Diagnosis of intra-abdominal infections and management of catastrophic outcomes
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Outcome of acute intestinal failure management according clinical quality indicators

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Chapter 10

ABSTRACT

Background
Type 2 acute intestinal failure is characterized by the need for parenteral nutrition (PN) for several months and is typically caused by complications of abdominal surgery with enteric fistulas or proximal stomas. This study aimed to evaluate clinical management according to quality indicators established by the Association of Surgeons of Great Britain and Ireland.

Methods
Retrospective cohort study in prospectively registered consecutive patients with type 2 intestinal failure referred to a specialised centre. Study outcomes included success of discontinuation of PN, morbidity and mortality.

Results
Eighty-nine patients were analysed, of whom 57 had enteric fistula, 29 a proximal stoma (some with distal fistula) and 3 intestinal failure due to other causes. One patient was deemed inoperable, while 9 patients died during initial management from their underlying illness. Prior to reconstructive surgery 94 per cent (65 of 66 operated and 4 soon to be operated patients) spent the period of rehabilitation at home. Discontinuation of PN due to restoration of enteral autonomy was achieved in 73 per cent of all patients (65 of 89), 87 per cent of surviving patients (65 of 75), and 83 per cent of patients who underwent reconstructive surgery (55 of 66). Seven patients developed a recurrent fistula, which was successfully managed with a reoperation in 4, eventually resulting in successful fistula takedown of 93 per cent (41 of 44 patients undergoing fistula resection). Postoperative in-hospital mortality was 5 per cent (3 of 66). Overall mortality in present series, including preoperative deaths from underlying diseases, was 16 per cent (14 of 89).

Conclusion
Specialised intestinal failure care and reconstructive surgery resulted in successful discontinuation of PN in the vast majority of patients, although disease related mortality was considerable.
INTRODUCTION

Intestinal failure, originally defined as ‘a reduction in functioning gut mass below the minimal amount necessary for adequate digestion and absorption of food’, was long considered synonymous with chronic dependency of parenteral nutrition (PN). During the last decades, awareness and interest for patients with temporary and reversible intestinal failure has increased. Three types of intestinal failure can be distinguished based on reversibility and duration. Type 1 and 2 are considered acute intestinal failure while type 3 includes chronic conditions associated with the long-term need for PN, such as absolute short-bowel syndrome or chronic intestinal motility disorders.

Type 1 is the most common form of acute intestinal failure and is characterized by a reversible and self-limiting disturbance in intestinal motility, seen in the postoperative period as a paralytic ileus. Specialised care is seldom needed and most cases can be managed conservatively with enteral or parenteral nutritional support during a limited period of time. Type 2 concerns complex patients with the need for PN for several weeks or months. This more severe type of acute intestinal failure typically occurs as a result of a complicated postoperative course following abdominal surgery, characterized by abdominal sepsis, intestinal fistula or the necessity to divert into a proximal stoma. Management and treatment of type 2 acute intestinal failure is complex, prolonged and follows a temporal sequence of various phases. Prompt and adequate treatment of sepsis with early nutritional support is the most important initial aspect. The next phase aims at restoration and maintenance of nutritional status and healing of the peritoneal cavity and abdominal wall. This process takes many months and is essential to enable safe surgical reconstruction. During this period, referred to as ‘bridging-to-surgery’, management is furthermore characterized by challenging skin, wound and stoma care and the difficulties associated with the provision of complex home (nutritional) care. After this necessary bridging period surgery to restore intestinal continuity and function, usually accompanied by reconstruction of the abdominal wall, can be considered when the patients’ status permits and the complete intestinal anatomy is delineated.

Data on both the incidence and outcome of type 2 acute intestinal failure is limited, partly because some patients are being managed in local non-specialized hospitals. Nevertheless, there is general agreement that the management of type 2 acute intestinal failure benefits from a multidisciplinary and specialized approach, not only in terms of morbidity and mortality, but also in weaning of parenteral nutrition and achieving enteral autonomy. In 2010, the Association of Surgeons of Great Britain and Ireland (ASGBI) proposed a set of quality of care indicators for acute intestinal failure.

