Gastrointestinal fistulae are usually very serious complications and are associated with high morbidity and mortality rates. They allow abnormal diversions of gastrointestinal contents, digestive juices, water, electrolytes, and nutrients from one hollow viscous to another or to the skin, thus causing a wide variety of pathophysiological effects. Fistulae can also prolong the patient’s hospital stay, which has obvious cost implications. Although gastrointestinal fistulae can occur spontaneously in IBD (for example, diverticular disease of the colon), cancer, or radiation enteritis, most fistulae are postoperative fistulae. Abdominal trauma can also lead to fistula formation although this is rare. Postoperative gastrointestinal fistulae can occur after any abdominal procedure in which the gastrointestinal tract is manipulated. Regardless of the cause, leakage of intestinal contents initiates a cascade of events: localized infection, abscess formation and, as a result of a septic focus, fistulae formation. The nature of the underlying disease may also be important, with some studies showing that fistula formation is more frequent following surgery for cancer than for benign disease. Fistula formation can result in a number of serious or debilitating complications, ranging from disturbance of fluid and electrolyte balance to sepsis and even death. The patient will almost always suffer from severe discomfort and pain. They may also have psychological problems, including anxiety over the course of their disease, and a poor body image due to the malodorous drainage fluid. Postoperative fistula formation often results in prolonged hospitalization, poor quality of life, and enormous cost. Therapy has improved over time with the introduction of parental nutrition, intensive postoperative care, and advanced surgical techniques, which has reduced mortality rates. However, the number of patients suffering from gastrointestinal fistulae has not declined substantially. This can partially be explained by the fact that with improved care, more complex surgery is being performed on patients with more advanced or complicated disease who are generally at higher risk. Therefore, gastrointestinal fistulae remain an important complication following gastrointestinal surgery.

The absolute definition of what constitutes a fistula is still unclear. For example, some studies have defined a pancreatic fistula as increased amylase/lipase in the drainage fluid for 3–4 days postoperatively with a drainage volume of >10 ml/day. However, other studies have defined a fistula as draining >50 ml/day. This latter definition is probably too high as a lower output volume can still be clinically relevant.

The type of fistula also has important clinical implications. In a lateral (side) fistula, continuity of the intestine is maintained allowing normal progression of intestinal contents beyond the fistula. This is a common type of fistula which usually closes spontaneously if not associated with any other anatomical abnormality. Conversely, with an end fistula, there is complete loss of intestinal continuity beyond the fistula and it generally requires surgery to achieve closure. Complex fistulae refer to multiple fistulae arising from different organs (that is, intestine, colon, and bile ducts) and pose challenging management problems. Spontaneous closure occurs but rates are much lower than in single organ fistulae. The presence of intra-abdominal abscesses also needs to be determined, as this would have clinical implications.

Various classification systems have been used to define gastrointestinal fistulae, of which fistula output is an integral part. The three schemes shown in table 1 (anatomical, output volume, and aetiological) have been most widely used. Each of these systems carries specific implications with regard to likeliness of spontaneous closure, prognosis, operative timing, and non-operative care planning. These classifications are often used in combination to achieve an integrated understanding of the fistula and its potential impact on the patient.

Gastrointestinal Fistulae

The relevance of gastrointestinal fistulae in clinical practice: a review

M Falconi, P Pederzoli

Gastrointestinal fistulae most frequently occur as complications after abdominal surgery (75–85%) although they can also occur spontaneously—for example, in patients with inflammatory bowel disease (IBD) such as diverticulitis or following radiation therapy. Abdominal trauma can also lead to fistula formation although this is rare. Postoperative gastrointestinal fistulae can occur after any abdominal procedure in which the gastrointestinal tract is manipulated. Regardless of the cause, leakage of intestinal juices initiates a cascade of events: localised infection, abscess formation and, as a result of a septic focus, fistulae formation. The nature of the underlying disease may also be important, with some studies showing that fistula formation is more frequent following surgery for cancer than for benign disease. Fistula formation can result in a number of serious or debilitating complications, ranging from disturbance of fluid and electrolyte balance to sepsis and even death. The patient will almost always suffer from severe discomfort and pain. They may also have psychological problems, including anxiety over the course of their disease, and a poor body image due to the malodorous drainage fluid. Postoperative fistula formation often results in prolonged hospitalisation, poor quality of life, and enormous cost. Therapy has improved over time with the introduction of parental nutrition, intensive postoperative care, and advanced surgical techniques, which has reduced mortality rates. However, the number of patients suffering from gastrointestinal fistulae has not declined substantially. This can partially be explained by the fact that with improved care, more complex surgery is being performed on patients with more advanced or complicated disease who are generally at higher risk. Therefore, gastrointestinal fistulae remain an important complication following gastrointestinal surgery.

