conclusion: The two groups had a similar outcome without statistically significant differences. We can safely conclude that the primary endorectal pull-through for HD is at least as safe as the staged approach in Sub- Saharan Africa. With this technique, we avoid a stoma and the necessity for two surgical procedures with added potential complications.

INTRODUCTION

Hirschsprung's disease (HD) is a congenital condition characterized by the absence of ganglion cells in the submucosal (Meissner's) and myenteric plexus of the distal bowel. [1,2] It is more common in males (M:F=3.2:1) and is the most common cause of distal bowel obstruction in both neonates and older children.[1,3]

HD can be classified as short-segment (recto-sigmoid) and long-segment HD. Long segment HD can be further subdivided into long segment colonic aganglionosis, total colonic aganglionosis, and small bowel aganglionosis.[4] Various surgical methods have been described over the years for definitive surgery, with endorectal pull-through (ERP) being the latest addition. De la Torre-Mondragon and J.A. Ortega –Salgado first described this method in 1998, which has since become the most popular surgery for short segment Hirschsprung's disease worldwide.[1,5,6] ERP is a minimally invasive technique, executed meticulously with good results. Both single and multicentric studies have shown it to be safe, easy to master, without potential risks of complications related to the laparotomy and stoma.[7-9]

New studies are being published with favorable short and long-term outcomes in patients undergoing this procedure.[10-13] To the best of our knowledge, this is the first review assessing the short and long-term outcomes of primary endorectal pull-through in Sub-Saharan Africa. Primary ERP for short segment HD was introduced in our unit in 2007 and is currently the preferred elective procedure for short segment Hirschsprung's disease.

METHODS

A retrospective data review was done of all patients diagnosed with Hirschsprung's disease (HD) at Tygerberg Children's Hospital, a tertiary care hospital, during an 11-year period (2007 – 2018). The patients were divided into two groups: the primary Endorectal pull-through (Primary) group and the staged (Staged) group.

Patient's medical records, operation theatre notes, discharge summaries, and patient questionnaires (completed by part of the surgical team) were used in the data collection. The age of the patient at the time of diagnosis and surgery, gender, type of surgery, length of hospital stay, perioperative complications (including intraoperative to six months post-surgery), and late complications (from six months post definitive surgery) were included in the data collection.

Also, late outcomes and complications were assessed by completion of an age-appropriate questionnaire for caregivers of children older than two years.[14] The questionnaire is based on the Krickenbeck classification system, which is currently one of the most used systems to assess bowel function in HD patients.

Patients with histological confirmation of the disease, those that signed consent, and those that had their definitive ERP done in our unit were included in the study. The exclusion criteria were pre-operative mortality, the definitive surgery done in another unit, and repeated complex surgery. Ethical approval was obtained from the HREC (S20/06/149).

The diagnosis of HD was confirmed on histology with either a rectal suction biopsy or a full-thickness rectal biopsy. A contrast enema was performed in all patients, to assess the level/length of diseased bowel and to assist with surgical planning.

The primary group included patients who had an ERP as the first surgery without a stoma. Patients that had a laparoscopically assisted or laparotomy assisted pull-through, as first surgery, were also included.

All patients who had a stoma first and then an ERP later with/or without laparoscopy or laparotomy were included in the staged group. The decision to fashion a stoma for patients mostly depended on his/her response to rectal washouts as well as the preference of the surgeon in the most recent cases.

Data was tabulated on an excel spreadsheet for quantitative assessments. The P-value was calculated using the t-test for 2 independent means and a value of < 0.05 was considered statistically significant.

RESULTS

Eighty patients with histologically confirmed Hirschsprung's disease (HD) were treated in our institution during the study period (2007 – 2018). Four patients did not meet the inclusion criteria and were excluded. Of those four, one was operated in another center, one died before definitive surgery and two were complicated cases and were excluded due to the repeated histological diagnosis being inconclusive leading to multiple complex surgeries. Of the remaining 76 who were included, forty-six patients (60.5%) had a primary endorectal-pull through (Primary) and 30 patients (39.5%) had staged procedures (Staged) with a stoma before the final ERP.

Thirty-five out of the 46 patients included in the primary group were males. The median age at surgery (ERP) was 6 weeks (2-364 weeks) and the mean hospital stays post-operatively was 5.5 days. Nineteen of the 46 patients (41%) had their ERP during the neonatal period.

