Nutritional Support in Gastrointestinal Disease

Module 12.3

Nutrition and Gastrointestinal Fistulas

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Learning objectives

- To learn about the general management of patients with gastrointestinal fistulas;
- To learn about the nutritional management of patients with gastrointestinal fistulas;
- To learn about the metabolic and nutritional complications of patients with gastrointestinal fistulas.

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Key messages

- The development of enterocutaneous fistulas is a major gastrointestinal complication with high morbidity and mortality requiring phased specialised treatment;
- Treatment focuses on controlling sepsis, optimisation of nutritional status, wound care, anatomical evaluation of the fistula, timing of surgery, and surgical strategy;
- 55-90% of the patients with an enterocutaneous fistula becomes malnourished, because of a combination of illness and starvation;
Nutritional screening and subsequent assessment provide important information regarding nutritional status and requirements;

Enteral nutrition has many advantages over parenteral nutrition and is the preferred route of nutrition;

Short bowel syndrome, ileus, high fistula output leading to malabsorption, are indications for parenteral nutrition;

The duration of convalescence must be at least six weeks to control sepsis, to clear inflammatory activity and regain normal body composition and function (normal nutritional status);

The majority of patients remains does not require additional artificial nutritional support after fistulas closure.
1. Introduction

Gastrointestinal fistulas are abnormal communications between the intestinal tract and another hollow organ, the skin or a distant part of the gut (1). Usually, they develop in patients who already suffer from severe illness, and they contribute considerably to morbidity and mortality. Especially fistulas in continuity with the skin (enterocutaneous fistulas; ECF) can lead to severe complications associated with a compromised gut (2). Intestinal content exits the body through the fistula and the distal gut is excluded from the absorption process (Fig. 1). Consequently, patients lose (macro)nutrients, fluid and electrolytes (3) through the fistula and absorption is limited to the intestine proximal of the fistula, resulting in malnutrition.

Fluid and electrolyte imbalances, malnutrition and infectious complications significantly influence outcome. Several developments and accumulating experience have led to a guided approach that has reduced mortality from 40% to 5-15% (4-6). Nevertheless, treatment remains complex and challenging to doctors, nutritional specialists, nurses, etc. The complications of ECF’s and the difficulties with their (nutritional) management are therefore the focus of this module and they are discussed below in more detail.

Figure 1 Enterocutaneous fistula in an abdominal wall defect

2. Pathogenesis of the ECF

A minority of ECF’s develops spontaneously (10-25%) as a result of Crohn’s disease, cancer or radiation damage and diverticulitis (the latter commonly leading to low-output fistulas) (4, 6-9). The majority of ECF’s (75-90%) occur postoperatively mainly because of iatrogenic lesions or suture failure in patients with malignancy of the digestive tract, Crohn’s disease or infectious diseases of the bowel (4, 6, 7, 10). The major risk factor for infectious complications, promoting ECF formation, includes malnutrition, including weight loss, low fat free mass and inflammatory activity.
Table 1 Common causes of fistula formation

<table>
<thead>
<tr>
<th>Formation</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous</td>
<td>Crohn’s disease</td>
</tr>
<tr>
<td>10-25%</td>
<td>Cancer</td>
</tr>
<tr>
<td></td>
<td>Diverticulitis</td>
</tr>
<tr>
<td></td>
<td>Radiation enteritis</td>
</tr>
<tr>
<td>Surgical</td>
<td>Iatrogenic lesion (sutures)</td>
</tr>
<tr>
<td>75-90%</td>
<td>Anastomotic failure</td>
</tr>
<tr>
<td></td>
<td>Abdominal wall dehiscence</td>
</tr>
<tr>
<td></td>
<td>Mesh rupture</td>
</tr>
<tr>
<td></td>
<td>Drain puncture</td>
</tr>
<tr>
<td>Traumatic</td>
<td>Diagnostic intervention (puncture)</td>
</tr>
<tr>
<td>&lt;5%</td>
<td>(Traffic) accident</td>
</tr>
</tbody>
</table>