GASTROINTESTINAL FISTULAE

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Abbreviations: IBD, inflammatory bowel disease.
The relevance of gastrointestinal fistulae in clinical practice

González-Pinto and Moreno González cover classification of fistulae and in particular classification by fistulae output in more detail elsewhere in this supplement (see page iv22).

**DIAGNOSIS**

The first diagnostic step in a patient suspected of having a gastrointestinal fistula is a thorough examination and medical history. Common symptoms include pain (first localised and then diffuse), illness, and fever, although occasionally a fistula can cause no symptoms. External fistulae are generally easier to diagnose due to the unusual effluent from drainage sites or abdominal incisions (purulent discharge and/or discharge of intestinal contents), cellulitic inflammation, and sepsis.

Internal fistulae are more difficult to diagnose although patients often suffer from diarrhoea, sepsis, and dyspnoea, as well as air, pus, or faeces in the urine.

Once a fistula has been confirmed, the daily output volume should be determined and biochemical (amylase, lipase, bilirubin, pH, etc.) and microbiological evaluations should be performed on the fistula fluid (table 2). Many techniques are available that can be useful in confirming the diagnosis and identifying the intrinsic anatomical and pathological features of a fistula. These are listed in table 2.

**AETIOLOGY AND EPIDEMIOLOGY**

The majority of gastrointestinal fistulae form following surgery (75–85%), most commonly after operations for cancer. IBD (for example, Crohn’s disease, diverticulitis), lysis of adhesions, and pancreatitis. The remaining 15–25% of fistulae usually form spontaneously, most commonly in patients with diverticular disease of the colon and other IBDs (for example, Crohn’s disease). Spontaneous fistulae are also reported in cancer patients or those who have received previous radiation therapy. A small number of fistulae form following abdominal trauma such as gunshot wound, stabwound (sharp trauma), or car accident (blunt trauma).

### Table 1

<table>
<thead>
<tr>
<th>Scheme</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anatomical</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td>External</td>
</tr>
<tr>
<td>Output volume</td>
<td>Pancreatic</td>
</tr>
<tr>
<td></td>
<td>Low (&lt;200 ml/day)</td>
</tr>
<tr>
<td></td>
<td>High (&gt;200 ml/day)</td>
</tr>
<tr>
<td>Intestinal</td>
<td>Low (&lt;500 ml/day)</td>
</tr>
<tr>
<td></td>
<td>High (&gt;500 ml/day)</td>
</tr>
<tr>
<td>Aetiologial</td>
<td>Underlying disease</td>
</tr>
</tbody>
</table>

Gastrointestinal fistulae can also occasionally occur following a sharp wound, such as that caused by a knife or bullet, or a blunt trauma, such as the impact of a steering wheel during a car accident. Blunt trauma to the abdominal wall can cause vascular injury, ischaemic problems, or abscess formation, all of which can lead to fistula formation. In one study of 44 consecutive patients, 15%–25% of all gastrointestinal fistulae form spontaneously. Diseases such as pancreatitis and IBD cause local inflammatory processes that can lead to local abscess formation, perforation, and distal obstruction, which are all potential causes of spontaneous fistula formation. Spontaneous oesophagotracheal fistulae can also form in patients with oesophageal cancer. Further causes of spontaneous fistulae include: radiation, diverticular disease, appendicitis, ischaemic bowel, erosion of indwelling tubes, perforation of duodenal ulcers, and pancreatic and gynaecological malignancies. In westernised populations, Crohn’s disease is the principal cause of spontaneous fistula formation. As shown in table 3, up to half of Crohn’s patients will develop a fistula at some stage during their disease, the majority of which will be external or perianal. Patients with diverticulitis are much less likely to develop a spontaneous fistula (1–12%) (table 3). Although fistulae that develop in the bowel are likely to close without the need for surgery, they often reopen as the underlying problem is still present.

