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ARM-Net Consortium; van Der Steeg, H. J. J.; van Rooij, I. A. L. M.; Iacobelli, B. D.; Sloots, C. E. J.; Leva, E.; Broens, P.; Leon, F. Fascetti; Makedonsky, I.; Schmiedeke, E.

Published in:
Journal of Pediatric Surgery

DOI:
10.1016/j.jpedsurg.2019.03.008

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2019

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

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The impact of perioperative care on complications and short term outcome in ARM type rectovestibular fistula: An ARM-Net consortium study

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Abstract

Background: The impact of perioperative care interventions on postreconstructive complications and short-term colorectal outcome in patients with anorectal malformation (ARM) type rectovestibular fistula is unknown.

Methods: An ARM-Net consortium multicenter retrospective cohort study was performed including 165 patients with a rectovestibular fistula. Patient characteristics, perioperative care interventions, timing of reconstruction, postoperative complications and the colorectal outcome at one year of follow-up were registered.

Results: Overall complications were seen in 26.8% of the patients, of which 41% were regarded major. Differences in presence of enterostomy, timing of reconstruction, mechanical bowel preparation, antibiotic prophylaxis and postoperative feeding regimen had no impact on the occurrence of overall complications. However, mechanical bowel preparation, antibiotic prophylaxis ≥48 h and postoperative nil by mouth showed a significant reduction in major complications. The lowest rate of major complications was found in the group having these three interventions combined (5.9%).

Multivariate analyses did not show independent significant results of any of the perioperative care interventions owing to center-specific combinations. At one year follow-up, half of the patients experienced constipation and this was significantly higher among those with preoperative mechanical bowel preparation.

Conclusions: Differences in perioperative care interventions do not seem to impact the incidence of overall complications in a large cohort of European rectovestibular fistula-patients. Mechanical bowel preparation, antibiotic prophylaxis ≥48 h, and postoperative nil by mouth showed the lowest major complications.

Level of evidence: III

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Anorectal malformations (ARMs) represent a complex group of congenital anatomical anomalies of the anorectum, characterized by the absence of a normal rectum and anal canal with the opening at its anatomic position central in the sphincter complex [1,2]. In females, the rectovestibular type is common [3,4]. Many different approaches have been used for reconstructive surgery for patients with an ARM in the past, but since the introduction of the posterior sagittal anorectoplasty (PSARP) in the early 1980’s, this approach and the more limited explorative anterior sagittal anorectoplasty (ASARP) have developed into preferred surgical techniques [5,6].

When performing reconstructive surgery, multiple perioperative interventions have to be considered, such as mechanical bowel preparation, antibiotic prophylaxis, and perioperative feeding regime. Based on literature and clinical experience, these interventions are addressed differently in international centers depending on country, center and/or surgeon [7,8]. These interventions, as well as timing of surgery and presence of a prior enterostomy, might have a potential influence on postoperative complications, recovery, and functional outcome, but their impact has not yet been established for reconstructive surgery in ARM patients.

The aim of this study was therefore to investigate which differences exist in perioperative care for rectovestibular fistula patients among pediatric surgery centers, joined in the ARM-Net consortium, and whether it led to different outcomes in terms of postreconstructive complications and colorectal outcome at one year follow-up. Our study was performed as a multicenter retrospective cohort study using data from the European ARM-Net registry [9].

1. Material and methods

Data regarding all ARM patients in the participating centers of the ARM-Net Consortium are registered in our joined ARM-Net data registry [10]. Available data involve pseudoanonymized background data, type of ARM, genetic and VACTERL-screening (with VACTERL-association defined as ≥3 different VACTERL-anomalies [11]), additional congenital anomalies, surgical procedures, postoperative complications, and 1 year follow-up outcome measures [10]. The registry presently contains data of 1600 ARM patients. For this study only those with a rectovestibular fistula were selected. Additional questions concerning perioperative care were developed, i.e. timing of surgery, preoperative mechanical bowel preparation, perioperative antibiotic prophylaxis, and postoperative (par)enteral nutrition. Possible answers were proposed based on literature [7] and on experience from different centers of expertise. For this expansion of required data, a separate database was developed, and all involved members were invited to include data of their prior entered patients with a rectovestibular fistula and all new patients that were treated since the start of this study (December 2016).

