Evaluation of Trans Anal Endorectal Pull-Through Outcomes in Hirschsprung Disease in Different Age and Gender Groups: A Comprehensive Systematic Review

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Research Article

Keywords: Systematic review, Hirschsprung's disease, trans-anal pull through, infant, neonate

Posted Date: July 11th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-3142661/v1

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Abstract

Introduction;

The timing of endorectal pull-through for Hirschsprung’s disease (HD) is controversial. Early endorectal pull-through avoids the occurrence of preoperative enterocolitis. However, delayed pull-through (≥31 days) enables postnatal maturation of the anal canal and sphincter complex. The aim of this study was to identify the best age to perform trans-anal pull-through according to the literature.

Methods and Materials:

This was a comprehensive systematic review. All published articles from 2010 to 2022 were searched through Web of Science, Ovid Medline, PubMed, CINAHL, and Embase databases, using the keywords Hirschsprung's disease, delayed or early treatment, trans-anal Pull-Through surgery, age, sex or gender, complications and outcomes. Articles that met the inclusion criteria along with good to fair quality according to the Newcastle-Ottawa quality assessment and low bias score in the Cochran collaboration tool were reviewed.

Results;

Sixteen studies were eligible to be reviewed. The overall results of this study showed that due to more common short-term complications at neonatal period and lower contrast enema diagnostic accuracy in determining the transition zone, postponing surgery until the child is several months old seems to be a reasonable decision. There was also no difference in terms of complications and outcomes of trans-anal Pull-Through surgery between females and males.

Conclusion;

it is not recommended to delay surgery too much for ages over 1 year. Ages between 3 and 12 months can be a good time to take interventional treatment for Hirschsprung's disease.

Introduction

Hirschsprung's disease is a pretty common surgical disease in children studied by pediatric surgeons and researchers. The prevalence of Hirschsprung is 1 per 5000 live births and the probability of transmission to the next generation is about 3% [1, 2]. This congenital disease is caused by a developmental disorder of the intestinal nervous system and is characterized by the absence of ganglion cells in the submucosal layer (Meissner) and the myenteric network of the distal colon. The ganglion-free segment in the intestine lacks normal movement, so the proximal intestine dilates, leading to functional bowel obstruction, putting these patients at high risk for enterocolitis [3].

Most cases of Hirschsprung's disease are now diagnosed in infancy. Hirschsprung's disease should be considered in neonates who do not have meconium excretion within 48 hours of birth or have vomiting and abdominal distention. Nonetheless, full-thickness biopsy of the rectal wall has been suggested as the most reliable test to endorse the diagnosis [4]. The normal relaxation of the internal sphincter in response to rectal dilation is also impaired, which forms the basis of manometric diagnostic modality [5].

Patients who have a confirmed diagnosis of Hirschsprung's disease undergo corrective surgery. In 1948, Swenson and Bill performed the first corrective surgery to remove the aganglionic segment of the colon followed by coloanal anastomosis [6, 7]. Traditionally, treatment involves a diverting colostomy at the time of diagnosis, and then, when the child grows older and weighs more than 10 kg, a definitive repair is considered. In 1998, De la Torre-Mondragón et al. developed a single stage transanal pull-through for Hirschsprung's disease [8].
In patients who respond to enema and rectal lavage, Botox can be used temporarily until the final pull-through operation is performed [9]. In the recent years, pull-through from the anal canal (TAEPT) has received much attention. In this method, laparotomy is not always required and the rectum is usually removed by maintaining the surrounding muscle cuff, leading to less damage to adjacent tissues and nerves [10, 11].

The advantages of TAEPT include easy technique, no need for colostomy, low bleeding rate and short hospital stay compared to other modalities. Despite the fact, there is no definite recommendation for the best age to perform the operation. Therefore in this study, we tried to investigate the best age group who are suitable to undergo corrective surgery with least complications and best outcomes. Besides, the operation outcomes in males and females were compared.