3. Management of ECF

3.1 Treatment strategy

Patients with enterocutaneous fistulas fortunately are rare occurrences in the careers of individual surgeon. Their incidence is low and they comprise a very heterogeneous population. RCT’s of this population are therefore very difficult to perform. Evidence mainly depends on cohort studies, case reports and expert opinion, which has led to an experience guided approach of fistula treatment, which has proven its clinical value (6, 9). A modest number of institutes has contributed to the development of practical guidelines (6, 11-13). In order of priority, the treatment strategy consists of treatment of sepsis, optimisation of nutritional status, wound care, anatomical evaluation, timing of surgery and surgical procedure (Table 2). Treatment implies a multidisciplinary approach adjusted to the individual needs of the patient.

Table 2 Treatment of patients with ECF according to the SOWATS guideline

<table>
<thead>
<tr>
<th>Step</th>
<th>Considerations and action</th>
</tr>
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<tbody>
<tr>
<td>Sepsis control</td>
<td>Signs of sepsis</td>
</tr>
<tr>
<td></td>
<td>Radiological drainage of abscesses</td>
</tr>
<tr>
<td></td>
<td>Relaparotomy on demand</td>
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<tr>
<td>Optimization of nutritional</td>
<td>Rehydration and electrolyte supplementation</td>
</tr>
<tr>
<td>status</td>
<td>Parenteral/enteral nutrition</td>
</tr>
<tr>
<td>Wound care</td>
<td>Wound care with wound managers</td>
</tr>
<tr>
<td></td>
<td>Sump suction</td>
</tr>
<tr>
<td>Anatomy of the bowel and</td>
<td>Contrast fistulography</td>
</tr>
<tr>
<td>fistula</td>
<td>Contrast enhanced MRI or CT imaging</td>
</tr>
<tr>
<td></td>
<td>Visualisation of the length of the intestine and the localization of the origin of the</td>
</tr>
<tr>
<td></td>
<td>fistula tract</td>
</tr>
<tr>
<td></td>
<td>Stenosis, obstruction, fluid collection</td>
</tr>
<tr>
<td>Timing of surgery</td>
<td>Clinically stable</td>
</tr>
<tr>
<td></td>
<td>Normalisation of laboratory values</td>
</tr>
<tr>
<td></td>
<td>&gt; 6 weeks after fistula development</td>
</tr>
<tr>
<td>Surgical strategy</td>
<td>Restore continuity</td>
</tr>
<tr>
<td></td>
<td>Careful dissection of the bowel</td>
</tr>
<tr>
<td></td>
<td>Cover sutures with healthy viable tissue</td>
</tr>
<tr>
<td></td>
<td>Stay away from compromised area</td>
</tr>
</tbody>
</table>
3.2 Treatment of septic complications

3.2.1 Diagnosis of abdominal infection and sepsis
Sepsis is the most common accompanying problem in the development of a fistula and the leading cause of death (5, 6, 14-17). The primary disease leading to fistula formation often includes inflammatory activity. The fistula is developing from a intestinal defect (spontaneous or surgical) leading to leakage of intestinal contents into the abdominal cavity, in turn leading to abscess formation or/and peritonitis. This often leads to sepsis which is difficult to treat. Adequate drainage or exclusion of the defect is necessary to treat sepsis. Primary closure of the intestinal defect is often impossible, so that adequate drainage often leads to a fistula with little accompanying infectious activity. In the septic period before the fistula has matured and drained mortality is high.

Therefore it is imperative to recognise early signs of sepsis. These are sometimes blunted because many patients with ECF’s are often severely malnourished and do not show clear signs of infection (fever, pus formation etc.). Clinical signs of sepsis include fluid retention and oedema, jaundice, organ failure and (not always) fever. Patients display laboratory signs of inflammation, including increased CRP, decreased, leucocytosis with lymphopenia, low haemoglobin, reduced plasma albumin and transferrin levels and liver test abnormalities. To achieve anabolism it is necessary to identify and treat the septic focus and to install nutritional support. Antimicrobial therapy alone will not resolve an abdominal abscess. However, patients with pneumonia or urinary tract infections will benefit from antibiotics. A central venous catheter must always be removed in case of sustained fever and the catheter tips should be cultured. When fever subsides a new lines can be re-inserted after 24 hours to resume parenteral nutrition (PN). Loss of oedema and subsequent weight loss, wrinkling of the skin, a negative fluid balance etc. indicate that sepsis and inflammatory activity subsides.