The aim of this study was to review all patients with acute type 2 intestinal failure referred to a specialized unit and to report and evaluate management and outcome, according to the aforementioned ASGBI quality of care indicators.
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METHODS

All consecutive patients referred to the acute intestinal failure unit of the Academic Medical Centre between January 2011 and October 2014 were prospectively registered in a database. The intestinal failure unit consists of a multidisciplinary staff including a gastrointestinal surgeon, an internist-endocrinologist, specialized dieticians, a TPN nurse, a nurse consultant, wound and stoma care nurses, and a plastic surgeon. The unit has treated patients with chronic intestinal failure and home TPN since 1986 and extended its care towards acute intestinal failure since 2011.

The manuscript was written in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. The Medical Ethics Review Committee of the Academic Medical Centre (Amsterdam, the Netherlands) approved the study protocol and waived the need for written informed consent.

Patient inclusion and data collection

Patients were eligible for retrospective inclusion if they had acute intestinal failure, received PN for more than 28 days and if the intestinal failure was considered potentially reversible (i.e., type 2 intestinal failure). Patients with apparent type 3 or chronic intestinal failure due to absolute short bowel syndrome, intestinal failure due to radiation enteritis or chronic intestinal pseudo-obstruction, or prolonged type 1 intestinal failure (i.e., temporary postoperative PN in stable patients without sepsis or fistula) were excluded. Furthermore, patients referred for a single consultation were also excluded.

After prospective registration, detailed data were retrospectively collected through medical chart review and included patient characteristics, characteristic of the provided nutritional support, details regarding the period of bridging-to-surgery, surgical details, postoperative morbidity and (postoperative) follow-up.

Outcome measures and definitions.

Outcome measures of this study were based on the quality of care indicators established by the Association of Surgeons of Great Britain and Ireland comprising (1) success in discontinuation of parenteral nutrition and (2) success in discontinuation of all types of artificial nutritional support (including parenteral fluids and electrolytes). Additional outcomes regarded morbidity of both medical and surgical management including (3) infection rate of catheters used for administration of parenteral nutritional support, (4) unplanned hospital admissions, (5) reoperation rate after surgery, (6) recurrent fistula rate after surgery for fistula, (7) unplanned postoperative intensive care and hospital readmission rate (within 30 days) and (8) 30-day and in-hospital mortality following surgery, and overall mortality rate.
Outcome of acute intestinal failure management

Aetiology of acute intestinal failure was categorized into enteric fistula, high-output stoma or other. If patients presented with both a stoma and a fistula, intestinal failure was considered to be caused by the orifice with the highest output. Fistulas were classified according to anatomy (enterocutaneous, enterovaginal etc.), output (high-output defined as more than 500cc per 24 hours) and source of fistulation (small intestine, colon). A catheter-related bloodstream infection was defined as positive blood cultures with no other focus for infection. Postoperative complications were graded according to the Clavien-Dindo classification, with grade III or higher regarded as major complications. If a reoperation was performed for recurrent fistula, postoperative follow-up time was calculated as time since the most recent surgery.

Intestinal failure treatment strategy

The specific treatment differed between patients but in general patients were managed using a standardized, multidisciplinary and comprehensive approach. Once acute intestinal failure had established, and the patient was referred, any signs of residual sepsis were aggressively treated with (preferably) percutaneous drainage and antibiotic treatment. To reduce overall output and gastrointestinal (hyper)secretion and to slow gut transition, a short bowel diet, (isotonic) fluid restriction, antimotility drugs, proton pump inhibitors and, on occasion, somatostatin analogues were prescribed. Enteral intake was desirable but the possibility depended on the length of remaining (functional) bowel, the anatomic location of fistulas and stomas, and the effect on manageable fistula output. In general nil by mouth was neither necessary nor desirable and trophic feeding was recommended. Some patients were additionally fed by fistuloclysis, if anatomy was suitable and patients were willing.11 By definition, intestinal failure patients are dependent of parenteral support. PN at home was administered by trained nurses from specialized home care organisations and prepared and delivered according to good manufacturing practice rules by a specialized pharmacy. Patients could be trained in self-administration of PN and central venous catheter care. The use of tunneled single-lumen central venous catheters in the jugular or subclavian vein or a peripherally inserted central catheter is preferred. Catheters are locked with taurolidine (although heparin or saline can be used as well) and all care of central venous catheter is carried out following a strict aseptic protocol.12 In case of a catheter-related bloodstream infection, intravenous systemic antibiotic or antifungal treatment was given according to the results of blood cultures. Removal of the central venous catheter was only performed in case of refractory or ongoing sepsis or blood cultures positive for fungi/yeasts or highly virulent bacteria such as Staphylococcus aureus.

