

# Should primary anastomosis be considered more? A retrospective analysis of anastomotic complications in young children

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## ABSTRACT

**Objective** Little is known about intestinal anastomotic leakage and stenosis in young children ( $\leq 3$  years of age). The purpose of this study is to answer the following questions: (1) what is the incidence of anastomotic stenosis and leakage in infants? (2) which surgical diseases entail the highest incidence of anastomotic stenosis and leakage? (3) what are perioperative factors associated with anastomotic stenosis and leakage?

**Methods** Patients who underwent an intestinal anastomosis during primary abdominal surgery in our tertiary referral centre between 1998 and 2018 were retrospectively included. Both general incidence and incidence per disease of anastomotic complications were determined. Technical risk factors (location and type of anastomosis, mode of suturing, and suture resorption time) were evaluated by multivariate Cox regression for anastomotic stenosis. Gender and American Society of Anaesthesiology (ASA) score of  $\geq$ III were evaluated by  $\chi^2$  test for anastomotic leakage.

**Results** In total, 477 patients underwent an anastomosis. The most prominent diseases are intestinal atresia (30%), Hirschsprung's disease (29%), and necrotizing enterocolitis (14%). Anastomotic stenosis developed in 7% (34/468) of the patients with highest occurrence in necrotizing enterocolitis (14%, 9/65). Colonic anastomosis was associated with an increased risk of anastomotic stenosis (hazard ratio (HR) = 3.6, 95% CI 1.8 to 7.5). No technical features (type of anastomosis, suture resorption time and mode of suturing) were significantly associated with stenosis development. Anastomotic leakage developed in 5% (22/477) of the patients, with the highest occurrence in patients with intestinal atresia (6%, 9/143). An ASA score of  $\geq$ III ( $p=0.03$ ) and male gender ( $p=0.03$ ) were significantly associated with anastomotic leakage.

**Conclusions** Both anastomotic stenosis and leakage are major surgical complications. Identifying more patient specific factors can result in better treatment selection, which should not solely be based on the type of disease.

## INTRODUCTION

Intestinal anastomotic stenosis and anastomotic leakages are serious postoperative complications which can lead to different outcomes ranging from sepsis to the necessity

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Anastomotic complications can lead to serious complications resulting in reoperation with a temporary stoma or even death. Due to these perceived risks, a primary anastomosis in young children is avoided by many surgeons.

## WHAT THIS STUDY ADDS

⇒ The extent of this risk in young children ( $< 3$  years of age) undergoing a primary anastomosis is not well studied. This study shows that the incidence of stenosis is 8% and that of leakage is 5%. Patients with necrotizing enterocolitis were most at risk of stenosis (8%) and patients with intestinal atresia were at risk of leakage (6%). Colonic anastomosis was associated with an increased risk (hazard ratio (HR) = 3.6) of stenosis, while American Society of Anaesthesiology score of  $\geq$ III ( $p=0.03$ ) and male gender ( $p=0.03$ ) are significantly associated with anastomotic leakage.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Anastomotic complications are uncommon following primary anastomosis, which should be taken into account when in doubt how to treat, by enterostomy formation or primary anastomosis. Identifying and using patient-specific risk factors, specifically within high-risk diseases, can further aid the decision between these options.

of reoperation with a temporary stoma, all of which will extend hospital stay, and increase morbidity and mortality.<sup>1,2</sup> In young children ( $\leq 3$  years of age) treated for abdominal birth defects, anastomotic leakage occurs in up to 7% of patients with colonic atresia, while 8% of patients treated for complex gastroschisis develop an anastomotic stenosis.<sup>3,4</sup> However, for many surgical procedures in young children, the incidences of these complications are unknown.

In critically ill infants, the risk of anastomotic leakage is perceived to be too high to

safely create a primary anastomosis. In these infants, an enterostomy is mostly created because this treatment is believed to create the best conditions to allow the underlying disease to heal. However, enterostomy can result in a high-output stoma, stoma prolapse, and wound infections and can significantly affect the quality of life of infants and parents. In addition, a secondary operation is necessary to restore bowel continuity, which might result in other postoperative complications including anastomotic leakage and stenosis.<sup>5,6</sup> Moreover, a history of enterostomy increases the risk of long-term complications such as incisional hernia.<sup>7</sup> Therefore, it seems advisable that enterostomies should only be performed in selective patient groups with an increased risk of anastomotic leakage.