3.2.2 Albumin
Albumin decreases as it becomes redistributed over the extra-vascular interstitial space, which increases substantially in volume during trauma and sepsis. In many disease states fractional synthesis rates of albumin are increased. A low albumin level is therefore a sign of the stress response in disease and inflammation and is associated with a negative outcome of treatment in patients with an ECF (6, 18). Nutritional support cannot normalise serum albumin levels in the presence of ongoing inflammation but promotes the adequacy of host defense and accelerates recovery when the inflammatory activity diminishes. An increasing albumin level is always a good sign and signifies that the stress response abates. There is no evidence that supplementation of albumin is of benefit and it may even have adverse effects (19). See also module nutritional screening and assessment.

3.3 Nutritional management

3.3.1 Malnutrition
Malnutrition can be defined as a condition in which a combination of varying degrees of over- or undernutrition and inflammatory activity causes measurable adverse effects on tissue/body form (body shape, size, and composition), body function and clinical outcome. Many patients with ECF’s show signs of malnutrition prior to fistula formation increasing the risk for its development. Most patients with an established ECF suffer from inadequate food intake and excessive loss of gastrointestinal contents in combination with an increased energy expenditure associated with the inflammatory state. This leads to stress starvation in which the normal adaptive responses of starvation without inflammation or infection, including conservation of body protein, are overridden by the neuro-endocrine and cytokine effects of inflammation. Metabolic rate rises rather than falls, ketosis is minimal, protein catabolism accelerates to meet the demands for tissue repair and for gluconeogenesis and there is hyperglycaemia and glucose intolerance. Subsequently, between 55 and 90% of patients with an ECF become severely malnourished (14, 20, 21). This decreases the capacity of the patient to heal and increases the susceptibility to infection. Edmunds et al. and Chapman et al. demonstrated that malnutrition in patients with fistulas resulted in increased morbidity and mortality (14, 15). In the 1970s it was generally accepted that adequate nutrition should be an essential part of conservative and operative

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fistula treatment. Techniques to administer enteral and parenteral nutrition rapidly improved and were successfully used in these complicated patients (Fig.2) (22, 23).

![Flow chart of nutritional management](image)

**Figure 2** Flow chart of nutritional management

### 3.3.2 Nutritional screening and assessment
Nutritional screening and assessment provides information about the risk of malnutrition and the basic energy requirements. Weight loss, body mass index, food intake and disease severity are easy screening measures during treatment. The Nutritional Risk Screening 2002 combines these parameters and can be used easily. Other validated tools include the Malnutrition Universal Screening Tool and the Subjective Global Assessment.

In patients who appear at risk according to the nutritional screening, a detailed assessment is advised in order to develop a nutritional plan. Because needs of patients with ECF depend on inflammatory activity, nutrient loss and co-morbidity, more sophisticated tools are of more value in these situations (see also Topic 3).