Patients visited the outpatient clinic frequently at 4-, 8- or 12-week intervals, depending on the patient’s condition. Electrolyte and metabolic derangements were addressed (with special interest to parenteral nutrition associated liver disease) and the maintenance of an optimal nutritional status was ensured. Complex large laparostomy wounds with fistulas or nearby
located stomas were frequently seen and required the involvement of specialized wound and stoma care nurses. Protection of skin from fistula or stoma effluents, prevention of infections, and adequate wound and stoma care enabled improvement of patient wellbeing and mobility. If an enteroatmospheric fistula could be isolated it was managed with use of a fistula-adapter and negative pressure wound therapy (100 mmHg). If isolation was not achievable, gauzes were applied covered by a wound manager or stoma bag.

After achieving a stable clinical condition and a good nutritional status, surgical repair of persistent fistulas and/or restoration of intestinal continuity were considered. Postponing reconstructive surgery at least 6 months after the last laparotomy or drainage of abdominal abscesses is rule of thumb. Detailed knowledge of the intestinal anatomy is imperative. Previous operative reports were studied. Oral and enema contrast studies or a MR enterography were used to assess the entire length of small intestine and colon, including segments distal to the fistula or stoma. A contrast-enhanced computed tomography (CT) was made to estimate the size and anatomy of the abdominal wall defect. If considered appropriate, e.g. patients with previous intestinal ischemia or severe cardiovascular comorbidity, patency of the mesenteric blood supply was assessed using CT angiography.

Surgical procedures were based on restoring intestinal continuity and closing the abdomen by reconstruction of the abdominal wall. Fistulating segments of bowel were resected with restoration of continuity by anastomosis, on occasion with constructing a defunctioning ileostomy. The use of non-absorbable synthetic meshes was avoided. Instead, component separation techniques and non-cross-linked biologic mesh (Strattice Reconstructive Tissue Matrix™, LifeCell, Branchburg, New Jersey, USA) were used for abdominal wall reconstruction. Parenteral nutritional support was usually continued postoperatively since recovery or adaptation of adequate gastrointestinal function takes several weeks to months. Outpatient monitoring was continued for at least 6 months or the time it took to successfully discontinue parenteral nutritional support.

**Statistical analysis**

All data were analysed with SPSS® software version 20.0 (IBM, Armonk, New York, USA). Normally distributed continuous data were expressed as mean (standard deviation), non-normally distributed continuous data as median (range). Comparisons between groups were made with use of the chi-square test, Fisher’s exact test or Mann-Whitney-U test, as appropriate.
RESULTS

A total of 179 consecutive patients were referred to the acute intestinal failure unit during the study period. Following chart review, 90 patients were excluded because of parenteral nutritional support for less than 28 days (26), apparent type III intestinal failure due to absolute short-bowel (12), prolonged type I intestinal failure (8), single consultation (9), radiation enteritis or chronic intestinal pseudo-obstruction (12), need for parenteral nutritional support due to malignancy (10), PN as management of postoperative chyle leakage (4), and miscellaneous reasons (9). The remaining 89 patients were included in the present analysis (figure 1).

Patient characteristics

Patient characteristics are depicted in Table 1. Mean age was 60 years (13) and 45 per cent (40 of 89) was female. At presentation, patients already had received parenteral nutrition for a median of 2 months (range 0-9). In 57 patients (64 per cent), intestinal failure was caused by one or more enteric fistulas. Twenty-nine patients (33 per cent) had intestinal failure due to a high-output stoma. Six of the patients with a high-output stoma had concomitant distal fistulas. Two patients were on parenteral nutrition after recent massive small bowel resection for intestinal ischemia with subsequent immediate restoration of continuity, while another patient had undergone massive small bowel resection with a stapled blind ending duodenal loop.