Currently, there is no consensus on which cases a primary anastomosis can be performed safely. For this reason, a temporary enterostomy is almost always created during primary surgery in certain diseases, such as necrotizing enterocolitis, deemed at high risk. However, the decision to perform a primary anastomosis or to create an enterostomy should be based on more patient-specific risk factors that predict the risk of complications. In this manner, anastomotic complications as well as possibly unnecessary enterostomies could be reduced. Therefore, identification of these risk factors is essential. For instance, factors describing the fitness of the infant prior to surgery such as the American Society of Anaesthesiology (ASA) score, could be related to anastomotic leakage.<sup>8</sup> Furthermore, surgical techniques creating an anastomosis, such as continuous stitching or side-to-side (s-s) anastomosis, might be of influence in anastomotic stenosis. Currently, there is no uniform surgical technique in which an intestinal anastomosis should be created to minimize the risk of postoperative complications in infants.<sup>9,10</sup>

The purpose of this retrospective cohort study, including young children ( $\leq 3$  years of age) who underwent a primary intestinal anastomosis between 1998 and 2018 in our tertiary clinic, is to answer the following questions: (1) what is the incidence of anastomotic stenosis and leakage in young children? (2) which surgical diseases entail the highest risk of anastomotic stenosis and leakage? (3) what are perioperative factors associated with anastomotic stenosis and leakage?

## METHODS

### Patients and management

All young children ( $\leq 3$  years of age) who underwent a primary anastomosis between January 1998 and December 2018 at the Amsterdam University Medical Centers were enrolled from a surgical administrative database. Data were stored in an electronic database (Castor EDC).<sup>11</sup>

### Data extraction

For anastomotic leakage, the definition and classification of the International Study Group of Rectal Cancer

(ISREC) was used, which was recently described in a Delphi study.<sup>12,13</sup> Since there is a lack of consensus for the definition for anastomotic stenosis, no strict definition was used. Anastomotic stenosis was assumed in patients with obstructive symptoms and an observation of a stenosis at the anastomotic sight during surgery or on contrast enema. Stenosis following treatment for Hirschsprung's disease was only noted if either redo-surgery was necessary without findings of residual aganglionosis or if anal dilatations were deemed necessary. Constipation that cleared following botulin injections was not included. In necrotizing enterocolitis, anastomotic stenosis was only included when it was described in the surgical report at the sight of anastomosis to distinguish it from postnecrotizing enterocolitis stenosis. Patients who died within a week following primary anastomosis were not included in the analysis of anastomotic stenosis but were included in the analysis of anastomotic leakage.

The time from surgery until the development of an anastomotic complication was recorded as well as the duration of follow-up, mode of diagnosing the complication, surgical and non-surgical reinterventions, and complications following reintervention. No procedures were excluded. The following data were retrieved from operative reports: surgical approach (laparotomy/laparoscopy), if surgery was urgent (executed within 72 hours following admission yes or no), history of prematurity (gestational age  $< 37$  weeks) and ASA score before operation (grouped as ASA score  $\leq II$  or  $\geq III$ ). Information on the location of the anastomosis (small intestine, colonic or ileocolic), type of anastomosis (end-to-end (e-e), end-to-side (e-s) or s-s), mode of creating the anastomosis (sutured or stapled), mode of suturing (intermittent or continuously) and type of suture material used (VICRYL®, Novosyn®, Monocryl®, Monosyn Plus®, or Polydiazone (PDS)) were recorded. The time to resorption of the used suture material was categorized as normal (Vicryl, Novosyn, and Monocryl) or slow (PDS and Monosyn plus).