In comparison, the staged group had 22 males and 8 females (Table 1). The median age of definitive ERP in the staged group was 40 weeks (15 – 520 weeks) with 20 of these patients being operated on between 1 and 12 months of age and a mean hospital stay post-ERP of 5.3 days. Although the mean hospital stay post-ERP was slightly less in the staged group, the extra days post-stoma was not added and in total this number would have been much higher making the total hospital stay longer in the staged group.

Table 1: Comparison between the Primary and Staged Group

	Primary Group	Staged Group
Total number	46	30
Male: Female	35:11	22:8
Median age at surgery (weeks)	6	40
Mean hospital stay post definitive surgery	5.5 days	5.3 days
Type of HD if documented: • Short segment • Long segment • Not documented	 34 5 7	 21 9 0
Patients with a family history of HD	2	2

We had 5 premature babies who were diagnosed with HD during the neonatal period, the youngest at a gestational age of 32 weeks. An interesting finding was that 4 out of the 5 were female and 1 of them was also diagnosed with Trisomy 21. Three of these babies had their primary ERP done during the neonatal period. The other 2 had stomas done after

28 days of age and an ERP during infancy. No complications were encountered in this sub-group of patients.

The overall rate of perioperative complications in the primary group was lower (24%) compared to the staged group (40%). We included all intraoperative complications up to 6 months post-ERP in this group of complications and sub-divided them into minor complications (needed non-operative treatment) and major complications (needed major surgery). The primary group had 6 (13%) minor peri-complications compared to 10 (33%) in the staged group (Table 2). With a p-value of 0.017, this difference was statistically significant. Anastomotic strictures were the most common complication in the primary group, while anastomotic strictures and abdominal wound infection being the most common in the staged group. The patients with anastomotic strictures were started on to anal dilatations and all patients in the staged group responded, while 1 case in the primary group eventually required myomectomy.

Table 2: Minor Perioperative complications

Complication	Primary Group (*N*: 46)	Staged Group (*N*: 30)	p-value
Colorectal anastomotic breakdown:			
• Minor (treated with local procedures and antibiotics only)	2	2	
Abdominal wound infection (ERP and stoma closure done at the same time)	0	3	
Abdominal wound dehiscence	0	2	
Anastomotic stricture	4	3	
TOTAL	**6 (13%)**	**10 (33%)**	**P=0.017**

Table 3: Major Perioperative complications

Complication	Primary Group (*N*: 46)	Staged Group (*N*: 30)	p- value
Colorectal anastomotic breakdown:			
• Major (requiring relook laparotomy and stoma)	2	1	
Adhesive bowel obstruction	2	0	
Twisted distal bowel	1	0	
Ureteric injury	0	1	
TOTAL:	**5**	**2**	**P=0.27**

The major perioperative complications between the two groups (Table 3) were not statistically significant (p-value = 0.27). We had one case in the primary group where the distal bowel was twisted during the ERP. This patient developed bowel obstruction and required a relook laparotomy with a colostomy to relieve the obstruction. The Duhamel procedure was done for him at a later stage.

When we looked at the perioperative complications in the different age groups, we found that most of the major complications (80%) in the primary group occurred in infancy (Fig 1). In comparison most of the minor complications in the staged group presented in patients that had their ERP after 1 year of age while the major complications were the same for both the infant group and late presenters.

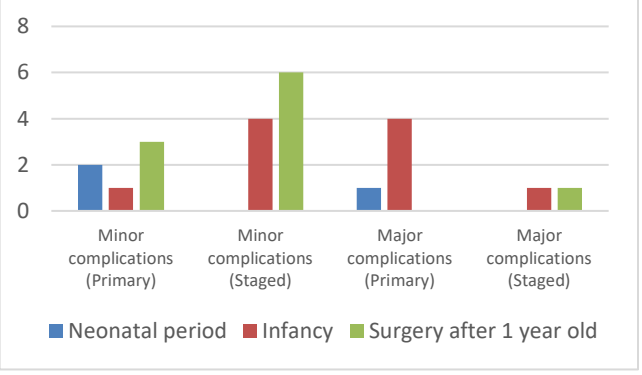

Fig 1: Age-group related perioperative complications

The age-appropriate follow-up questionnaires were completed by 22 caregivers of patients in the primary group (48%) and 15 (50%) in the staged group (Table 4). The average age of follow-up and completion of the questionnaire was 6 years for both groups. Only one child in the primary group complained about soiling (Gr 3 that was later treated with an ACE) and 10 children had constipation (8 were of Grade 2 and were treated with laxatives). In comparison, two patients in the staged group complained about soiling at the time of follow-up while 5 complained about constipation (managed with regular laxatives).