Table 1 Characteristics of 89 patients with type 2 acute intestinal failure referred to a specialised unit

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value 1</th>
<th>Value 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (SD)</td>
<td>60</td>
<td>(13)</td>
</tr>
<tr>
<td>Female, %</td>
<td>40</td>
<td>(45)</td>
</tr>
<tr>
<td>Aetiology of acute intestinal failure, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enteric fistula</td>
<td>57</td>
<td>(64)</td>
</tr>
<tr>
<td>High-output stoma</td>
<td>29</td>
<td>(32)</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>(3)</td>
</tr>
<tr>
<td>Duration of PN at presentation in months, median (range)</td>
<td>2</td>
<td>(0-9)</td>
</tr>
<tr>
<td>History of catheter-related bloodstream infection, %</td>
<td>17</td>
<td>(19)</td>
</tr>
<tr>
<td>Number of previous abdominal operations, median (range)</td>
<td>4</td>
<td>(1-17)</td>
</tr>
<tr>
<td>History of constructed laparostomy, %</td>
<td>42</td>
<td>(47)</td>
</tr>
<tr>
<td>Remaining small bowel length ≤ 150 cm, %</td>
<td>21</td>
<td>(24)</td>
</tr>
<tr>
<td>Remaining colon = hemi-colon or less, %</td>
<td>38</td>
<td>(43)</td>
</tr>
<tr>
<td>Ileocecal valve in situ, %</td>
<td>51</td>
<td>(57)</td>
</tr>
</tbody>
</table>

SD = standard deviation, PN = parenteral nutrition,
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Figure 1 Flowchart depicting patient selection, management and outcome

- 179 Referred patients with intestinal failure
- 90 Patients not fulfilling inclusion criteria
- 89 Patients with type 2 intestinal failure
- 10 Patients managed conservatively
- 1 Patient with no surgical options: type 3
- 3 Patients currently bridging-to-surgery
- 9 Patients died before surgical attempt
- 66 Patients underwent reconstructive surgery
- 1 Patients with chronic parenteral fluid dependency
- 2 Patients with chronic type 3 intestinal failure
- 4 Patients currently in post-operative adaptation phase
- 5 Patients died before discontinuation of PN
- 54 Patients regained enteral autonomy
The majority of the enteric fistulas developed as consequence of a complicated postoperative course following abdominal surgery (53 of 57; 95 per cent). The initial operations had been performed for colorectal carcinoma (12), other intra-abdominal malignancies (9), Crohn’s disease (6), diverticulitis (6), abdominal wall repair (6), intestinal ischemia (5) and miscellaneous (11). In two patients fistulas arose spontaneously due to chronic infection of a synthetic mesh. One patient had an enteric fistula between small bowel and a Bricker ileal conduit due to anastomotic leakage. The remaining fistulas were enterocutaneous or enterocutaneous fistula, all originating from the small bowel (4 patients had a concomitant colocutaneous, enterovaginal or enterovesical fistula). Of the 57 patients with an enteric fistula, 36 (63 per cent) had a fistula classified as high-output, 14 (24 per cent) as low-output, while in 7 (12 per cent) output was unclear. Of the 29 patients with a high-output stoma, 18 (62 per cent) had a jejunostomy and 11 (38 per cent) an ileostomy. Stoma construction was performed during surgery for severe abdominal sepsis (17 of 29; 59 per cent) or resection for intestinal ischemia (12 of 29; 41 per cent).

All patients had a history of abdominal surgery, with a median of 4 (range 1-17) laparotomies. In 47 per cent (42 of 89) of the patients, a laparostomy was constructed during one of these previous operations.

Outcomes of intestinal failure management according to ASGBI criteria

Outcomes of management of all 89 included patients with type 2 acute intestinal failure based on the quality indicators as established by the ASGBI are depicted in Table 2, overall and for patients with intestinal failure (predominantly) due to enteric fistula or high-output stoma separately.

Discontinuation of parenteral nutritional support, overall and after reconstructive surgery

While being managed by the intestinal failure unit for a median duration of 12 months (range 1-45) 65 of 89 patients (73 per cent) achieved enteral autonomy and could be successfully discontinued from PN, and 64 of 89 (72 per cent) from PN including fluids and electrolytes. Successful discontinuation of both PN and all other types of nutritional support was more frequently achieved in patients with intestinal failure due to enteric fistula compared to patients with high-output stoma (p=0.030 and p=0.049, respectively). Of the 89 referred patients with type 2 intestinal failure, ten (11 per cent) were successfully conservatively managed after a median overall duration of nutritional support of 5 months (range 1-11; Figure 1). These ten patients included eight with conservatively managed enteric fistula and two patients who were referred after resection for intestinal ischemia with restoration of continuity during the same procedure. Nine patients (10 per cent) died before surgical restoration was attempted. Death was attributed to an underlying disease in 5 patients, while 4 patients died of sepsis related to
the cause of intestinal failure. One patient was deemed inoperable after thorough analysis, and parenteral nutrition could not be discontinued (i.e. type 3 intestinal failure). Three patients were still in the rehabilitation phase prior to reconstructive surgery.