### Statistical analysis

Descriptive data were reported according to distribution as median with range or mean with standard deviation (SD). Multivariate Cox regression was performed using anastomotic stenosis as the outcome. A subgroup analysis using only handsewn anastomosis was also performed using multivariate Cox regression. The proportional hazard assumption was graphically checked by log-minus-log plot for every included variable. Forward Wald selection was used for selection of variables and assessment of confounding (increase in B coefficient of  $> 10\%$ ) and effect modification (significant interaction term). Significant risk factors were reported in hazard ratio (HR) with complementary 95% confidence intervals (CIs). Due to insufficient events per variable for anastomotic leakage, Cox regression analysis was not possible. Therefore,  $\chi^2$  (dichotomous and categorical variables) and Fisher's

**Table 1** Baseline characteristics

| Variables                                    | Total with primary anastomosis (n=477) |
|--|--|
| Male, n (%)                                  | 290 (61)                               |
| Preterm birth, n (%)                         | 221 (53) (missing=61)                  |
| Surgery for congenital disease, n (%)        | 376 (79)                               |
| Median age (days), median (range)            | 49 (0–1095)                            |
| Median weight (g), median (range)            | 3230 (600–16 000) (missing=238)        |
| Urgent procedure, n (%)                      | 255 (54)                               |
| ASA score ≥III, n (%)                        | 92 (29) (missing=165)                  |
| Laparotomy, n (%)                            | 443 (93 (missing=1)                    |
| Mean duration of surgery in hours, mean (SD) | 2.2 (1.0) (missing=80)                 |
| Location of anastomosis, n (%)               |  |
| Small intestine–small intestine              | 262 (56) (missing=9)                   |
| Ileocolic                                    | 73 (16)                                |
| Colon–colon                                  | 133 (28)                               |
| Type of anastomosis, n (%)                   |  |
| End-to-end                                   | 302 (64) (missing=10)                  |
| End-to-side                                  | 32 (7)                                 |
| Side-to-side                                 | 96 (21)                                |
| Heineke-Mikulicz stricturoplasty, n (%)      | 36 (8)                                 |
| Stapled, n (%)                               | 61 (13)                                |
| Technique of handsewn sutures, n (%)         |  |
| Continues                                    | 116 (43) (missing=207)                 |
| Interrupted                                  | 154 (57)                               |
| Suture resorption time, n (%)                |  |
| Normal                                       | 176 (50) (missing=126)                 |
| Slow   | 175 (50)                               |

ASA, American Society of Anaesthesiology; IQR, interquartile range; SD, standard deviation.

exact test (dichotomous variables not meeting criteria for  $\chi^2$ ) were used for this outcome accordingly.

## RESULTS

A total of 477 patients, distributed in 23 different conditions (online supplemental appendix A), were treated with a primary anastomosis. Patient characteristics are described in [table 1](#). Out of all 477 patients undergoing an anastomosis, 30% (143/477) were created to treat intestinal atresias, 29% (136/477) to treat Hirschsprung's disease and 14% (67/477) to treat necrotizing enterocolitis. In 8% (36/477) of the patients, the intestine was longitudinally incised and closed (Heineke-Mikulicz stricturoplasty) as part of treatment, of which 39% (14/37) were patients treated for duodenal atresia. A stapled anastomosis was created in 13% (61/477) of patients, of whom 92% (56/61) underwent a Duhamel procedure for Hirschsprung's disease and 8% (5/56) for intestinal atresia. The median follow-up was 770 days

**Table 2** Anastomotic complications per condition

| Variables, n (%)             | Anastomotic stenosis* | Anastomotic leakage |
|------------------------------|-----------------------|---------------------|
| Intestinal atresia           | 9/142 (6%)            | 9/143 (7%)          |
| Hirschsprung's disease       | 12/136 (9%)           | 3/136 (2%)          |
| Necrotizing enterocolitis    | 9/65 (14%)            | 3/67 (5%)           |
| Meckel's diverticulum        | 0/18 (0%)             | 1/18 (6%)           |
| Focal intestinal perforation | 2/12 (17%)            | 1/12 (8%)           |
| Midgut volvulus              | 1/12 (8%)             | 0/12 (0%)           |
| Malrotation                  | 1/7 (14%)             | 0/8 (0%)            |
| Meconium peritonitis         | 0/2 (0%)              | 2/3 (67%)           |
| Incarcerated inguinal hernia | 0/2 (0%)              | 2/2 (100%)          |
| Diaphragmatic hernia         | 0/1 (0%)              | 1/1 (100%)          |

\*Nine patients died within 1 week.