Table 4: Main results from the follow-up questionnaire

		Primary 22/46 (48%)	Staged 15/30 (50%)
1	Voluntary bowel movement	21	13
2	Soiling: Grade 1: Once or twice per week Grade 2: Everyday, no social problems Grade 3: Constant, social problems (e.g., Nappies)	1 0 0 1	2 0 1 1
3	Constipation: Grade 1: Diet changes only Grade 2: Regular laxatives Grade 3: Daily bowel washouts	10 1 8 1	5 0 4 1

The late complications were similar in both groups (Table 5). Constipation was the most common complication in both groups, followed by soiling. One patient in the primary group presented with severe

soiling and required an Antegrade Continence Enema (ACE) to keep him clean. Both the patients in the staged group responded to conservative management (laxatives and bowel washouts) and symptoms improved gradually over 2 years.

One patient from the staged group was diagnosed with a hyper-motile colon (diagnosed with manometry and exclusion of other causes) and was treated empirically with Loperamide and Clonidine. The patient responded to treatment and is doing well on follow-up.

Table 5: Late complications

Complications	Primary (*N*:46)	Staged (*N*:30)	p-value (Total only)
Constipation	10	5	
Soiling	1	2	
Anastomotic stricture	1	0	
Hyper-motile colon	0	1	
Perianal abscess and fistula	0	1	
Mortality	0	1	
TOTAL	**12 (26 %)**	**10 (33 %)**	**P = 0.43**

Hirschsprung's related enterocolitis (HREC) were encountered in both groups but were excluded from both peri-operative and late complications as we did not consider this a surgery-related complication, but rather a complication related to the nature of the disease.

We had three mortalities in the cohort. Two were in the staged group and one was in the primary group. Two deaths were not surgery-related (1 patient demised secondary to pneumonia and the second from pneumonia and missed enterocolitis). The only one surgery-related mortality was in the staged group where the patient died secondary to sepsis from an anastomotic breakdown post stoma closure.

One of the 46 patients in the primary group had a covering stoma due to difficult surgery and this was closed 3 months later without any complication. A further six patients required stomas after the definitive surgery, 2 from the staged group, and 4 from the primary group (already mentioned in the complications above). The reasons for stomas post-definitive surgery included a stricture in the transverse colon in a patient that was later diagnosed with skip lesions, 1 patient with a complicated peri-anal fistula not improving with conservative treatment, 2 patients with an anastomotic breakdown, 1 twisted pull-through, and 1 patient with repeated episodes of severe enterocolitis.

DISCUSSION

Bowel obstruction in infancy is often due to Hirschsprung's disease (HD).[15] Histology is the gold standard for diagnosis. A contrast enema, showing the level of the diseased bowel, is essential to assist the diagnosis and also for surgical planning.[15]

In 2007 we started with primary ERP as a surgical option for HD patients in our unit. Recently, there is a surge in publications about the outcome of primary ERPs from developing countries. Al-Baghaday et al from Egypt reviewed 84 patients and reported a zero-conversion rate, no intraoperative complications, and no significant early complications.[7] Ghorbanpour et al., from Iran, reviewed 55 patients and reported intestinal obstruction (25.5%) and constipation (27.3%) as the most common early and late complications, respectively.[16]

Anastomotic strictures account for the most common cause of mechanical obstruction after ERP.[17] The symptoms of obstruction may present as abdominal distension, bloating, borborygmi, vomiting, or severe constipation.[18] Anastomotic strictures are diagnosed on digital rectal examination. Pratap et al. claimed that a "flimsy synechiae" (early fibrosis) can be present as early as 7 days post-surgery. They recommend starting daily anal dilatation on day 7 post-operatively and continuing up to 3 months postoperatively to reduce the rate of anal stricture.[19] In comparison, Rouzrokh et al recommend starting anal dilatation after 2 weeks post-operatively. They claimed that starting earlier dilatation may cause damage to the anastomotic site.[20] In our unit, we bring the patients back for either an EUA in theater or a rectal examination in the clinic (depending on the age of the patient and the primary surgeon) two weeks post ERP. We only start dilatations if a stricture is present at that time.