### 3.3.3 Enteral nutrition
EN has several advantages over PN. It has been claimed to reduce the inflammatory response (24), maintains the enterohepatic circulation and the secretion of slgA (25), maintains gut function and structure (26), decreases bacterial overgrowth (27), avoids intravenous access complications (28), and has been claimed to decrease organ failure (29). However, in severe illness leading to multiple organ dysfunction syndrome, bowel function is compromised and enteral nutrition is not always tolerated. Especially patients with a high output small bowel fistula may have all the symptoms of short bowel syndrome and need nutritional support (see also Module 12.2). Complications caused by EN include aspiration, diarrhoea, misplacement of the tube, nausea/vomiting, adynamic ileus. They therefore require intensive follow up and monitoring.
The general considerations for enteral nutrition also apply to patients with an ECF. An enteral intake of 500 ml clear fluids per day is always allowed for psychological reasons and to exploit the beneficial effects of intraluminal intake: maintenance of intestinal mass and structure, diminution of bacterial overgrowth and improvement of intestinal immune function. It has also been claimed that EN blunts the hypermetabolic stress response (30). Restriction of enteral nutrition to 500 ml/day has been applied because this was considered to promote spontaneous closure of suitable fistulas, and to facilitate wound care by diminution of fistula output. At present artificial enteral nutrition is administered more liberally.

Techniques have been described to administer proximal secretions of the intestine or/and a nutrition formula into the intestine distal to the ECF. A first technique involves collection of succus intestinalis and reinfusion into the distal part of the intestine. Reinfusion of secretions from high output proximal stomas or fistulas into the distal defunctionalised part of the small bowel has proven to normalise alkaline phosphatase, γ-glutamyl transpeptidase and bilirubin in patients with ECF-associated liver disease and PN (10). Refunctionalisation of the gut restores liver abnormalities implying that a non-functioning gut, including a disrupted enterohepatic circulation, has toxic effects on the liver. These methods can be considered when parenteral nutrition associated cholestasis, hepatic steatosis and hypertriglyceridemia develop (31). A second technique is fistuloclysis, in which nutritional formulas are infused into the intestine distal to the fistula. In preparation of the restorative procedure fistuloclysis has been successfully applied in 11 out of 12 patients in a study by Teubner et al (32).

3.3.4 Parenteral nutrition
Patients who are not able to meet nutritional demands through the enteral route alone benefit from parenteral supplementation in order to maintain or improve nutritional status. Especially in patients with small bowel ECF and high output ECF, the intestine distal to the fistulous tract is not involved in the absorption process resulting in malabsorption. Furthermore, high output fistulas may cause difficulties during wound care when enteral nutrition is provided. Severe sepsis and ileus also contraindicate enteral intake. The great advantage of PN has been that it allowed postponement of surgical intervention in severely ill patients in whom re-operation would be extremely hazardous, but who could not be fed adequately enterally because of their high-output fistulae or because of intolerance for enteral nutrition due to sepsis (5, 33). PN can at least maintain or slow down deterioration of nutritional status during this period. PN also has been claimed to contribute to the rate of spontaneous closure of enterocutaneous fistulas with low but also with high output (22).

3.3.5 Parenteral fat
Patients normally receive parenteral nutritional formulas containing tri-acylglycerols, containing long chain fatty acids (LCFA). LCFA provide the patient with essential fatty acids and also furnish a caloric source. However, the clearance of LCFA is not always optimal causing liver steatosis which is also promoted by chronic underlying disease. The LCFA administration can lead to steatohepatitis and results in insulin resistance by cytosolic fat accumulation and overproduction of reactive oxygen species, mainly from beta-oxidation (34). Several other lipid solutions are available but their value in clinical practice is not yet fully established. Structured triacylglycerols (STG) are lipid solutions containing triglycerides in which the glycerol backbone is randomly esterified with medium chain fatty acids (MCFA) or LCFA. MCFA are metabolised more rapidly because its transfer occurs independent from cell membrane transport proteins, are released into the portal venous system and allow the administration of lesser amounts of LCFA, diminishing their negative effects. Compared to the standard lipid emulsions, STG may result in lower triglyceride and fatty acids levels, less ketosis and metabolic acidosis and possibly less liver dysfunction especially in patients receiving long-term parenteral nutrition (35). Recent reports indicate that STG improve nitrogen balance and cause fewer disturbances in liver enzymes and bilirubin clearance than the standard LCFA containing lipid emulsions (36).

