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Chinese expert consensus statement on the diagnosis and treatment of Hirschsprung disease

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Hirschsprung disease (HSCR) is a congenital anomaly of the intestine caused by the developmental absence of the enteric nervous system, which results in variable lengths of intestinal dysfunction and requires surgical intervention.[1] Due to the complex etiology, multiple surgical procedures and postoperative complications, the diagnosis and treatment strategies of HSCR have always been the focus of pediatric surgeons around the world. Seventy pediatric surgical experts with rich clinical experience from almost all national and provincial children's medical centers in China constituted the Chinese Research Group of Hirschsprung disease (CRGHSCR). All members discussed and compiled the disagreements concerning the diagnosis, treatment [Supplementary File, http://links.lww.com/CM9/B890], and perioperative management of HSCR based on existing evidence from previous articles, in combination with the latest high-quality evidence. The current consensus statement is aimed at standardizing the diagnostic and surgical strategies, and emphasizing postoperative rehabilitation training, to systematically improve postoperative recovery and to improve the quality of life in long-term follow-up.

The consensus was reached through a total of three rounds of discussions between February 2019 and June 2022. A modified Delphi method was used for as many reiterative rounds as necessary. The quality of evidence and recommendations were evaluated according to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system.

Diagnosis of HSCR

Meconium is delayed 24 h after birth in approximately 90% of HSCR patients.[1] The symptoms of premature infants with HSCR are similar to those of full-term infants.

Recommendation 1: HSCR should be considered for all neonates who fail to pass meconium within 24 h after birth. (Grade 1A)

Digital rectal examination (DRE) is an important method for screening HSCR. It is also a simple method for the differential diagnosis of anorectal malformations.

Recommendation 2: DRE can exclude anorectal malformations and screen for HSCR. (Grade 1B)

In contrast enema (CE) test, the most intuitive manifestation of HSCR is the transition zone (TZ) between the narrow distal segment without ganglion cells and dilated proximal colon with normal ganglion cells. In a systematic review, CE had a mean sensitivity of 70% (95% confidence interval [CI]: 64–76%) and a mean specificity of 83% (95% CI: 74–90%) for the diagnosis of HSCR.[2]

Recommendation 3: Preoperative CE can detect the TZ and provide information, which can be beneficial to determine the lesion range in HSCR. (Grade 1A)

Anorectal manometry (ARM) is used to evaluate the voluntary and involuntary properties of the anorectum. One of the most important manometry assessment indicators for anorectal function is the recto-anal inhibitory reflex (RAIR). In a systematic review, the mean sensitivity and mean specificity of ARM were 91% (95% CI: 85–95%) and 94% (95% CI: 89–97%), respectively.[2] However, in a subgroup analysis of the diagnostic accuracy of ARM in infants younger than 6 months, ARM had a lower sensitivity of 88% and specificity of 89%.[3]

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Recommendation 4: ARM can be a routine method for the preoperative diagnosis of HSCR. (Grade 1A)

The preoperative diagnosis of HSCR mainly depends on the histopathological analysis of rectal biopsies, including rectal suction biopsy (RSB) and full-thickness rectal biopsy (FTRB). A systematic review demonstrated that the mean sensitivity of RSB was 96.84% (95% CI: 95.57–97.47%), and the mean specificity was 99.42% (95% CI: 99.17–99.57%), but 8.46% (95% CI: 7.55–9.46%) repeated RSB was required due to insufficient specimens. Systematic review showed that the conclusive rates of RSB and FTRB did not significantly differ.[4]

Commonly used histological staining methods include hematoxylin and eosin (HE), enzyme histochemical staining for acetylcholinesterase (AChE), and immunohistochemical staining for calretinin. In a systematic review and meta-analysis, HE staining alone and AChE alone obtained pooled proportions of 89% (95% CI: 83–93%) and 95% (95% CI: 90–99%) conclusive results, respectively. In addition, 89% (95% CI: 81–95%) in the HE + AChE group and 94% (95% CI: 89–98%) in the HE with calretinin with or without AChE group were found.[4]

Recommendation 5: RSB or FTRB should be used as the gold standard for the preoperative diagnosis of HSCR, but consensus on the preferred histological staining method is lacking. (Grade 1A)

Intraoperative frozen sections are commonly used to identify ganglion cells at the resection margin of the bowel. Generally, the most commonly cited features of TZ are partial circumferential aganglionosis (absent myenteric and/or submucosal ganglion cells in a contiguous eighth of the circumference), myenteric hypoganglionosis (as defined above of ≥1/8 circumference), and submucosal nerve hypertrophy (e.g., >2 submucosal nerves with >40 μm-thickness in one high-power field).[5]

Recommendation 6: Intraoperative frozen sections could be used to guide the length of bowel resection. (Grade 1D)

At present, establishing ideal guidelines for diagnosing neonatal HSCR remains challenging. Although a recent study showed that the sensitivity and specificity of CE examination exceeded 80% and 90% for neonatal HSCR, respectively, it is less reliable in the neonatal period than in older children.[6] Furthermore, the accuracy of CE in neonatal total colonic aganglionosis (TCA) is only approximately 25%.[7]

Typically, ARM is still used as a screening tool for HSCR, although the accuracy of ARM in the diagnosis of HSCR in neonates varies among the literatures.[3]

As for rectal biopsies, infants ≤3 months of age (43.5%) had a significantly higher risk of inconclusive results than infants >3 months of age (25.7%).[8]

Recommendation 7: Neonates with clinical symptoms of suspected HSCR can be screened using CE and ARM, and histopathological evaluation, such as RSB or FTRB, is the most important examination for diagnosing neonatal HSCR. (Grade 2C)

Preoperatively radiological patterns of TCA in CE examination include microcolon, a question mark-shaped colon, or a lack of distinct features in an otherwise normal colon. In clinical practice, multisite biopsies on the terminal ileum and whole colon during primary exploratory laparotomy are recommended to confirm the diagnosis if TCA is suspected.