El-sawaf et al. also compared primary ERP with a staged procedure. They found anastomotic strictures to be more common in the staged group (26.6 %) compared to the primary group (15.4%).[21] The reason for this may be that two surgical procedures increase the risk of compromised blood supply and subsequently leads to strictures at the anastomotic site.[11] One way to avoid this might be by using bipolar diathermy for the dissection instead of monopolar diathermy to decrease the chances of injury to the blood supply. In our cohort, 10% (3 cases) of patients in our staged group developed anastomotic strictures as a perioperative complication compared to 8.7% (4 cases) in the primary group. The difference between the two groups was statistically insignificant. Worth mentioning is that all the patients in our series who developed anastomotic strictures postoperatively were male.

This finding correlates with a recent study from Neuvonen et al. who describes being male as one of the indicators for a worse surgical outcome.[22]

Romero et al. in 2001 studied that partial anastomotic dehiscence (not complete dehiscence) post-ERP were more common in their staged group (n=29) compared to primary-ERP (n=24). They had 4 anastomotic leaks in their primary group (16.7%) and 5 in their staged group (17.2%). One patient from each group complicated with abscess formation at the site of the leakage (which required reoperation) and the rest healed uneventfully after re-suturing.[23] In another multicenter comparative study, Kim et al. reported an anastomotic leak rate of 1% in patients who underwent a staged approach.[24] In contrast, Teitelbaum et al. reported a higher rate of anastomotic leakage (it is not specified if it was partial or complete) in their staged group (9.7% compared to the 2.6% in their primary group).[11] The rate of colorectal anastomotic leaks in our cohort is higher in the staged group (10%) compared to the primary group (8.6%). We do accept that the statistical significance of this difference is limited may be due to the small sample size.

Stensrud et al. reported no adhesive intestinal obstruction in cases who underwent primary endorectal approach and 4% in those with laparotomy assisted approaches.[25] Torre-Mondragon et al. in 2000 reported only 1 case in their staged group (10%) that developed adhesive bowel obstruction and nil in patients who underwent endorectal or laparotomy assisted pull-through.[26] We had 2 cases of adhesive intestinal obstruction, both in the Primary group. The most common causes of obstructive symptoms after pull-through include mechanical obstruction, persistent or acquired aganglionosis, internal sphincter achalasia, motility disorders, and functional megacolon (stool-holding behavior).[7,17] The main aim of the workup for patients with postoperative obstruction is to exclude any mechanical causes.[17]

Pratap et al. reported a peri-anal abscess rate of 3.07% in their retrospective review. The reasons for peri-anal abscesses post-pull-through included damage to the mucosal tube, retraction of anastomosis, and/or poor blood supply due to massive dissection.[19]

The constipation rate after surgical repair of Hirschsprung's disease varies significantly in the literature, ranging from 0% - 25% in the primary group and 4.76% -27.6% in the staged group.[2,23,24,25,27] Bjornland et al. reported 25% constipation rate in their multicenter study.[28] This confirms that constipation is a common and long-standing complication even after a properly performed surgical procedure. The constipation rate in our cohort was 21.7 % in the primary group and 16.7% in the staged group.

Stool-holding behavior (functional megacolon) is responsible for up to half of constipation cases in normal children. It is suspected to be more common in Hirschsprung's patients because of their susceptibility to developing constipation.[7,17] It is a known fact that Hirschsprung disease patients do not have a normal recto-anal inhibitory reflex. For unknown reasons, some patients restore the reflex after surgical repair, but most patients wouldn't be able to restore this reflex.[29] Loss of this reflex contributes to persistent internal sphincter spasm (Achalasia).[30] This shows that the pathology in Hirschsprung disease is not localized to the aganglionic segment. Local applications of Nitroglycerin paste, injections of botulinum toxin, and internal sphincter myectomy have been suggested for the management of internal sphincter achalasia.[18] Motility disorder of proximal bowel may also play role in some patients presenting with constipation postoperatively. Abnormalities in the ganglion cells in the proximal bowel are responsible for hypoperistalsis. These abnormalities could be in the number of ganglion cells, the size, or the distribution thereof.[31] Meinds et al. emphasized another reason that could contribute to constipation after resection of the aganglionic segment which is a pelvic floor dyssynergia that leads to paradoxical external sphincter contractions.[32] Treatment of this condition includes a high fiber diet, hydration, toilet training, and pelvic floor muscles exercises.[30]