(IQR=225–2125 days); 12% (59/477) had a follow-up of less than a year.

## Anastomotic stenosis

Nine patients died within a week following surgery and were therefore not included. Anastomotic stenosis occurred in 7% (34/468) of patients after a median of 44 days (IQR=25–209 days) following primary surgery, and 83% (28/34) of the stenosis occurred within 1 year following surgery. In [table 2](#), the incidences of stenosis for each condition are described. Anastomotic stenosis developed in 8% (9/142) of patients treated for intestinal atresias, 9% (12/136) of patients treated for Hirschsprung's disease, and 14% (9/65) of patients treated for necrotizing enterocolitis. Of the patients treated for intestinal atresia, 2% (2/93) of the patients treated for a duodenal atresia developed a stenosis, while 14% (7/49) of the patients treated for jejunoileal atresia developed a stenosis. The characteristics of the anastomoses are described in [table 3](#). Stenosis developed in the colon in 53% (18/34) of the cases, and 85% (29/34) developed following the usage of e-e anastomoses. In none of the stapled anastomoses a stenosis occurred. In the subgroup of handsewn anastomoses, 63% (19/30, four unknowns) of the stenoses developed after using intermittent sutures and 59% (17/30, four unknowns) after using fast absorbing sutures.

Redo-surgery was necessary in 68% (23/34) of all stenoses. The 11 patients who did not need redo-surgery were patients with a stenosis following treatment for Hirschsprung's disease. Of the patients experiencing a stenosis with the need for redo-surgery, a new handsewn anastomosis was created in 75% (17/23); a stoma was created in 17% (4/23); a stapled anastomosis was performed in 4% (1/23); and a stricturoplasty was performed in 4% (1/23) (Heineke-Mikulicz).

Following redo, three patients died (8% of all stenosis, ≤1% of all patients), of which two patients with

**Table 3** Characteristics of anastomotic complications

| Variables  | Anastomotic stenosis (n=34) | Anastomotic leakage (n=22) |
|--|-----------------------------|----------------------------|
| Male, n (%)                                      | 14 (41)                     | 18 (82)                    |
| ASA ≥III score prior to operation, n (%)         | 7 (27) (missing=8)          | 9 (53) (missing=5)         |
| Location of anastomosis, n (%)                   |                             |                            |
| Small intestine                                  | 11 (32)                     | 13 (65) (missing=2)        |
| Ileocolic  | 5 (15)                      | 5 (23)                     |
| Colon  | 18 (53)                     | 3 (14)                     |
| Type of anastomosis, n (%)                       |                             |                            |
| End-to-end                                       | 29 (85)                     | 12 (57) (missing=1)        |
| End-to-side                                      | 0 (0)                       | 0 (0)                      |
| Side-to-side                                     | 3 (8)                       | 5 (23)                     |
| Closed longitudinal incision intestine, n (%)    | 2 (5)                       | 5 (23)                     |
| Stapled, n (%)                                   | 0 (0)                       | 0 (0)                      |
| Technique of handsewn sutures, n (%)             |                             |                            |
| Continuous                                       | 11 (37) (missing=4)         | 10 (67) (missing=7)        |
| Interrupted                                      | 19 (63)                     | 5 (33)                     |
| Suture resorption time, n (%)                    |                             |                            |
| Normal   | 12 (41) (missing=4)         | 6 (38) (missing=6)         |
| Slow   | 17 (59)                     | 10 (62)                    |
| Median days until the complication, median (IQR) | 44 (25–209)                 | 6 (4–7)                    |
| Reoperation needed, n (%)                        | 23 (68)                     | 21 (96)                    |
| Death related to complication, n (%)             | 3 (9)                       | 2 (9)                      |
| Recurrence in surviving patients, n (%)          | 1 (5)                       | 0 (0)                      |

ASA, American Society of Anaesthesiology; IQR, interquartile range.

necrotizing enterocolitis both died of multiorgan failure due to abdominal sepsis caused by multiple perforations and stenosis. One patient with intestinal atresia was diagnosed with a stenosis by contrast enema, but, due to the combined impact of multiple congenital defects and sepsis, the patient passed away before surgery could be performed. Of the patients who survived and in whom redo-anastomosis was performed, recurrence developed in 5% (1/20).