Concerning timing of surgery, neonatal repair was defined as reconstruction within the first 7 days of life. Mechanical bowel preparation was defined as any preoperative intervention to limit the feces and therefore colonic bacterial load. Groups were divided into no mechanical bowel preparation and any bowel preparation (strict fluid diet less than 24 h prior to surgery, laxatives, rectal wash outs, and total irrigation, or combinations of these). Although strict fluid diet less than 24 h prior to surgery is not an actual mechanical intervention (‘modified’ bowel preparation), we considered this as mechanical bowel preparation, as it is a means of diminishing fecal load [12]. Based on differences in use, antibiotic prophylaxis was divided into prophylaxis, defined as perioperative use ≤24 h after surgery, and prolonged prophylaxis, defined as ≥48 h after surgery. Postoperative feeding regime was divided into a group of immediate postoperative oral feeds and a group of prolonged nil by mouth, independent of the number of days (>3, 3–7 and > 7 days postoperatively). Dilatation therapy was generally started 2–3 weeks after surgery, and the protocol used was at the discretion of the treating surgeon.

Complications were recorded, i.e. wound dehiscence, wound infection, urinary tract infection, gluteal abscess, anal stenosis, mucosal prolapse, recurrent fistula, megacolon, incisional hernia and indication for redo surgery (not otherwise specified). These complications were not further defined, but judged by the surgeon of the center where the patient was treated. In order to substantiate complications, we made a distinction between minor and major complications based on the Clavien–Dindo classification of surgical complications [13]. Grades 1 and 2 are considered as minor, 3 and 4 as major.

Short-term colorectal outcome was described by the items constipation (the incapacity to empty the rectum spontaneously without help every day), consistency of feces, diaper rash, and circumferential or partial anal mucosa prolapse at 1 year follow-up. Within the ARM-Net consortium, 1 year follow up was defined as the moment 1 year after reconstructive surgery, whether or not a (prior) enterostomy was closed. Because of the fact that in this study all pseudoanonymized data were extracted through patient medical files, and additional short-term follow-up scores are considered to be standard of care, the local Institutional Review Board of the principal investigator (HJJvdS) waived the study.

1.1. Statistical analyses

Descriptive analyses have been carried out to show frequencies and percentages of general and clinical characteristics, perioperative interventions, complications, and short-term outcome. Differences in all complications and major complications according to the Clavien–Dindo classification after reconstructive surgery between several perioperative care interventions were tested using the chi-square or Fisher’s exact test, as appropriate. The same has been done for the short-term outcome items (constipation, consistency of feces, diaper rash, and mucosa prolapse) at 1 year follow-up with the perioperative care interventions. Multivariate logistic regression analyses were performed in the associations between complications and the perioperative mechanical bowel preparation, antibiotic prophylaxis, and feeding regime to adjust for the effect of timing of reconstruction and use of an enterostomy. A combination of perioperative care interventions was constructed and differences among these combination groups in complications after reconstructive surgery (all and major) were tested using the chi-square test. Multivariate logistic regression analyses were performed to investigate whether independent associations exist between bowel preparation, antibiotic prophylaxis, or feeding regime and major complications by adjusting for each other. A p-value of <0.05 was considered statistically significant. Statistical analyses were performed using SPSS 22.0 for Windows (IBM SPSS, Chicago, IL, USA).

2. Results

Out of the 205 patients with a rectovestibular fistula from the ARM-Net registry, 169 (82%) were entered in the additional database, and eligible for study analyses. Four patients did not have any surgical reconstruction, two because of early death and two of unknown reasons, and were therefore excluded from the analyses, leaving 165 patients in this study. These patients were collected in 18 different European centers from 9 different countries (Austria (n = 6), Belgium (4), Germany (9), Italy (66), the Netherlands (59), Spain (9), Sweden (1), Ukraine (10), United Kingdom (1)).