**Methods and Materials**

This was a comprehensive systematic review. The present study included all studies regarding transanal pull-through in patients with Hirschsprung’s disease. All studies evaluating this method in children with different age groups from 2010 to 2022 were included. Non-English articles were excluded. Case report, case series and expert opinions were also excluded. If necessary, the authors were contacted to provide more information. Besides, studies that did not report information regarding response to transanal pull-through surgery and its complications in Hirschsprung patients or did not have sufficient data were ignored. Five main databases were searched, including Web of Science, Ovid Medline, PubMed, CINAHIL, and Embase. Google Scholar database was searched finally to ensure that the systematic search was complete. Abstracts published in conferences or dissertations on transanal pull-through in patients with Hirschsprung’s were also considered as much as possible. Those studies that included patients with concurrent congenital abnormalities were excluded.

Main keywords included Hirschsprung’s, Hirschsprung’s disease, Congenital megacolon, Transanal, Pull-through, Aganglion, Aganglionosis, Aganglionic segment, Aganglionic bowel, Rectosigmoid colon, Anorectal stenosis, Enterocolitis, Soiling, Fecal continency, Bowel continency, Fecal soiling, Pediatric, newborn, child, Infant, Infancy, Neonate and Bowel obstruction.

**Bias assessment tool**

The bias of included studies was checked by two independent authors. In case of disagreement between the two authors, a consensus was reached through discussion and exchange of views or by requesting a third opinion. The Joanna Briggs Institute Critical Appraisal tool [12] was used to assess the eligibility of studies. The Joanna Briggs Institute Critical Appraisal tool consists of 10 questions in three main sections of design, conduct and analysis. Each question scores yes, no, unclear or not applicable. For instance, question No. 1 is “Was the sample representative of the target population?”[12].

Data were extracted according to a standard protocol. The extracted information included study design, year of publication, authors’ name, sample size, surgical complications including enterocolitis, anastomotic stenosis, fecal continence and constipation, age and sex.

**Results**

Initially, 149 studies were found. After the primary review, duplicate studies (21 records) were excluded. After evaluating these 128 studies by their titles and abstracts, 61 articles were considered for full-text evaluation. Of these 61 studies, 45 studies were omitted for various reasons depicted in Fig. 1, and 16 studies remained for the final analysis. The study flowchart is depicted in Fig. 1. Our results were classified into two main categories including the results of transanal pull-through surgery based on age and gender.

**A) Age**
In a large retrospective cohort study by Lu et al. In both neonatal and non-neonatal groups (650 patients), it was found that a single-stage transanal pull-through in non-neonatal period may be more appropriate than in the neonatal period. There was a higher rate of perianal excoriation, anastomotic stenosis and leakage, postoperative enterocolitis, and postoperative incontinence in neonates than non-neonates [13]. Furthermore, in another study by the same author, Lu et al. recommended to perform home rectal irrigation, followed by a delayed and planned surgery, as intervention at neonatal period lacks enough diagnostic accuracy and higher rate of post-op enterocolitis [14]. Moreover, Zhu et al. in a retrospective cohort study in 2019 stated that children with Hirschsprung's below 3 months had lower rates of accurate diagnostic results and poorer postoperative outcomes. They suggested that it may be more appropriate to wait until the child is above three months to perform surgery [15].

A study by Freedman-Weiss et al. on 282 patients found that for appropriately selected patients with Hirschsprung disease, delaying pull-through until the second month of life is associated with lower total and postoperative stays without increased readmissions or complications [16]. However, in another study by Beltman, L., et al, multivariate analysis showed that older age at surgery (median 105 days) increases the risk of developing postoperative complications (OR = 1.00, 95% CI = 1.00-1.01, p = 0.041) [17].