In addition to PN, sepsis and high output fistulas also relate to disturbances in lipid metabolism. Cytokines, such as TNF-α, up-regulated during sepsis, directly inhibit lipoprotein lipase causing an increase in triglyceride concentration. Exclusion of the distal bowel and loss of proximal gut secretions
lead to a disruption in the enterohepatic cycle (bile acid pool) and subsequently in lipid metabolism. Reinfusion of secretions from high output proximal small bowel fistulas aims to restore this cycle and has proven its effectiveness in restoring liver test abnormalities (10). Other treatment options are hardly described but withholding lipid emulsions from the nutritional regimen has proven its clinical effectiveness.

Immunonutrition (glutamine, arginine, omega-3 fatty acids, and nucleotides) may be of benefit in patients with ECF’s. Their efficacy has not been investigated specifically in patients with ECF’s, but extrapolating from surgical patients they may reduce infectious complications and length of hospital stay (37, 38, 39).

3.4 Wound care

3.4.1 The problematic wound
ECF can produce staggering amounts of fluid. A high output fistula is defined as a fistula producing more than 500 ml of enteral secretions per 24 hours, and is very often associated with malnutrition. An output volume between 200 ml and 500 ml per 24 hours is regarded by some authors as a moderate output fistula and leads in most cases to mild but significant malnutrition if not nutritionally supported. When fluid loss is less than 200 ml per 24 hours, the fistula is defined as a low output fistula (1, 40). In addition to fluid, electrolytes and nutrients, the fistula output contains proteolytic enzymes and bile acids that damage the skin surrounding the external opening. The skin becomes red, painful and macerated and loses its normal barrier function leading to infection. Healthy cutaneous tissue is essential for proper abdominal closure during the restorative procedure. Healthy granulating skin defects with showing successful epithelialization and the absence of pus indicate that sepsis is controlled and the patient is becoming anabolic.

Normally, the abdominal wound is odourless. A foul smelling wound indicates an infection with mainly anaerobic bacteria (41) which can be treated with proper management, cleaning and antibiotics (42). The granulating process may also be hampered by the infectious state originating from other parts of the body.

3.4.2 Treatment of wound surfaces
A dedicated team of wound nurses is of great value for proper wound and stoma care, collection of intestinal output and wound discharge, and for proper skin protection. An large array of products is available, including powders, pastes, adhesions materials, barriers, wound bags, etc. Fistulas with a single orifice and intact skin will suffice with a silicone barrier surrounding the fistula after cleaning and drying of the skin. The fistulas residing in an abdominal wall defect constitute the biggest challenge and present more frequently during the past decades (6, 17, 43). The fistula in a large abdominal wall defect is treated most adequately with a wound manager, with or without sump suction. Placement of a suction drain causes a slight vacuum in the bag resulting in a constant diversion of fluid from the wound. This system also creates a moist environment stimulating the production of healthy granulating tissue (Fig. 3).
3.4.3 Supportive methods in wound care
Proton pump inhibitors reduce gastric acid secretion. Somatostatin analogues are not routinely advised. It can be used to reduce output (44), facilitating wound care and possibly accelerating the closure of suitable fistulas. There is no advantageous effect on outcome (45). If the output remains unchanged within the first 48 hours administration can be discontinued.

The application of a vacuum assisted closure technique has been suggested to be of benefit but applied to bowel exposed in an abdominal wall defect is more likely to cause damage to the bowel than to promote fistula and wound closure (46).

3.5 Anatomical evaluation
Oral ingestion of methylene blue and subsequent effusion from the skin proves the presence of a fistula, but the diagnostic method is only reliable in very high proximal fistulae. If the fistula is in the lower jejunum or ileum the methylene blue is absorbed, colouring plasma serum, interstitial fluid and intestinal secretions. Analysis of the fistula fluid is an easy method to establish the origin of the fistula. A biliary fistula mainly contains bilirubin, a pancreatic fistula contains amylase whereas a small bowel fistula contains both in relatively high amounts. For a complete evaluation of the fistula tract, radiological imaging with water-soluble contrast (fistulography) remains vital (47). Computer tomography with enteral and intravenous contrast enhancement provides information regarding the location of the fistula, length of the intestine proximal and distal to the origin of the fistula and the presence of abscesses, stenoses and obstructions (48).