Preterm birth was documented in a fifth of the patients (Table 1). Low birth weight (<2500 g) was present in 26.3%, and 5.1% was even very low birth weight (<1500 g). Seven patients were part of a twin. The VACTERL association was present in 18.3% of the patients. The most prevalent associated anomalies were cardiac (40.5%). Other associated anomalies, reported in VACTERL order, were: vertebral anomalies (16.5%), esophageal atresia (11%), renal anomalies (22.1%), and upper limb deformities (5.5%). Spinal cord anomalies were present...
in 18.3%, the majority of which being tethered cord. Vescicoureteral reflux was checked in only 29% of the patients, and present in 20.3% of those. Genetic abnormalities, not necessarily syndromic, were documented in 10.9%. Of 165 patients, 33 (20%) received an enterostomy prior to definitive surgery for different reasons (Table 2). PSARP was performed in 61%, in 25% an ASARP was done, and in 12.8% a mini-PSARP. One patient had a laparoscopic dissection. A total of 16 patients (10.1%) were reconstructed in their neonatal period; the remaining were reconstructed at least more than 1 week after birth, with a median of 3 months after birth (5–95% range: 0–14 months). Patients with low birth weight (<2500 g) and preterm babies (<37 weeks) were distributed equally among the neonatal repair group and the delayed repair group. Preoperative mechanical bowel preparation was performed in 63.6% of the patients; most of them had rectal washouts one or more days preoperatively. Others had a range of possible preparative interventions, ranging from strict fluid diet less than 24 h prior to surgery to laxatives and total irrigation. Regarding antibiotic prophylaxis, 32.9% of the patients received antibiotics with a maximum duration of 24 h and the rest received antibiotics for at least 48 h, of whom 52.2% received them for more than 5 days. All antibiotic treatments were broad spectrum and covered both aerobic Gram positive and negative microorganisms, as well as anaerobic. Concerning postoperative feeding, 31.4% of the patients were allowed immediate enteral feeds after surgery. The rest either were administered iv fluids (14%) or received total parenteral nutrition (50.9%). Of the latter group, the majority received it for more than 7 days.

### 2.1. Postreconstructive complications

Overall complications after reconstructive surgery were encountered in 26.8% and ranged from wound dehiscence, gluteal abscess to megalon and indications for redo surgery (Fig. 1). The most prevalent complication was wound dehiscence. According to the Clavien–Dindo classification of surgical complications, 59% of these complications were considered minor (grade 1 or 2) and 41% major (grade 3 or 4).

Complications were seen in 18.8% of the patients after a neonatal reconstruction versus 27.5% in those having a delayed reconstruction (p = 0.56). Patients with a prior enterostomy had an almost equal rate of complications after reconstruction to those undergoing a primary reconstruction (30.3% vs 26%; p = 0.61; Table 3). When focusing on major complications, there was no significant difference either (Table 4). Mechanical bowel preparation was used as much in patients with a prior enterostomy as in patients with a primary reconstruction. Whether or not mechanical bowel preparation was used did not influence the occurrence of overall complications. Mechanical bowel preparation did, however, show a statistically significant decrease in major complications (6.7%) when compared to no mechanical bowel preparation (18.3%; p = 0.02; Table 4). Prophylactic antibiotic use was associated with complications in 24.5% of the cases, compared to 27.8% in the group with prolonged prophylaxis (p = 0.66; Table 3). Correction for the presence of a prior enterostomy did not change the impact, nor did the type of antibiotics prescribed. When only major complications were analyzed, prolonged prophylaxis showed a significant decrease (7.4%) compared to prophylaxis (18.9%; p = 0.03; Table 4). Prolonged nil by mouth did not protect against overall complications compared to immediate enteral feeds, but did lead to a significant decrease in major complications (7.3% vs 20%; p = 0.02; Table 4). The presence of a prior enterostomy did not change this significant impact of prolonged nil by mouth on the observed complication rate.