On the other hand, Zakaria's study compared two groups of patients regarding outcome and complications. The mean age in groups A and B were 14.02 ± 10.3 and 69.9 32 months, respectively. They suggested that it may be better to perform surgery at a younger age and delaying surgery is associated with comorbidities. Most children at younger age showed no abnormal defecation problems, and had excellent fecal continence score rate (FCSR) [18]. Besides, in another study by the same author, fecal incontinence was less occurred when the operation was performed between 6 months to 2 year [19]. Moreover, in Khalil's study, higher ages at surgery significantly affected physical function (β = -0.686, p = 0.001) and reduced school performance (β = -0.2279, p = 0.027). They indicated that age at surgery (patients age was 7–19 month) had a significant negative correlation with quality of life, as children who underwent surgery at a younger age had a better quality of life [20].

In another study by Kumar et al., the implications of the single-stage transanal endorectal pull-through was assessed retrospectively. Perianal excoriation was reported in 60% of patients, more commonly in neonates. Besides, stool frequency was reported to be more than 5 to 7 per day in all neonates early after the procedure. Moreover, blood transfusion was higher in children above one year. They concluded that delaying surgery is not logical and neonates and infants might benefit most than other age groups [21]. Besides, Kastenberg et al., compared delayed primary endorectal pull-through (≥ 31 days) [The median age at operation 98 days (IQR 61–188 days)] with neonates. They assess 82 patients, 49 neonates and 33 non-neonates. Fifteen of neonates compared to five non-neonates developed fecal incontinence (P value = 0.13). Besides, enterocolitis and other complications were not different between the two groups [22].

Anyways, in a retrospective study by Dahal et al. on 113 children, younger age at surgery (less than 3 years) was associated with lower bowel frequency (less than 3 times a day) (p < 0.05). There was a significantly higher frequency of stool in patients aged more than 36 months and those with a resected colon more than 30 cm [23].

On the other hand, Miyano study showed that age at surgery was not correlated with postoperative bowel function in Hirschsprung's disease [24]. They reported that only the operation duration was significantly more in patients older than 4 years, and other outcomes did not differ significantly. Furthermore, in a study by Hoff et al., there was no risk factor for short-term complication using the Clavien-Dindo-grading system, including age at surgery [median age 62days] (OR = 2.97, 95% CI = 9.93 – 0.92) [25].

Nonetheless, in Byström et al. study, children who underwent TERPT (Transanal endorectal pull-through) for Hirschsprung had significantly impaired bowel function score compared with healthy controls in several aspects. There were no differences between age groups in this study [median age at TERPT was 57 days(12 – 3,355)], indicating impaired bowel function childhood after TERPT [26].
On the other hand, in a multicenter study in Scandinavia to evaluate the predictors of functional outcomes, age at surgery did not have a significant effect on poor outcomes using a multivariate model [27]. This study was a retrospective investigation mainly to identify long-term complications of children with HDs after operation. In addition, in a very recent study by Yanan Zhang et al., 229 neonates who underwent TEPT were reviewed. They reported that operation in the neonatal period was quite safe with few complications (age of 6–28 days) [28]. In 62 patients, there was no radiological transition zone (27.1%). Early post-op (wound infection, dehiscence, sepsis, etc.) complications occurred in 26 (11.4%) patients. Enterocolitis was noted in 16 (7%). The follow-up period ranged from 1.2 years to 14 years. Delayed complications (stricture, fistula, prolapse) were reported in 6 patients. Soiling was remained in 22 (20.8%) patients.

**B) Gender**

Dahal et al. reported the same incidence of postoperative complications in both males and females. There were no statistically significant differences in terms of stool frequency less than 3 times a day (male/female; 70%/100%, p = 0.09), soiling (male/female; 7%/12.5%, p = 0.4) and constipation (male/female; 3%/0%) [23]. In another study, the prevalence of social problems after surgery was not affected by gender (p < 0.05) [29]. In addition, Dehghan et al. compared the two methods of trans-abdominal or transanal pull through in children with Hirschsprung, and reported no significant differences regarding complications in males and females [30]. In another study, sphincter function was not related to patients’ gender [31].