The remaining 66 patients had undergone reconstructive surgery. With a median postoperative follow-up of 8 months (range 1-13), PN could successfully be discontinued in 55 of these 66 patients (83 per cent). In one of these patients, PN was discontinued but parenteral supplementation of fluids and electrolytes remained necessary. Five patients (5 of 66; 8 per cent) deceased before PN could be discontinued (three patients died postoperatively after a (re)operation for intestinal failure and two died of postoperatively diagnosed metastasised malignancies). The remaining six patients (9 per cent) failed to achieve enteral autonomy despite undergoing surgery with a median follow-up of 6 months (range 3-25 months). The success rate of discontinuation of PN in all surviving patients was 87 per cent (65 of 75 patients).

Infection rate of catheters used for administration of parenteral nutritional support

When all 89 included patients were analysed, the median duration of parenteral nutritional support, while under the care of the team, was 6 months (range 0-37) or 22909 catheter days. During this period, a total of 22 catheter-related bloodstream infections occurred in sixteen patients. Therefore, the overall catheter-related bloodstream infection rate of the study population was 0.96 per 1000 catheter days.

Unplanned hospital admissions

The majority of the 66 surgically managed patients and the 3 patients in the bridging-to-surgery phase were rehabilitated at home. Only four patients remained hospitalised while the remaining 65 (94 per cent) patients could be discharged. Of these 65 discharged patients, 44 (67 per cent) needed no readmission during their rehabilitation period, 15 (23 per cent) had to be readmitted to the hospital once, while 6 (9 per cent) patients were admitted more than once. Most of these unplanned hospital admissions were related to a catheter-related bloodstream infections or an episode of recurrent abdominal sepsis.

Reconstructive surgery and postoperative morbidity

Operative details of the 66 patients undergoing reconstructive surgery are depicted in Table 3. The operation was performed in the referral hospital in 53 of 66 (80 per cent) patients, and in 13 of 66 (20 per cent) patients in the referring hospital, some with assistance of the intestinal failure team surgeon. Surgery was performed after a median of 9 months since the last abdominal intervention (range 3-26). One or more enteric fistulas were resected in the majority of patients (44 of 66; 67 per cent). Restoration of continuity, other than fistula
resection, was performed in 32 patients (48 per cent). In 7 patients (11 per cent) an infected synthetic mesh was removed during surgery. Primary fascial closure was achieved in 55 of 66 patients (85 per cent), if necessary with use of an unilateral or bilateral component separation technique. In 34 of 66 patients (52 per cent) a non-cross-linked biologic mesh (Strattice™) was placed intraperitoneally; in 23 patients as reinforcement of primary fascial closure and in 11 patients as bridging mesh without primary fascial closure despite component separation.

Table 2 Outcomes of 89 patients with acute intestinal failure based on the ASGBI set of clinical quality indicators, overall and for patients with intestinal failure (predominantly) due to enteric fistula or high-output stoma separately