The associations between several combinations of perioperative care interventions and the postreconstructive complications showed no differences in the overall complication rate. When analyzing the major complications, the best combination was preoperative mechanical bowel preparation, antibiotic prophylaxis ≥48 h, and a postoperative feeding regime of nil by mouth, with a major complication rate of 5.9%. When performing multivariate analyses, we were not able to identify perioperative care interventions that independently decreased the risk of major complications. This was owing to the large impact

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### Table 1

<table>
<thead>
<tr>
<th>General characteristics of the study population of 165 patients with anorectal malformation type rectovestibular fistula.</th>
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<tbody>
<tr>
<td>N (%)</td>
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<tr>
<td>Preterm birth (&lt; 37 weeks of gestation)</td>
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<td>Birth weight</td>
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<tr>
<td>Low birth weight (&lt;2500 g)</td>
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<tr>
<td>Very low birth weight (&lt;1500 g)</td>
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<tr>
<td>Twin</td>
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<tr>
<td>Associated anomalies</td>
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<tr>
<td>VACTERL-association</td>
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<tr>
<td>Type of associated anomalies:</td>
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<tr>
<td>Vertebral (not sacral/coccyx)</td>
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<tr>
<td>Sacral</td>
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<tr>
<td>Cardiac</td>
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<tr>
<td>Esophageal atresia</td>
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<tr>
<td>Renal</td>
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<td>Limbs (upper)</td>
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<tr>
<td>Spinal cord</td>
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<td>Genetic abnormalities</td>
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### Table 2

<table>
<thead>
<tr>
<th>Clinical characteristics of the study population of 165 patients with anorectal malformation type rectovestibular fistula.</th>
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</thead>
<tbody>
<tr>
<td>N (%)</td>
</tr>
<tr>
<td>Type of reconstructive surgery</td>
</tr>
<tr>
<td>PSARP</td>
</tr>
<tr>
<td>mini-PSARP</td>
</tr>
<tr>
<td>ASARP</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Timing of reconstructive surgery</td>
</tr>
<tr>
<td>≤ 7 days after birth</td>
</tr>
<tr>
<td>&gt; 7 days after birth</td>
</tr>
<tr>
<td>Preoperative enterostomy</td>
</tr>
<tr>
<td>Preoperative mechanical bowel preparation</td>
</tr>
<tr>
<td>Perioperative antibiotic prophylaxis</td>
</tr>
<tr>
<td>Prophylaxis (≤ 24 h postoperatively)</td>
</tr>
<tr>
<td>Prolonged prophylaxis (≥ 48 h postoperatively)</td>
</tr>
<tr>
<td>Postoperative feeding regime</td>
</tr>
<tr>
<td>Immediate oral feeds</td>
</tr>
<tr>
<td>Nil by mouth</td>
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</tbody>
</table>

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*a Percentages are calculated leaving out missing values in several clinical characteristics.
*b Including among others: Cat Eye Syndrome, Turner syndrome with mosaicism, Kabuki syndrome, 5q2 duplication, 22q11 deletion, and caudal regression syndrome.

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**Fig. 1.** Type and number of complications after reconstructive surgery. *In 44 patients (26.8%) complications were encountered: some patients had more than 1 complication (total 51). **A few more redo operations were performed owing to mentioned complications as wound dehiscence, but only these two were mentioned as an isolated complication, without specifying the reason for the redo.
of certain center-specific combinations of interventions on major complication occurrence.

2.2. One year follow-up

Constipation was present in approximately half of the patients after one year follow-up (Table 5), and was not affected by timing of surgery. Necessary treatment was by a diet (8%), stool softener (40%), stimulant laxatives (39%), or enemas (14%). Consistency of the feces (solid, soft or liquid) was mainly soft (71.8%). Frequent diaper rash was documented in 7% of all patients. At physical examination a partial or circumferential anal mucosal prolapse was observed in 4.2% of the patients. Most patients (85.6%) had finished dilation therapy, while only 2.3% never received any dilation therapy. Pain or discomfort during dilation was experienced by 41.5% of the patients initially, and by 5.1% continuously.