Radiation therapy for malignant disease is also associated with fistula development and other complications in approximately 5–10% of patients. In a recent review that examined 41 publications, 17% of radiotherapy patients presented with a fistula after a mean interval of 3.4 years following radiotherapy. The clinical presentation varied from mild disease to debilitating rectal bleeding, diarrhoea, obstruction, and fistula formation. Mucosal ulceration may persist following high dose radiation and indeed, intestinal complications may manifest weeks or even years after radiotherapy. Furthermore, bowel resection and anastomosis in previously irradiated tissue increases the risk of anastomotic failure and, consequently, of fistula formation.

### Table 2

<table>
<thead>
<tr>
<th>Scheme</th>
<th>Clinical-instrumental methods used for diagnosing gastrointestinal fistulae (adapted from Falconi and colleagues)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Monitor</td>
</tr>
<tr>
<td></td>
<td>— Fistula output volume</td>
</tr>
<tr>
<td></td>
<td>— Fistula aspect (colour, etc.)</td>
</tr>
<tr>
<td></td>
<td>— Water-electrolyte balance</td>
</tr>
<tr>
<td></td>
<td>— Biochemical evaluation (amylase, lipase, bilirubin, pH, etc.)</td>
</tr>
<tr>
<td></td>
<td>— Infection status</td>
</tr>
<tr>
<td></td>
<td>— Nutritional/metabolic status</td>
</tr>
<tr>
<td></td>
<td>• Methylene blue test</td>
</tr>
<tr>
<td></td>
<td>• Upper or lower gastrointestinal endoscopy</td>
</tr>
<tr>
<td></td>
<td>• Digestive tract x-rays with water soluble contrast medium</td>
</tr>
<tr>
<td></td>
<td>• Fistulography with water soluble contrast medium</td>
</tr>
<tr>
<td></td>
<td>• Ultrasonography</td>
</tr>
<tr>
<td></td>
<td>• Computed axial tomography</td>
</tr>
<tr>
<td></td>
<td>• Magnetic resonance imaging</td>
</tr>
</tbody>
</table>

### Postoperative fistulae

Both local and systemic factors may contribute to postoperative fistula formation, including infection or breakdown of an intestinal anastomosis due to ischaemia, tension, or distal obstruction. They generally form as external rather than internal fistulae because of the presence of a drain. Technical problems that can lead to fistula formation include inadvertent full thickness bowel injury, deserosalisation of the bowel, suture-line defects, and tight suture causing ischaemic necrosis. Further factors include inadvertent injury to the mesenteric vessels, poor haemostasis resulting in a peristure haematoma, inappropriate use of drains, and a loop of intestine caught in a fascial suture. When an abscess cavity is associated with a fistula, infected material tends to collect adjacent to the gastrointestinal tract defect, preventing adequate healing of this defect. Healing is also compromised by malnutrition, immunosuppression secondary to medications, or specific disease states.

Fistulae can occur at any time following gastrointestinal surgery. The time elapsed to fistula appearance is an important guideline for management and prognosis. Early fistulae arising in the first 48 hours post surgery can be considered as technical errors and would occasionally require further surgical intervention. Low output well drained fistulae appearing late after surgery have a good prognosis and can generally be treated conservatively. However, in the case of late high output complex fistulae of upper gastrointestinal origin, reoperation would be required in most cases to achieve closure.

### Spontaneous fistulae

Approximately 15–25% of all gastrointestinal fistulae form spontaneously. In a recent review that examined 41 publications, 17% of radiotherapy patients presented with a fistula after a mean interval of 3.4 years following radiotherapy. The clinical presentation varied from mild disease to debilitating rectal bleeding, diarrhoea, obstruction, and fistula formation. Mucosal ulceration may persist following high dose radiation and indeed, intestinal complications may manifest weeks or even years after radiotherapy. Furthermore, bowel resection and anastomosis in previously irradiated tissue increases the risk of anastomotic failure and, consequently, of fistula formation.