In two different studies, there were no significant differences in terms of Clavien-Dindo-grading, anastomotic stenosis, postoperative enterocolitis, bleeding and wound infection, length of hospital stay after surgery, readmission within 30 days after surgery, and the need for reoperation between males and females during the first 30 days after surgery [25, 26].

In the study of Byström et al. [26], the comparison of bowel function score between males and females with Hirschsprung disease showed no significant difference. In another study [17], in univariate analysis, gender was not reported as a risk factor for postoperative complications (OR = 1.27, 95% CI = 0.38–4.23, p = 0.698). In Gunadi et al.’s study [32], no association between gender and voluntary bowel movement (VBM) was observed in Hirschsprung patients after TEPT. A summary of main studies used in this systematic review and their outcomes is depicted in Table 1.
<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Publish year</th>
<th>Subjects</th>
<th>Male</th>
<th>Female</th>
<th>Study design</th>
<th>Quality</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lu et. al.</td>
<td>2017</td>
<td>650 children in two groups of neonates and non-neonates</td>
<td>497</td>
<td>153</td>
<td>Retrospective cohort</td>
<td>Good</td>
<td>TAEPT in the non-neonatal period may be more appropriate than in the neonatal period, especially regarding post-op complications</td>
</tr>
<tr>
<td>Zhu et. al.</td>
<td>2019</td>
<td>62 infants ≥ 3 months and 136 infants aged 3–12 months</td>
<td>158</td>
<td>40</td>
<td>Retrospective cohort</td>
<td>Good</td>
<td>Infants with ≤ 3 months old Hirschsprung disease showed lower rates of accurate and conclusive diagnostic results and more postoperative complications.</td>
</tr>
<tr>
<td>Freedman-Weiss et. al.</td>
<td>2019</td>
<td>282 patients in two groups of &lt; 31 days and 31–120 days old</td>
<td>231</td>
<td>51</td>
<td>Retrospective cohort</td>
<td>Good</td>
<td>Delaying pull-through until the second month of life is associated with lower total and postoperative stays without increased readmissions or complications.</td>
</tr>
<tr>
<td>Beltman et. al.</td>
<td>2021</td>
<td>106 patients underwent TERPT (Median age at time of surgery: 105 days)</td>
<td>80</td>
<td>26</td>
<td>Retrospective</td>
<td>Good</td>
<td>Older age at time of surgery was a risk factor for postoperative complications.</td>
</tr>
<tr>
<td>Zakaria</td>
<td>2012</td>
<td>40 patients in two age groups (6–42 months and 3.5–13 years old)</td>
<td>28</td>
<td>12</td>
<td>Comparative retrospective cohort</td>
<td>Good</td>
<td>Group A had fewer defecation problems, and had excellent fecal continence score.</td>
</tr>
<tr>
<td>Zakaria et. al.</td>
<td>2012</td>
<td>50 patients in two age groups</td>
<td>27</td>
<td>23</td>
<td>Retrospective cohort</td>
<td>Good</td>
<td>The earlier the surgery of HD, the lower the incidence of fecal incontinence (6-month – 2-year better results than &gt; 2-year)</td>
</tr>
<tr>
<td>Author(s)</td>
<td>Publish year</td>
<td>Subjects</td>
<td>Male</td>
<td>Female</td>
<td>Study design</td>
<td>Quality</td>
<td>Outcome</td>
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<tr>
<td>Khalil et. al.</td>
<td>2015</td>
<td>70 patients underwent Transanal Pull-Through</td>
<td>37</td>
<td>16</td>
<td>Retrospective</td>
<td>Fair</td>
<td>Surgery at a younger age 7 month (patients age 7-19 month) is associated with a better quality of life</td>
</tr>
<tr>
<td>Kumar et. al.</td>
<td>2019</td>
<td>30 patients including 10 neonates, 13 infants and 7 children</td>
<td>26</td>
<td>4</td>
<td>Retrospective/Prospective cohort</td>
<td>Good</td>
<td>Excoriation was more in neonates, but overall outcomes better in neonates</td>
</tr>
<tr>
<td>Kastenberg et. al.</td>
<td>2021</td>
<td>82 Hirschsprung patients underwent endorectal pull-through</td>
<td>68</td>
<td>14</td>
<td>Retrospective</td>
<td>Good</td>
<td>fecal incontinence more seen in neonates ((P \text{ value} = 0.13)), but overall equivalent outcomes</td>
</tr>
<tr>
<td>Dahal et al.</td>
<td>2011</td>
<td>131 children with HD aged 7 days to 14 years</td>
<td>112</td>
<td>19</td>
<td>Retrospective</td>
<td>Good</td>
<td>younger age at surgery (less than 3 years) was associated with lower bowel frequency (less than 3 times a day)</td>
</tr>
<tr>
<td>Miyano et. al.</td>
<td>2017</td>
<td>106 patients underwent laparoscopic pull-through in 4 age groups (&lt;3 months, 3–11 months, 1–3 years and &gt;3 years)</td>
<td>68</td>
<td>38</td>
<td>Prospective cohort</td>
<td>Good</td>
<td>Age at surgery was not correlated with postoperative bowel function in Hirschsprung’s disease</td>
</tr>
<tr>
<td>Hoff et. al.</td>
<td>2019</td>
<td>69 children underwent TERPT</td>
<td>51</td>
<td>18</td>
<td>Cohort</td>
<td>Fair</td>
<td>There is no risk factor for short-term Clavien-Dindo complication, including age at surgery[median age 62 days]</td>
</tr>
<tr>
<td>Byström et. al.</td>
<td>2020</td>
<td>30 Hirschsprung patients treated with TERPT and 30 healthy controls matched for age and gender</td>
<td>22</td>
<td>8</td>
<td>Cross-sectional case–control study</td>
<td>Good</td>
<td>Post-operative BFS (bowel function score) did not show a significant difference in Hirschsprung patients between age groups. [median age at TERPT was 57 days(12 – 3,355)]</td>
</tr>
</tbody>
</table>
Discussion