Recommendation 8: If TCA is suspected, a multisite biopsy involving the terminal ileum and whole colon during primary surgery is needed. (Grade 2D)

Surgery for HSCR

Compared with multistage surgery, the single-stage pull-through procedure has the prominent advantages of shortening the length of hospital stay, reducing the number of operations, decreasing hospitalization costs, and avoiding complications of enterostomy.

Recommendation 9: A single-stage pull-through procedure is recommended; however, for patients with complicated conditions, a multistage operation should be performed. (Grade 1C)

In recent decades, the primary pull-through approach for HSCR has gradually transformed from traditional laparotomy to minimally invasive surgeries (MIS), such as robot or laparoscopic techniques and transanal endorectal pull-through (TERPT). Evidence from a meta-analysis indicated that compared with laparotomy, laparoscopic-assisted pull-through is associated with less visible scarring, enhanced postoperative recovery, and shorter hospitalization time.[9]

Recommendation 10: Generally, the TERPT or laparoscopy approach is recommended for short-segment HSCR, and the laparoscopy or laparotomy approach is recommended for long-segment HSCR or TCA. (Grade 1B)

Whether primary pull-through should be performed in neonates remains controversial. In a recent meta-analysis, Westfal *et al*[10] suggested that patients with short-segment HSCR who were less than 2.5 months of age at the time of TERPT had higher rates of postoperative complications, such as soiling and anastomosis problems, including stricture and leak.

Recommendation 11: Single-stage pull-through is not recommended in the neonatal period. (Grade 2B)

Successful treatment of TCA using a single-stage laparoscopic technique has been reported. The opposite view tends to multi-stage operation, which is helpful to perform multi-site biopsies in the initial exploration operation to detect the range of the affected intestines. More importantly, multi-stage surgery reduces the risk of severe perianal irritant dermatitis and provides a window of time for behavioral training, which can improve patients' ability to control defecation after definite operation.

Recommendation 12: For TCA patients, staged ileostomy with multi-site biopsies before definite operation is preferred, and a single-stage operation is not recommended. (Grade 2D)

Perioperative Management

Effective colonic emptying is believed to reduce the risk of postoperative anastomotic leakage and Hirschsprung disease associated enterocolitis (HAEC). European Reference Network for rare Inherited and Congenital Anomalies (ERNICA) guidelines recommended preoperative saline rectal irrigation to overcome functional bowel obstruction and to enable enteral feeding.[11]

Recommendation 13: Preoperative rectal irrigation is required; it is beneficial to recovery after the pull-through procedure. (Grade 1D)

Malnutrition has been identified as a risk factor for postoperative recurrent HAEC, and it is related to long-term quality of life.[12] Recently, according to a multi-center cross-sectional study conducted in China screening for undernutrition in children with HSCR, moderate to severe malnutrition rate was as high as 18.1%.[13] In a multicenter random controlled trial (RCT), Tang *et al*[14] reported that preoperative nutritional intervention improved the nutritional status of HSCR patients in the early postoperative period and promoted postoperative recovery.

Recommendation 14: HSCR patients with malnutrition should receive personalized nutritional intervention before the pull-through procedure, including enteral nutrion (EN) or parenteral nutrition (PN). (Grade 1C)

In a multicenter RCT, early postoperative EN helped to reduce insulin resistance and promote intestinal peristalsis, which help to improve the nutritional status of HSCR patients after pull-through.[14]

Recommendation 15: Postoperative early oral feeding should be encouraged. (Grade 1B)

As a part of the continuous nursing management strategy of HSCR, postoperative behavioral intervention involves dietary adjustment and toilet training. In a prospective RCT, Wang *et al*[15] demonstrated that such a postoperative rehabilitation protocol can reduce the recurrence rate of postoperative HAEC and improve the defecation control and quality of life of HSCR patients during long-term follow-up.

Recommendation 16: Postoperative behavioral interventions, including dietary adjustment and toilet training, could improve HSCR patients' quality of life in long-term follow-up. (Grade 1C)

Clinical practice indicates that the application of anal dilatation is based on different anastomosis methods, and the main indication is anastomotic stenosis.

Recommendation 17: Postoperative regular anal dilation in the short term is beneficial to the recovery of HSCR. (Grade 2D)

It is important to insist on structural follow-up for HSCR patients after pull-through procedures.

Recommendation 18: HSCR patients need regular long-term follow-up after the pull-through procedure. (Grade 1C)

Conflicts of interst

None.

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