The literature review suggests the rate of soiling ranging from 4.8%-29.2% for primary ERP and 9.5%-41.4% the staged surgery.[2,33,34] In our cohort, 3 patients had soiling: 1 in the Primary group (2.17%) and 2 in the Staged Group (6.67%). A big concern in the literature seems to be the long-term effects of over-stretching of the sphincter mechanism while doing a primary ERP.[35] A multicenter Nordic study, looking at the long-term outcome of the endorectal pull-through, showed that it has a legitimate concern.[28] The soiling due to damage of the anal canal is a "preventable, irreparable, and irreversible complication".[36] To avoid such a devastating complication, Torre-Mondragon et al. recommended that one should protect the entire anal canal and start the incision 2 cm above the dentate zone to preserve the highly sensitive area, which is essential for fecal continence.[36] They further recommended dilating the anus before placement of the lone star retractor® with a Hagar dilator up to 2 numbers higher than the number that corresponds to the age of the patient, to relax the sphincter muscle.[36] Applying traction sutures on the proximal end of the mucosa further helps dissection without aggressive

retraction on the sphincter mechanism.[15] In a review of fecal incontinence after surgical repair of Hirschsprung's disease in 2017, Bischoff et al. concluded that a meticulous surgical technique may further avoid this complication.[37]

Soiling after surgical repair for HD can be categorized into the hyper-motile colon and hypo-motile colon. Radiology (plain abdominal X-rays and contrast enema) can help to differentiate between these two conditions. The hypo-motile colon has fecal loading (X-ray) and increased diameter of the colon, while no fecal loading and a normal or decreased diameter of the colon will be seen in the hyper-motile colon. In the hyper-motile group, multiple factors play a role in its pathophysiology which includes persistent or non-coordinated contractions.[38,39] Furthermore, these patients have a loss of their sigmoid colon which has 2 roles in the continence, the first being a reservoir for stool and the second that it does not respond to high amplitude propagated contractions (HAPCs) which have an essential role to move the stool from the right side to the left side of the colon. Resection of the sigmoid colon results in the loss of these protective mechanisms. The dissection during surgery may also affect the anorectal angle of the puborectalis muscle which helps in the continence leading to postoperative soiling.[40]

In our cohort, 1 patient was diagnosed with a hyper-motile colon postoperatively. Abdominal X-ray did not show fecal loading, and contrast enema showed a normal caliber colon and the examination under general anesthesia was normal. This patient was treated empirically with Loperamide and Clonidine and responded well.

In our experience, patients presenting in the neonatal period respond well to rectal washouts and are more suitable for a primary-ERP. It correlates with the finding of Lu et al.[41] In addition, the safety of a primary pull-through in the neonatal period has been well documented in the literature.[11,42] Rectal washouts alone for decompression of the bowel seems less successful in late presenters, as documented by Ekenze et al. from Nigeria who showed a failure rate (of rectal washouts to adequately decompress the bowel) of more than 80% in their patients older 1 year and eventually needing a colostomy for effective decompression.[43] It correlates with Stensrud et al. and our experience.[44]

Small sample size and inherent bias in a retrospective study cannot be eliminated. We also acknowledge that we have a small sample size. Bigger, multi-centric studies are proposed to eliminate bias and explore the ideal age for primary vs staged procedures. It is important to highlight that 33.3% of the staged group had stoma-related complications including prolapse and a leaking Hartman's pouch which required another laparotomy. This should be taken into consideration when looking at the overall results.

CONCLUSION

The two groups had a similar outcome without significant statistical differences. We can safely conclude that the primary endorectal pull-through for HD is at least as safe as the staged approach in Sub-Saharan Africa. We recommend a primary endorectal pull-through for HD in the neonatal period, as they respond better to rectal washouts. A primary ERP avoids stomas and their added (often-severe) complications, as well as the additional burden of two surgical procedures. A careful patient selection should be done for ERP. In our experience, infants (patients between 1-12 months of age) should undergo a staged approach, as primary ERP in them has higher complication rates.

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