Outcomes of technical factors that were analyzed as risk factors for stenosis are reported in [table 4](#). Cox regression analysis showed that colon–colonic anastomoses were of significantly increased hazard (HR=3.0, 95% CI 1.4 to 6.7,  $p \leq 0.01$ ) for anastomotic stenosis development when compared with small intestine–small intestine anastomoses. Colon–colonic anastomoses were not significantly more at risk ( $p=0.327$ ) of stenosis than ileocolic anastomoses. The type of anastomosis was not significantly associated with the development of a stenosis (s-s,  $p=0.29$ ; e-e,  $p=0.29$ ; e-s,  $p=0.98$ ).

A subgroup analysis, using Cox regression, of all handsewn anastomoses (excluding stapled anastomoses) showed no significant hazard in resorption time ( $p=0.27$ ) or mode of suturing (continuous or interrupted) ( $p=0.60$ ).

### Anastomotic leakage

Anastomotic leakage was diagnosed in 5% (22/477) of the children after a median of 6 days (IQR=3–7 days) following primary surgery. Diagnosis was made using abdominal radiograph (n=14), ultrasound (n=4), CT scan (n=1) or during surgery (n=3). All leakages were

**Table 4** Cox regression into technical factors associated with anastomotic stenosis

| Variables               | HR (95% CI)       | P value     |
|-------------------------|-------------------|-------------|
| Location of anastomosis |                   |             |
| Small intestine         | Comparator        | Comparator  |
| Ileocolic               | 1.6 (0.6 to 4.6)  | 0.54        |
| Colon                   | 3.0 (1.4 to 6.7)  | $\leq 0.01$ |
| Type of anastomosis     |                   |             |
| Side-to-side            | Comparator        | Comparator  |
| End-to-end              | 2.0 (0.9 to 4.5)  | 0.07        |
| End-to-side             | 1.2 (0.1 to 11.4) | 0.89        |
| Handsewn anastomosis    |                   |             |
| Suture resorption time  | 1.4 (0.5 to 4.4)  | 0.53        |
| Mode of suturing        | 0.5 (0.3 to 1.3)  | 0.23        |

CI, confidence interval; HR, hazard ratio.



ISREC classification C ('anastomotic leakage requiring relaparotomy'). In table 2, the occurrence of anastomotic leakages is described per condition. An anastomotic leakage developed in 6% (9/143) of the patients treated for intestinal atresias, in 2% (3/136) of the patients with Hirschsprung's disease, and 5% (3/67) of the patients treated for necrotizing enterocolitis. In the patients treated for intestinal atresia, 6% of the patients treated for a duodenum atresia (6/94) and jejunoileal atresia (3/49) developed a leakage. Half (3/6) of the leakages following treatment for duodenum atresia occurred in patients with a duodenal web treated by longitudinal incision, removal of the web, and closure of the intestinal incision.

While four patients died following an anastomotic leakage, two patients died more than 100 days after redo-surgery due to factors unrelated to the anastomotic leakage. The other two patients' deaths were directly related to the anastomotic leakage resulting in a direct mortality of 9% (2/22) within all patients with a leakage and  $\leq 1\%$  (2/477) of all patients undergoing a primary anastomosis. In one patient treated for a focal intestinal perforation, the anastomotic leakage resulted in death before reoperation could be performed. Another patient with Down syndrome died 10 days after treatment of a duodenal atresia. Following primary anastomosis, the patient developed an *Escherichia coli* sepsis as a result of an anastomotic leakage. Despite treatment by redo-anastomosis 8 days after the initial surgery, the patient died as a result of ongoing sepsis.