<table>
<thead>
<tr>
<th>Primary outcomes</th>
<th>Overall (n=89)</th>
<th>Enteric fistula (n=57)</th>
<th>High-output stoma (n=32)†</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success in discontinuation of PN, %</td>
<td>65 of 89</td>
<td>46 of 57</td>
<td>19 of 32</td>
<td>0.030</td>
</tr>
<tr>
<td>Success in discontinuation of all types of nutritional support, %</td>
<td>64 of 89</td>
<td>45 of 57</td>
<td>19 of 32</td>
<td>0.049</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Catheter-related bloodstream infections per total number of catheter days, rate per 1000 catheter days</td>
<td>22 per 22909</td>
<td>11 per 12128</td>
<td>11 per 10781</td>
<td>0.302</td>
</tr>
<tr>
<td>Unplanned hospital admissions during rehabilitation phase, %</td>
<td>21 of 65</td>
<td>11 of 40</td>
<td>10 of 25</td>
<td>0.171</td>
</tr>
<tr>
<td>Reoperation rate after reconstructive surgery, %</td>
<td>5 of 66</td>
<td>2 of 42</td>
<td>3 of 24</td>
<td>0.345</td>
</tr>
<tr>
<td>Recurrent fistula rate after first reconstructive surgery for fistula, %</td>
<td>7 of 44</td>
<td>7 of 42</td>
<td>0 of 2</td>
<td>0.704</td>
</tr>
<tr>
<td>Unplanned postoperative intensive care admission rate, %</td>
<td>15 of 66</td>
<td>9 of 42</td>
<td>6 of 24</td>
<td>0.778</td>
</tr>
<tr>
<td>Hospital readmission rate (within 30 days), %</td>
<td>7 of 66</td>
<td>4 of 42</td>
<td>3 of 24</td>
<td>0.662</td>
</tr>
<tr>
<td>30-days postoperative mortality rate, %</td>
<td>2 of 66</td>
<td>2 of 42</td>
<td>0 of 24</td>
<td>0.530</td>
</tr>
<tr>
<td>In-hospital postoperative mortality rate, %</td>
<td>3 of 66</td>
<td>2 of 42</td>
<td>1 of 24</td>
<td>0.702</td>
</tr>
<tr>
<td>Overall mortality rate, %</td>
<td>14 of 89</td>
<td>8 of 57</td>
<td>6 of 32</td>
<td>0.382</td>
</tr>
</tbody>
</table>

PN = parenteral nutrition

† Including three patients who underwent resection for intestinal ischemia and had immediate restoration of continuity (2) or construction of a stapled blind ending duodenal loop (1)
## Table 3 Operative details and postoperative morbidity in 66 patients with type 2 acute intestinal failure undergoing reconstructive surgery

<table>
<thead>
<tr>
<th></th>
<th>Overall (n=66)</th>
<th>Enteric fistula (n=42)</th>
<th>High-output stoma (n=24)†</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time since last abdominal intervention in months, median (range)†</td>
<td>9 (3-26)</td>
<td>9 (3-26)</td>
<td>9 (3-21)</td>
<td>0.523</td>
</tr>
<tr>
<td>Resection of one or more enteric fistulas, %</td>
<td>44 (67)</td>
<td>42 (100)</td>
<td>2 (8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Restoration of continuity*, %</td>
<td>32 (48)</td>
<td>8 (19)</td>
<td>24 (100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Operative time in minutes, median (range)</td>
<td>404 (45-747)</td>
<td>455 (148-747)</td>
<td>218 (45-421)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of constructed anastomoses, median (range)</td>
<td>1 (1-4)</td>
<td>1 (1-4)</td>
<td>1 (1-3)</td>
<td>0.977</td>
</tr>
<tr>
<td>Removal of infected synthetic mesh, %</td>
<td>7 (11)</td>
<td>7 (17)</td>
<td>0 (0)</td>
<td>0.035</td>
</tr>
<tr>
<td>Component separation technique performed, %</td>
<td>41 (62)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral</td>
<td>6 (9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral</td>
<td>35 (53)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary fascial closure achieved, %</td>
<td>55 (85)</td>
<td>31 (74)</td>
<td>24 (100)</td>
<td>0.004</td>
</tr>
<tr>
<td>Implantation of biologic mesh (IPOM), %</td>
<td>34 (52)</td>
<td>28 (67)</td>
<td>6 (25)</td>
<td>0.002</td>
</tr>
<tr>
<td>Sublay reinforcement</td>
<td>23 (35)</td>
<td>17 (41)</td>
<td>6 (25)</td>
<td></td>
</tr>
<tr>
<td>Bridging</td>
<td>11 (17)</td>
<td>11 (26)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Postoperative complication grade III or IV according to the Clavien-Dindo classification, %</td>
<td>26 (39)</td>
<td>15 (36)</td>
<td>11 (46)</td>
<td>0.418</td>
</tr>
<tr>
<td>Reoperation during admission, %</td>
<td>5 (8)</td>
<td>2 (5)</td>
<td>3 (13)</td>
<td>0.250</td>
</tr>
<tr>
<td>Length of postoperative hospital stay in days, median (range)</td>
<td>20 (4-104)</td>
<td>22 (6-104)</td>
<td>18 (4-71)</td>
<td>0.193</td>
</tr>
<tr>
<td>Readmission within 30 days, %</td>
<td>7 (11)</td>
<td>4 (10%)</td>
<td>3 (13)</td>
<td>0.502</td>
</tr>
<tr>
<td>Recurrent fistula, %‡</td>
<td>7 (16)</td>
<td>7 (17)</td>
<td>0 (0)</td>
<td>0.820</td>
</tr>
<tr>
<td>Resolved by reoperation, %‡</td>
<td>4 (9)</td>
<td>4 (10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unresolved due to death before or following reoperation, %‡</td>
<td>3 (7)</td>
<td>3 (7)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IPOM = intraperitoneal onlay mesh