3.6 Monitoring and timing of re-intervention
Spontaneous closure ranges from 20 to 70% and depends on many variables (Table 3) (6, 8, 9, 22, 43, 49). The majority of ECF’s will need operative closure. Before planning the restorative procedure the patient must be in a stable healthy condition, both physically as well as mentally. The patient must be
willing to proceed with the operation to close the fistula and feel confident that outcome will be successful. Improved health status is characterized by the fact that the patient is mobile, is interested in his/her surroundings and is eager to return home.

Clinical signs of improvement include reduction of oedema, a negative fluid balance and increased muscle strength. Infection parameters must normalise and the plasma albumin level must increase to normal or near-normal level (18, 50). Abatement of sepsis allows improvement of the nutritional status. Before the introduction of parenteral nutrition the restorative procedure was performed early because nutritional state deteriorated due to the inability to nourish adequately. This led to a high mortality rate (15). Since the introduction of parenteral nutrition it has been possible to postpone surgical intervention until sepsis has been adequately treated and patient’s health status is stabilised (51).

A minimal period of six weeks is required for the abdomen to become accessible again. Before that period adhesions are too dense and can not be dissected properly without inducing secondary lesions (6, 16). During that period the patient Most authors advise a three to six months waiting period, although no additional advantage in survival has become apparent (4, 11-13). Low albumin level has undeniably been associated with negative outcome and should normalise before commencing the restorative procedure (6, 18, 20). Other undisputed variables negatively associated with outcome include sepsis (49) and high APACHE II score (18). Additional variables include location of the jejunum, presence of multiple fistulas (20) and high output ECF (49).

Table 3 Factors associated with failure of an ECF to close spontaneously

<table>
<thead>
<tr>
<th>Major dehiscence of the anastomoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short fistula tract</td>
</tr>
<tr>
<td>Distal obstruction</td>
</tr>
<tr>
<td>Epithelialised fistula tract</td>
</tr>
<tr>
<td>Sepsis or nearby abscess cavity</td>
</tr>
<tr>
<td>High output ECF</td>
</tr>
<tr>
<td>Fistula in an abdominal wall defect</td>
</tr>
<tr>
<td>Non-surgical cause</td>
</tr>
<tr>
<td>Referrals</td>
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<tr>
<td>Jejunoileal ECF</td>
</tr>
</tbody>
</table>

**3.7 Surgical strategy**

At present 60 to 80% of patients will usually require a restorative procedure which is successful in 85 to 90% of these cases (6, 9, 20). This constitutes 45-70% of the overall closure rate.

The restorative operation is a laborious process and should be performed with utmost patience. Abdominal access has become difficult and freeing of the bowel is fraught with renewed damage to the bowel because of dense adhesions. Subsequently, the fistula tract including the diseased part of the bowel should be cleaned and excised as much as possible. Anastomoses must be covered with healthy surrounding tissue. In these situations it is often difficult to close the muscle/fascia layers of the abdominal wall. The remaining defect is therefore closed with two-three layers of bio-degradable Vicryl mesh and the skin is closed over it.

**4. Recovery**

After the restorative procedure for many patients a long period of rehabilitation follows. The chronic inflammatory state has often led to substantial loss of muscle mass which requires months to years to restore. In severe cases the patients a long rehabilitation process under the guidance of a rehabilitation physician and a physiotherapist. The quality of life in these patients is in the long run satisfactory.
A minority of patients has insufficient intestine left to assure adequate absorption of nutrients and remains dependent on supplementary home parenteral nutrition. These patients require lifelong guidance and specialized support (see Module 13.2 and Topic 19).

5. Summary

Metabolic and nutritional complications in patients with an ECF are associated with high morbidity and mortality. Treatment aims are directed towards achieving anabolism by resolving sepsis and by instituting nutritional support. Intensive and complex nutritional and metabolic support creates a favourable basis for spontaneous closure of ECF’s or for successful surgical closure.

References