Consequences of transanal pull-through surgery for Hirschsprung's disease are not always as favorable as the surgeon imagines. Incomplete continence, constipation and postoperative enterocolitis should not be ignored [33–36]. Previous studies have attempted to investigate the relationship between preoperative characteristics and surgical outcomes in patients with Hirschsprung's such as age, gender, length of aganglionosis, age at surgery, preoperative enterocolitis, comorbidities, and genetic background [37–40]. Despite the fact, there is always a challenge for the best age of operation. Therefore, here we mainly tried to categorize studies that prefer the neonatal period as the best age against those who believe to postpone it. We mostly focused on 16 studies according to our inclusion and exclusion criteria. in summary 11 investigations were in favor of postponing the operation above one month, 2 studies found no difference and 3 reported better outcomes in the neonatal period.

One important issue here is the accuracy of diagnostic modalities to detect patients. A recent study by Chen et al. showed a 88.5% correlation between radiological and pathological TZ in rectosigmoid Hirschsprung. This was depended on the patient's age. They showed 69% correlation for children below 3 months versus 85.3% (strong severity) for older ones [41]. Overall, different studies mentioned above indicated that longer periods of disease may lead to better development of radiological TZ. Therefore, determining the transition zone with a high accuracy is necessary. Most children with Hirschsprung's disease present during the neonatal period with delayed passage of meconium beyond the first 24 hours, abdominal distention, bilious vomiting and feeding intolerance and are diagnosed by a rectal biopsy in the first month of life. However, a definite diagnosis before surgery is mandatory.

The extent of colon caliber changes depend on the duration of distal bowel obstruction, which is limited in newborns. Therefore, contrast enema is not appropriate in newborns. This is the reason why some surgeons prefer to wait for 1–2 months. A colon enema performed before the age of 30 days had a sevenfold higher probability of false-negative results [42].