Children with an enterostomy more often experienced diaper rash (21%) and circumferential or partial anal mucosal prolapse (13%) one year after reconstruction than those without (4% and 2%, p = 0.01 and p = 0.05, respectively). There was no difference in frequency of constipation or consistency of stool. Analyzing the impact of perioperative care interventions on one year colorectal function, mechanical bowel preparation vs no preparation (35%; p = 0.01). Other short term colorectal outcome items did not show any difference between mechanical bowel preparation vs no mechanical bowel preparation. Differences in antibiotic prophylaxis and postoperative feeding regimen did not show any effect on short term colorectal outcome, nor did the timing of reconstruction or surgical approach.

### 3. Discussion

To date, this is the largest study addressing perioperative care interventions for reconstructive surgery in ARM type rectovestibular fistula patients. As more than 80% of the available patients in the ARM-Net registry have been included in this study, it gives a good reflection of current perioperative practice in European centers of expertise for ARM. Our study illustrates that the different perioperative care interventions in the treatment of rectovestibular fistula patients among individual countries and centers do not significantly impact outcome regarding overall postoperative complications. Three interventions, however, showed a significant reduction of the risk of major complications. These were mechanical bowel preparation, prolonged antibiotic prophylaxis ≥ 48 h and postoperative nil by mouth feeding, and their combination gave the lowest rate.

In this study, mechanical bowel preparation showed to reduce major complications. This is in contrast to the few small, mainly retrospective, studies on mechanical bowel preparation in diverse pediatric colorectal surgery that have been published up to date. These studies showed no benefit from mechanical bowel preparation, regardless of differences in regimens used [14–17]. This is in accordance with adult literature, in which compelling evidence exists that mechanical bowel preparation alone does not protect against the occurrence of complications, e.g. surgical site infections [18]. Although in adults the addition of nonabsorbable oral antibiotics significantly reduces complications [19], pediatric studies have failed to demonstrate any effect of additional oral antibiotics [15,16,20]. Likewise, none of our patients were recorded to receive oral antibiotics as an adjunct means of bowel preparation. All these diverse data, adult and pediatric, give rise to the limited agreement in the pediatric surgical community regarding the effectiveness and therefore utilization of mechanical bowel preparation and additional nonabsorbable oral antibiotics as an adjunct therapy in mitigating postoperative infectious complications [12,21–23]. Further research into the role of preoperative mechanical bowel preparation with or without additional nonabsorbable oral antibiotics in pediatric colorectal surgery is therefore warranted.

A further means to reduce postoperative surgical site infections is the use of perioperative systemic antibiotic prophylaxis. Our study showed that all patients received some form of systemic prophylaxis. The regimens used were in general in accordance to the recommended antibiotics in literature for colorectal procedures [24,25] and with the main goal to broadly cover aerobic as well as anaerobic bacteria. Concerning the duration of prophylaxis, there is no evidence in literature to support the continuation of antimicrobial prophylaxis longer than 24 h after the procedure [25–27]. Only one prospective study has suggested a protective effect of therapeutic (2–5 days) antibiotics over prophylaxis concerning wound infections [28]. The majority of guidelines concerning gastrointestinal surgery in general recommend either a single preoperative dose or cessation within 24 h [25–27,29]. There is even increasing evidence that prolonging antibiotic prophylaxis beyond 24 h leads to an increasing risk of adverse effects, development of resistance, and increased costs [25,27]. Therefore, our results of
a reduction of major complications after prolonged prophylaxis were somewhat unexpected. It could be hypothesized that contemporary prophylaxis guidelines, which are based on general adult colorectal surgery data, do not necessarily apply for this specific reconstructive surgery in infants with a subcutaneous wound and an anocutaneous anastomosis.