Of the patients who underwent redo surgery because of anastomotic leakage, a stoma was created in 50% (10/20) and a new anastomosis in 50% (10/20).

Both male gender ( $p=0.03$ ) and an ASA score of  $\geq III$  ( $p=0.03$ ) were significantly associated with anastomotic leakage.

## DISCUSSION

This study evaluates the incidence of anastomotic complications in young children, which is 7% for anastomotic stenosis and 5% for anastomotic leakage. Anastomotic stenosis occurs most often in patients treated for necrotizing enterocolitis (14%), Hirschsprung's disease (9%), or intestinal atresia (6%), which is in line with previous reports.<sup>4</sup> Anastomotic leakages develop most often after treatment for intestinal atresia (6%) followed by treatment for necrotizing enterocolitis (5%). The evaluation of technical factors as possible predictors for the development of anastomotic stenosis shows that colonic anastomosis is associated with an increased risk of the development of stenosis compared with those located in the small intestine. Other technical factors (type of anastomosis, suture resorption time, and mode of suturing) are not significantly associated with the development of a stenosis, although e-e anastomosis shows a trend towards increased risk of stenosis. A higher ASA score ( $\geq III$ ) and male sex are significantly associated with

the development of anastomotic leakage. In all patients undergoing a primary anastomosis, less than 1% died because of an anastomotic complication.

Compared with small intestinal anastomosis, colonic anastomoses are most at risk of stenosis development. Although an explanation cannot be retrieved from our data, there are multiple hypotheses provided for this effect by the literature. The simplest explanation might be that, due to fluid resorption in the colon, the increased fecal consistency also increases the chances of a stenosis in the colon to become symptomatic.<sup>14</sup> Additionally, it could be that the healing process between the two intestinal locations differ, resulting in different anastomoses. This process of anastomotic healing is to a great extent unclear, which is why there is no clear narrative yet.<sup>9 15</sup> However, there seem to be pathobiological differences between the small intestine and colon, such as the reaction to ischemia and reperfusion, which could reasonably have an effect on the extent of anastomotic scarring.<sup>16</sup>

None of the technical factors in the creation of an anastomosis seem to be associated with stenosis development, and therefore no recommendations can be given on this topic based on our data. However, it must be noted that e-e anastomosis shows a trend towards increased risk of stenosis, which was borderline non-significant ( $p=0.07$ ) in our cohort. The diameter of the intestinal lumen is smaller in an e-e anastomosis than in a s-s anastomosis. As the anastomosis heals and the patients grow, the lumen of an e-e anastomosis might more easily get obstructed, which might explain these results.

Previous studies have suggested that stenosis following Hirschsprung's disease treatment could be prevented by routine dilatations during the first week postsurgery, although conflicting results on this method have been reported.<sup>17 18</sup>

There is no consensus on how long the follow-up should be when conducting research into anastomotic stenosis in infants. The median time from operation to anastomotic stenosis was 44 days in our cohort; however, stenosis developed both within 10 days and up to 6 years after surgery. In our cohort, 80% of the stenoses developed within 1 year and 90% within 2 years. For this reason, 2 years seems to be an acceptable cut-off as not to miss a significant amount of stenosis.

An anastomotic leakage is a feared and unpredictable complication due to the possible severe consequences. The most feared consequence of anastomotic leakage, mortality, occurred in two children in our cohort, which is less than 1%. These fatalities show that when an anastomotic leakage occurs in vulnerable patients with multiple comorbidities, the chances of mortality are high. However, if a leakage occurs in patients who are fit enough to undergo redo-surgery, most recover. Moreover, half of the patients with a leakage recover without an enterostomy.