Despite the fact, the main risk of postponing surgery is the possibility of enterocolitis during the waiting period. This risk can be lessened by ensuring rectal pressure relief with adequate irrigation (usually 10–20 ml/kg, several times daily), administration of prophylactic metronidazole or probiotics. Due to the risk of enterocolitis, many pediatric surgeons believe
that once a diagnosis is made, even in small infants, a laparoscopic or transanal operation can be performed successfully and safely [43]. A survey by the European Society of Pediatric Surgeons found that 33% of pediatric surgeons prefer to perform endorectal pull-through surgery at diagnosis and 67% prefer a delayed approach (4 months or > 5 kg) [44].

In addition, anorectal manometry is an effective and safe method that complements the diagnosis of HD in newborns. Anorectal sphincter pressure progressively matures with incremental increase during the first months of life [45–47].

Kaiser Decker et al. reported that the sensitivity of a rectal suction biopsy (RSB) was 81% and its specificity 97%. Therefore, a repeated sampling may be necessary. They found that RSB can also be reliable and safely performed in preterm born infants [48]. However, repeated biopsies in neonates may lead to intestinal perforation. In the study of Putnam, L.R., et al, in clinically suspicious neonates for HD, contrast enema studies showed inconclusive results in 32% of cases [49].

Kumar et al., concluded that delaying surgery is not logical and neonates and infants might benefit most than other age groups. As their study design was retrospective with few number of patients in each sub group, they could not provide a detailed comparison between neonates and those between 1–12 months. However, the risk of reported complications was more in neonates [21].

Besides, Kastenberg et al., compared delayed primary endorectal pull-through (≥ 31 days) [The median age at operation 98 days (IQR 61–188 days)] with neonates. They assess 82 patients, 49 neonates and 33 non-neonates. Fifteen of neonates compared to five non-neonates developed fecal incontinence (P value = 0.13). Besides, enterocolitis and other complications were not different between the two groups. As fecal incontinence was more reported in neonates, but without a statistically significant difference, the authors tend to conclude that operation in neonates is as safe as those above one month, which is not logical in our opinion. This study had good mythological design but with a small sample size. Therefore, we might not rely completely on this analysis to advocate surgery in neonates [22].

In another investigation, Remi Andre Karlsen compared the outcomes of laparoscopic and trans-anal pull-through and reported poorer outcomes in the neonatal period. This study did not fulfill our inclusion and exclusion criteria but higher complications were reported in neonates [50].

In another study by Ivana et al. [32], no association was found between age at surgery and functional outcomes in Hirschsprung patients. In our idea this study lacks a large sample size. Also they categorized their patients into two groups of below 4 years and above it, which ignores any classification regarding neonates, therefore, the results might not be very helpful in our data interpretation. Despite the fact, soiling was more reported in patients older than 4 years which is consistent with some other reports. Accordingly, delaying surgery above 2–4 years is completely erroneous.

On the other hand, Miyano study showed that age at surgery was not correlated with postoperative bowel function in Hirschsprung’s disease. However, they emphasized to validate and highlight their modified laparoscopic technique for HD and their main goal was no comparison between neonates and non-neonates regarding outcomes [24].

In addition, Hoff et al., reported no risk factor for short-term complication using the Clavien-Dindo-grading system, including age at surgery [25]. They only evaluated outcomes during the first months after surgery, as early post-operation complications, and long-term outcomes were not assessed.