### Trauma induced fistulae

Gastrointestinal fistulae can also occasionally occur following a sharp wound, such as that caused by a knife or bullet, or a blunt trauma, such as the impact of a steering wheel during a car accident. Blunt trauma to the abdominal wall can cause vascular injury, ischaemic problems, or abscess formation, all of which can lead to fistula formation. In one study of 44 consecutive patients, 15%–25% of all gastrointestinal fistulae form spontaneously. Diseases such as pancreatitis and IBD cause local inflammatory processes that can lead to local abscess formation, perforation, and distal obstruction, which are all potential causes of spontaneous fistula formation. Spontaneous oesophagotracheal fistulae can also form in patients with oesophageal cancer. Further causes of spontaneous fistulae include: radiation, diverticular disease, appendicitis, ischaemic bowel, erosion of indwelling tubes, perforation of duodenal ulcers, and pancreatic and gynaecological malignancies. In westernised populations, Crohn’s disease is the principal cause of spontaneous fistula formation. As shown in table 3, up to half of Crohn’s patients will develop a fistula at some stage during their disease, the majority of which will be external or perianal. Patients with diverticulitis are much less likely to develop a spontaneous fistula (1–12%) (table 3). Although fistulae that develop in the bowel are likely to close without the need for surgery, they often reopen as the underlying problem is still present.

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patients with pancreatic or duodenal injuries admitted to a trauma centre over a six year period, an incidence of pancreatic fistulae of 16% was reported in patients with pancreatic injury. Another example of formation of trauma induced fistulae is in response to prolonged intubation with a cuffed tube (tracheotomy or nasotracheal intubation).

**RISK FACTORS FOR POSTOPERATIVE FISTULA FORMATION**

Univariate and multivariate (*) logistic regression models have identified the following as risk factors in patients undergoing pancreaticoduodenectomy: soft pancreas, ampulla or duodenum disease (rather than pancreas or bile duct disease)*, advanced age, long duration of jaundice*, high total bilirubin, low creatinine clearance*, shock during operation, long operating time, high intraoperative blood loss*, and low patient volume per surgeon*. Other risk factors that have been suggested, although not proved, for postoperative gastrointestinal fistula formation include malnutrition,* immunocompromised state, infection, bacterial peritonitis, IBD,* renal insufficiency,* cirrhosis, mesenteric vascular disease,* previous surgery, low quality suture, low hospital volume, and inadequate surgical training or experience. Patients undergoing emergency surgery may also be more likely to develop a fistula than patients undergoing elective surgery, as patient preparation may have been poor or the patient may be chronically malnourished.1

**Factors affecting spontaneous closure**

Fistula closure is considered to be spontaneous if no surgical intervention is required although artificial nutrition and drug therapy may have been administered. Many factors may adversely affect spontaneous closure rates (table 4) although to date, most have not been properly evaluated. The majority of adverse prognostic factors are anatomical, such as the presence of a distal obstruction, diseased adjacent bowel, or an associated abscess. It has also been suggested that complex or external fistulae are generally more resistant to healing. The site of the fistula also affects the likelihood of spontaneous closure—gastric, ileal, and lateral duodenal fistulae may be less likely to heal than oesophageal, jejunal, pancreaticobiliary, or duodenal stump fistulae.1

Cancer, chemotherapy, and radiation are all thought to reduce the likelihood of spontaneous fistula closure. However, postoperative fistulae and those caused by appendicitis or diverticulitis are more likely to close spontaneously. The presence of sepsis or local infection can also adversely affect the likelihood of closure. Other factors that can adversely affect prognosis include diabetes, corticosteroid use, and renal failure. However, opinion is divided on the effect of output on spontaneous closure—high output may or may not be associated with reduced closure rates.

**MORBIDITY**

A patient with a gastrointestinal fistula will probably suffer much more than severe discomfort and pain. A gastrointestinal fistula is associated with a considerable mortality rate, the knowledge of which can distress the patient greatly. The psychological effect of a drainage bag and malodorous fistula fluid can have an adverse effect on body image, as can pathological changes in the skin at the fistula orifice. A postoperative fistula will almost invariably lengthen hospitalisation, which increases morbidity as well as the time taken to return to work and social activities. In addition to the morbidity directly associated with the fistula, further complications often occur, such as fluid and electrolyte disturbances, abscess formation or local infection (for example, urinary tract infection, bronchitis), general infection, multiorgan failure, sepsis, and bleeding.