† Including one patient who underwent resection for intestinal ischemia and with construction of a stapled blind ending duodenal loop

* Excluding patients with a spontaneous fistula

* Restoration of continuity, other than restoration achieved by fistula resection, by stoma reversal or anastomosis of blind bowel loops; not per se meaning that all remaining intestinal segments were connected

‡ Of all patient undergoing fistula resection
No patients with intestinal failure due to a high-output stoma had bridged repairs compared to 11 of 42 patients with enteric fistula (p=0.004). Furthermore, a biologic mesh was more frequently used during reconstructive surgery for enteric fistulas compared to surgery for high-output stomas (28 of 42 (67 per cent) versus 6 of 24 (25 per cent), p=0.002).

A total of 26 of 66 patients (39 per cent) developed a major postoperative complication graded as III or IV according to the Clavien-Dindo classification. Four patients (4 of 66; 6 per cent) underwent a reoperation because of anastomotic leakage, whereas one patient was reoperated because of a stenotic jejunal segment. One patient died 50 days postoperative after restoration of continuity and abdominal wall reconstruction due to end-stage heart failure superimposed on pre-existing severe heart failure. Of the 66 patients undergoing reconstructive surgery, 15 (23 per cent) developed a complication requiring intensive care management. The 30-day hospital readmission rate was 11 per cent (7 of 66 patients).

Of the patients in whom one or more enteric fistulas were resected, 7 of 44 (16 per cent) developed a recurrent fistula. In four patients the recurrent fistula was successfully resolved by reoperation, resulting in an overall success rate of fistula takedown of 93 per cent (41 of 44). Two patients underwent a reoperation for recurrent fistula but subsequently died postoperatively due to abdominal sepsis and multi-organ failure. The remaining patient with a recurrent fistula was diagnosed with metastasised recurrent rectal cancer, received best supportive care and deceased four months after the initial reconstruction.

**Postoperative and overall mortality rate**

The 30-day and in-hospital mortality rate among the patients undergoing the 66 initial reconstructive surgeries and 6 reoperations combined was 3 per cent (2 of 66) and 5 per cent (3 of 66), respectively. Overall mortality for all 89 included patients with acute intestinal failure while being managed by the intestinal failure team for a median duration of 12 months (range 1-45 months), including deaths from underlying diseases, was 16 per cent (14 of 89 patients).

**DISCUSSION**

To increase awareness and offer guidance and advice on management of type 2 intestinal failure, the Association of Surgeons of Great Britain and Ireland has published a booklet in 2010, including clinical indicators to assess quality of care. This retrospective study of a prospectively registered consecutive cohort of patients with type 2 acute intestinal failure managed by an intestinal failure referral centre reported outcomes according to the ASGBI clinical indicators. In present series, parenteral nutrition could be discontinued after conservative management in a minority of patients, but in the vast majority of patients after reconstructive
surgery. During the essential rehabilitation period prior to surgical reconstruction almost all patients were safely discharged home without compromising central venous catheter care, as demonstrated by acceptable catheter-related bloodstream infection rates and readmission rates. Discontinuation of PN due to restoration of enteral autonomy was achieved in 73 per cent of all patients (65 of 89), 87 per cent of surviving patients (65 of 75), and 83 per cent (55 of 66) of patients undergoing reconstructive surgery.

Interest in type 2 acute intestinal failure has increased over the past decades, and several publications have reported on the most important aspects of management. However, few data on cohorts of acute type 2 intestinal failure patients are available. Although there are multiple large published series of patients with enterocutaneous fistula, most included patients are without the need for parenteral nutritional support and predominantly focussed on surgical outcome and postoperative morbidity. Moreover, only few reported on other aspects and complications of (preoperative) management such as catheter-related bloodstream infections.