Enterostomy formation does not prevent complications, as previously described.<sup>5-7</sup> Because of the associated complications of enterostomy formation, both

short-term (eg, high-output stoma, stoma prolapse, and wound infections) and long-term (eg, adhesive obstructions, incisional hernia, and anastomotic stenosis), a primary anastomosis must be preferred.<sup>5 6 19</sup> Because of these risks of enterostomy and the relatively low incidence of anastomotic leakage, one could argue that it is unwise to decide on enterostomy creation in all patients with high-risk diseases (ie, necrotizing enterocolitis and intestinal atresia patients). Identifying patient-related factors of those patients who are at increased risk of the development of anastomotic leakage could better help surgeons in the decision when not to perform a primary anastomosis. Although one should look for these factors within high-risk diseases, we feel that the decision of treatment should not solely be based on type of disease. This is underlined by our results showing ASA score to be of more importance than type of disease. An ASA score of  $\geq$ III was significantly associated with the development of anastomotic leakage in our cohort, as is the case in adults.<sup>8</sup> In necrotizing enterocolitis, none of the 12 patients with a low ASA score (I or II) developed a leakage following primary anastomosis, while 2 out of 2 patients with an incarcerated inguinal hernia warranting resection of the incarcerated intestine with primary anastomosis with an ASA score of III developed an anastomotic leakage. The ASA score seems to reflect disease severity preoperatively and thereby possibly healing capacity of the anastomosis postoperatively.

Regarding the ASA score, male sex seems to be associated with the occurrence of anastomotic leakage. Out of 15 patients who developed a leakage in high-risk diseases (necrotizing enterocolitis, Hirschsprung's disease, and intestinal atresia), only 1 patient was female. Our results do not provide any insights on an explanation for this finding. The increased risk of anastomotic leakage related to gender is not fully clear; however, it seems that female patients are better resistant to the damage occurring from ischemia-reperfusion-induced intestinal injury that occurs during surgery.<sup>20</sup> Patients with Hirschsprung's disease, which occurs predominantly in male subjects, only reported three leakages in our cohort, although these patients made up 14% of our total cohort.<sup>21</sup> If male sex is of key importance, we would have expected more leakages in this group. This suggests that other factors should be of importance.<sup>21</sup> Nevertheless, the factor gender seems of influence and, in combination with other factors such as ASA score, might be informative when deciding on type of treatment.

Previous studies describe fewer complications, leakages, and stenosis, in stapled anastomosis than in sutured anastomosis in young children.<sup>22 23</sup> These studies retrospectively included a diverse set of diseases including intestinal atresias, intussusception and necrotizing enterocolitis. In our cohort, the majority of the stapled anastomoses was created as part of pouch formation in the treatment of Hirschsprung's disease, although some patients with intestinal atresia also underwent a stapled anastomosis. Although this is a selective group of patients

and type of anastomosis, making comparison with the rest of the cohort difficult, no stenosis or leakages developed following these stapled anastomoses.

Due to the retrospective nature of our analysis, we were limited to perioperative factors described in the patient's files. Possibly other perioperative factors such as intestinal size discrepancy, infectious state of the patient, or (faecal) peritonitis could influence the healing process of the anastomosis and thereby the occurrence of anastomotic stenosis and leakage.<sup>24</sup> Moreover, the small number of anastomotic complications, especially for anastomotic stenosis, might have increased the chances of type II errors. Another result of the small number of cases was that we were unable to perform regression analysis on the outcome of anastomotic leakage. Therefore, we are unable to determine the strength of the association of male sex and high ASA score with the development of a leakage.

Nevertheless, owing to our large cohort of young children undergoing a primary anastomosis, we were able to determine that anastomotic stenosis seem to occur more often in colonic anastomosis, and occurrence does not seem to be related to other technical features of anastomotic creation (other types of anastomosis, suture resorption time, or mode of suturing). The occurrence of anastomotic leakage is associated with ASA score of  $\geq$ III and male gender. Identifying more patient specific factors can result in better treatment selection, which should not solely be based on type of disease.

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**Contributors** LES contributed to study conception and design, data acquisition, analysis, and data interpretation, drafting of the manuscript, and critical revision. GDM and JPMD contributed to study conception and design, drafting of the manuscript, and critical revision. LWEvH and WJdJ contributed to critical revision. The guarantor (LES) accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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