On the other hand, in a multicenter study in Scandinavia to evaluate the predictors of functional outcomes, age at surgery did not have a significant effect on poor outcomes using a multivariate model [27]. This study was a retrospective investigation mainly to identify long-term complications of children with HDs after operation. Age classification in this study is only given in a table categorized as 0.4 to 1, 1-2.9, 3-7.5 and 7.9–133 months. No detailed information regarding the number of patients in each quartile was found. Despite the fact, their main goal was to assess long-term bowel function and not to compare complications at different age groups. Therefore, we cannot conclude that the results are against our recommendation.
The most reliable study against postponing the operation to above one month was belonged to Yanan Zhang et al. on 229 neonates [28]. They reported that operation in the neonatal period was quite safe with few complications (age of 6–28 days). This is approximately the only well-organized study to defend the operation in neonatal period with a quite large sample size. We admire the authors to have such a settings. Despite the fact, We believe that these outcomes are due to high expertise of staff in this center as they could record 229 patients in 13 years. As most studies reported smaller number of patients, we think delaying the operation to above one month is logical in smaller centers. However, in very few tertiary centers with highly organized settings and experienced pediatric surgeons, we might recommend surgery in neonates.

In terms of postoperative complications, infants who undergo transanal pull-through surgery are exposed to undesirable short-term consequences. Huang et al. [51] reported that neonates have a longer recovery period after surgery than non-neonates. Furthermore, active immunodeficiency and inactive immunity of maternal antibodies result in low resistance to infection in neonates. In a retrospective study evaluating the results of a single-stage transanal pull-through on 650 children, the authors concluded that the operation might be more appropriate in non-neonatal period than the neonatal period. Because there was a higher rate of perianal excoriation, anastomotic stenosis and leakage, postoperative enterocolitis and incomplete postoperative continence in neonates than non-neonates [13]. In addition, Stensrud [31] compared two groups of patients who underwent trans-anal and trans-abdominal surgery regarding anal sphincter damage using ultrasonography. They showed that children who underwent trans-anal pull-through had higher rates of injury. The median age of patients in trans-anal and trans-abdominal surgery were 1.8 (0.4–133) and 13 (1.2–100) months. We might conclude that operation at lower ages and using trans-anal approach would increase the likelihood of sphincter injury.

A meta-analysis by Maggie et al. [52] published in 2021 included 4 studies in addition to their own center data to assess the best time to perform the operation for children with Hirschsprung disease. They included Miyano et al., Zhu et al, Lu et al and Chung et al. investigations in their pool analysis. The first three were discussed above, but the Chung et al. [53] study could not be entered because they did not include a clear age classification to separate neonates versus non-neonates. However, as they provided their data sheet, Maggie could include it. Overall, Maggie et al. claimed that children below 2.5 months old at surgery would have poorer outcomes, which is somehow in line with the results of our systematic review.

This study had some limitations. As all systematic reviews, we had to rely on other studies information. A recall bias is inevitable when compiling information from other investigations. Some studies did not include necessary information needed for our review. Therefore, some high-quality studies might have been excluded due to a high bias score using the checklist. Besides, some studies included patients with concurrent syndromes which were not assessed in our review. We do not know whether Down syndrome might affect the decision for age selection. It is suggested to perform large multicentric studies to collect data on different ethnicities.

Conclusion

Despite the recommendation of most studies to treat Hirschsprung's disease as early as possible, due to more common short-term complications and lower contrast enema diagnostic accuracy in neonates, postponing surgery until the child is several months old seems a reasonable decision. However, it is not recommended to delay surgery over 1 year. Overall view on most reviewed articles indicate that ages between 3 and 12 months can be a good time to take interventional treatment for Hirschspring's disease. However, we cannot complain performing surgery in high-volume advanced tertiary centers in the neonatal period.

Declarations

Acknowledgement

None
Financial support

This was part of a thesis to obtain specialty degree in general surgery by one of the authors and supported by Iran University of Medical Sciences (IUMS).

Disclosure

None

Authors' contribution

All authors helped in writing the manuscript according to the ICMJE criteria for authorship.

References


**Figures**
Figure 1

The Study Flow Chart

149 records found

21 removed due to duplications

128 records remained after duplication removal

67 studies were excluded due to irrelevancy based on two authors' opinions

61 manuscripts considered for full-text assessment

45 studies excluded; 13 case series or case report
5 review article
14 not available full-text
9 non-English full-text
4 studies with syndromic patients

16 studies remained