Another point of discussion in perioperative care is the postoperative feeding regime. The main concern with regard to early enteral feeding is the presumed increased risk of wound infection or dehiscence of the anocutaneous anastomosis [4]. Stool passes a newly created anorectoplasty and therefore stretches the wound, potentially evoking dehiscence and interference with wound healing. On the other hand, it is widely recognized that early enteral feeding in adult patients undergoing colorectal surgery, decreases the risk of wound infections and enhances early recovery [30,31]. Furthermore, enteral nutrition is considered superior to conventional parenteral nutrition because it is more physiologic, safer and less expensive [32]. Although widely debated, data concerning these topics in the pediatric surgical population are scarce. Regardless of the presence of a diverting colostomy, some advocates prolonged fasting for 2 weeks [33], while others allow earlier oral feeds [34-38]. In our study, a third of the patients were allowed immediate oral feeds directly after surgery, not just those already protected by a prior enterostomy. Our study showed that immediate oral feeds did not result in an increase in overall postoperative complications compared to prolonged nil by mouth. It did, however, lead to a significant increase in major complications. An enterostomy, interestingly enough, did not prevent the occurrence of wound infections and dehiscences, even though stool does not pass the neonate. One could suggest that the mere presence of colonic bacteria at the surgical site and their role in the development of surgical site infections has more impact on wound infection and dehiscence than stool passing. Details regarding many factors, such as experience of the surgical team and the weight and nutritional status of the patient at the time of surgery were not available and may have influenced this outcome. Why immediate oral feeds in this regard leads to more major complications, remains unclear.

Although we have been able to identify three interventions that reduce the risk of major complications, they have not been shown to independently do so through our multivariate analyses. This was because of combinations of interventions that were rather center-specific. A few large centers had limited to no complications, and therefore a large impact on the success of specific combinations in limiting the occurrence of major complications.

One year follow up shows us that almost half of the patients experience constipation. This is according to other studies, with recorded constipation rates of 25%-61% [1,36,39]. In our study, mechanical bowel preparation resulted in a significant increase of constipation at 1 year follow up. It is unclear how this intervention is related to constipation. One potential explanation might be that preoperative bowel preparation disturbs the microbiome of the gut, with recolonization by less healthy hospital flora. A prior enterostomy was associated with more diaper rashes, a known complication after enterostomy closure. Anal prolapse was also more present in patients with a prior colostomy. This is possibly more related to the associated problems in this group of patients, particularly sacral anomalies that indicate a lesser developed pelvic floor. Anal prolapse was seen only in 3.9% of our patients, similar to earlier reports [36,40], although 27% has also been described in this type of ARM [41], suggesting potential underreporting in our study.

When we consider the impact of perioperative care in ARM patients with a rectovestibular fistula in this study, we need to appreciate some limitations of the study. Data from the ARM-Net registry are collected prospectively, but the additional questions concerning perioperative care interventions were collected retrospectively. Some degree of error, i.e. misclassifying or omitted data, is inherent. All investigated perioperative interventions show a wide variety of practices, and merging them into groups may introduce type II errors of one specific form of intervention. Furthermore, the indication to treat complications such as a wound dehiscence by surgical interventions instead of by conservative measures, therefore shifting from minor to major complication, is not standardized over the centers. In addition, some major complications, such as a malpositioned anus for which redo surgery was indicated, may not be attributed to perioperative care. With small numbers these issues may have a profound impact on the grading of complications, and therefore its interpretation. Finally, there may remain factors, potentially center-specific, contributing to the occurrence of complications that have not been accounted for.

In conclusion, this study identified differences in perioperative care in European centers of pediatric colorectal expertise. Although there was no evidence to support impact of differences in perioperative care on overall complications, it did show that mechanical bowel preparation, prolonged antibiotic prophylaxis ≥48 h and postoperative nil by mouth feeding all reduced the risk of major complications, with the best protection when combined. Ultimately, these identified protective interventions and its combination, together with determined differences among centers in general, urge us to develop multicenter studies on the topics of this study. We then have to take into account the current best available evidence, and the potential negative impact of these interventions on short term functional outcome, as was seen in our study with mechanical bowel preparation and the associated increase in constipation at one year follow up. Randomizing patients with rare diseases in such trials will be a challenge. Until then, in absence of high level evidence, the ARM-Net consortium and recently established European Reference Networks dealing with congenital malformations of the digestive and urogenital tract [42], will try to reach consensus in the near future. It is well established that standardized care reduces or eliminates institutional and provider-level variation and improves outcomes [43,44]. Guidelines on perioperative care in rectovestibular fistula patients should therefore be developed, preferably extending to all ARM patients, taking into account any cultural, local, or national contextual differences. By doing so, a comprehensive standardized approach to perioperative care is achievable.


References