In general, all patients in the present study developed intestinal failure in the setting of an intra-abdominal catastrophe, illustrated by the high number of previously performed abdominal surgeries. The majority of patients had intestinal failure due to loss of functional bowel length associated with the presence of one or more postoperative enteric fistula. Fistula as the main cause of intestinal failure has been described previously. Especially fistula in conjunction with an open abdomen or laparostoma, so called entero-atmospheric fistula, are at risk of causing severe intestinal failure. In present series, 47 per cent of patients presented with a laparostoma. A constructed proximal stoma was the main reason of intestinal failure in the patients without fistulas. Not all patients with a proximal stoma classified as high-output stoma. This is most likely explained by the fact that all patients were already on parenteral nutrition and fluid restriction, although enteral intake according to the short bowel diet recommendations was allowed and stimulated.

Only few patients achieved enteral autonomy conservatively. Eight of the conservatively managed patients had spontaneous closure of a fistula, resulting in a spontaneous closure rate of 14 per cent (8 of 57 patients with fistula). This rate is somewhat lower than described spontaneous closure rates in literature but can be explained by the fact that the patients in this cohort were referral patients, mostly referred due to complexity or after an attempt to spontaneous closure was not accomplished.

It is generally accepted that surgical restoration should be delayed for several months in order for the patient to rehabilitate and a neoperitoneum to form. A minimum of six months since the last abdominal intervention is frequently advocated as preferred period. Preferably, patients spend this period at home. In present series, with only a few exceptions all patients deemed to undergo reconstructive surgery could be discharged and managed at home. An expert support team and dedicated pharmacy for the provision of home PN is essential,
and can reduce catheter-related bloodstream infection rate, one of the most frequent and serious complications of PN. The catheter-related bloodstream infection rate in present series falls within the range of 0.38 to 4.58 episodes per 1000 catheter days reported in literature on adults receiving home parenteral nutrition.

Reconstructive surgery was associated with considerable morbidity. Despite advances in care and surgical technique, high rates of postoperative morbidity are still being described. Postoperative in-hospital mortality in present series is comparable to the range of 2-5 per cent reported in published series. Recurrence fistula rate was also comparable to previous reports (11-30 per cent described in literature).

In total, 73 per cent (65 of 89) successfully achieved enteral autonomy. The majority of patients who did not successfully achieve enteral autonomy died prior to surgery or postoperatively, due to an underlying disease or sepsis. The overall mortality in present series was considerable, illustrates the severity of the disease and is comparable to overall mortality rates in other series. The number of patients who remained dependent of PN after undergoing reconstructive surgery was 9 per cent (6 of 66 operated patients), while in another patient parenteral supplementation of fluids and electrolytes remained necessary. In some patients dependency was decreasing so discontinuation can still be hoped for. Owen et al. reported a rate of postoperative chronic PN dependency of 14 per cent after surgical treatment of enterocutaneous fistula. However, they also included patients with a preoperative diagnosis of absolute short-bowel syndrome, while in the present study, patients in whom achieving enteral autonomy was deemed impossible due to absolute short-bowel were excluded. Other comparative data on achievement of enteral autonomy in type 2 intestinal failure patients is scarce and the different underlying conditions make generalised prognoses difficult.

Several limitations of this study need to be addressed. Firstly, it can be argued that the inclusion of both patients with fistulas and patients with a proximal stoma makes present study population heterogeneous. Indeed, some aspects differ between these two possible aetiologies of acute intestinal failure, such as the chance of spontaneous healing (closing of a fistula). However, most aspects of management of acute intestinal failure, whether caused by a proximal stoma or an enterocutaneous fistula, are comparable. The importance of adequate sepsis control, the difficulties of provision of (home) parenteral nutrition, fluids and electrolytes support, the challenging wound and skin-care, and the complexity of surgery with respect to gaining access to the abdominal cavity and performing adhesiolysis in patients with a history of multiple abdominal surgeries; all these issues are encountered in all patients with acute intestinal failure. Another potential limitation is the lack of data on initial sepsis control because most of the patients were referred after the initial phase. However, although sepsis is the most common cause of death in patients with acute intestinal failure and adequate treatment is essential, care for septic patients is based on several general treatment principles.
which fall outside the scope of this article.\textsuperscript{21} A final limitation is the retrospective nature of data on patient history prior to referral.

With the introduction of clear definitions and a set of quality measures, the first steps towards more uniform data and evidence on acute intestinal failure has been made. The use of similar definitions and outcome measures enable benchmarking and introduction of new ways to improve care, organisation and ultimately outcome.
REFERENCES