**FACTORS AFFECTING MORTALITY**

Gastrointestinal fistulae are associated with considerable mortality, most commonly due to sepsis, although bleeding due to erosion of a large blood vessel can cause acute blood loss which is often fatal very quickly. A number of factors are known to affect mortality rate such as fistula site; underlying disease, low hospital volume and surgeon experience, high intraoperative blood loss, high preoperative serum bilirubin,
large diameter of the pancreatic duct, and the occurrence of complications.\textsuperscript{34} The effect of advanced age on operative outcome has also been studied.\textsuperscript{40-43} Perhaps surprisingly, operative mortality did not increase with advancing age in any of these studies although the complication rate in patients aged >80 years was higher than those <80 years in one study (57\% v 41\%, respectively; \textit{p}=0.05).\textsuperscript{40} Hospital volume has been shown to have a significant effect on total inhospital mortality following pancreatic surgery\textsuperscript{44-45} and other complex high risk gastrointestinal surgical procedures,\textsuperscript{46} although no analysis of the link to fistula formation was made. All of these studies found a significant correlation between high hospital volume and low mortality, although definitions of “high volume” and “low volume” varied considerably. The study by Lieberman and colleagues\textsuperscript{47} also found an association between high volume pancreatic surgeons and reduced perioperative mortality—5\% for high volume (>41 cases) surgeons versus 16\% for low volume (<9 cases) surgeons (\textit{p}=0.001). Despite these results, it has also been reported that pancreaticoduodenectomy can be successfully performed in low volume hospitals provided the surgeon is adequately trained in the procedure.\textsuperscript{7} In such hospitals, the case load should be restricted to a minimal number of trained surgeons to concentrate the experience.

**POSTOPERATIVE COMPLICATION RATES, FISTULA INCIDENCE, AND MORTALITY RATES**

As the majority of fistulae are caused by surgery, the remainder of this paper will focus on postoperative gastrointestinal fistulae. Truly representative epidemiological data are difficult to obtain as clinical trials tend to be conducted in specialist centres, which often treat the most complex cases and patients in the worst clinical condition. The frequency of fistulae depends on many surgeon and patient related factors, which are hard to assess for epidemiological purposes. The proposed submission of this paper is as part of a supplement, and therefore the values can only be used as a guide.

### Oesophagus and stomach

As can be seen in table 5, oesophagectomy or transhiatal oesophagectomy is associated with a much higher incidence of complications than resection or subtotal oesophagectomy (23–62\% v 10–14\%). However, the incidence of fistulae/leaks was higher following resection or transhiatal oesophagectomy (0–15\%) than after subtotal oesophagectomy or oesophagectomy (1–2\%). The mortality rates after oesophagectomy varied from 0\% up to 16\%.

The risk of complications in patients undergoing gastric surgery also varies with operative procedure, with a value of up to 68\% in patients with perforated ulcer undergoing omental patch closure. The incidence of fistulae/leaks also varies widely—up to 35\% in patients undergoing left upper abdominal exenteration plus Appleby’s method. Mortality in patients with perforated ulcer is very high (30–36\%) but much lower in other patient groups. The underlying pathology also has an effect on the incidence of fistulae in patients undergoing gastric surgery—those with cancer were more likely to develop a fistula (9\% (0–31\%))\textsuperscript{48,49} as high as 19\%\textsuperscript{50}.

**Liver or biliary tree**

In patients undergoing liver surgery, the overall complication rate, anastomotic leak rate, and mortality were generally low (table 6). However, surgery on the biliary tree is much more likely to result in complications, with up to half of all patients suffering at least one complication. The incidence of anastomotic leaks in patients undergoing biliary surgery varied according to the procedure from only 1\% in patients undergoing biliary-enteric anastomosis or pylorus preserving pancreatcduodenectomy to 19\% in patients undergoing choledochojunostomy. Mortality also ranged from 1\% in patients undergoing biliary-enteric anastomosis to 12\% in patients undergoing choledochojunostomy.

**Lower gastrointestinal tract**

The studies that examined surgery on the lower gastrointestinal tract all used various methods and patient groups and therefore it was difficult to group the results. Table 7 shows that the complication rate varied widely, from as low as 6\%\textsuperscript{51} to as high as 69\%.\textsuperscript{52} The incidence of fistulae was low, with the majority of studies reporting rates of 0–7\%, although rates as high as 19\%\textsuperscript{53} have been found. Similarly, mortality rates were generally low (0–9\%), although one study reported 17\% mortality\textsuperscript{54} The presence or absence of cancer did not appear to affect the fistula rate overall (1–19\%\textsuperscript{50,52,55-57} v 0–16\%,\textsuperscript{50,58-61} 3\%–1\% respectively).

**Pancreas**

It is well documented that pancreatic surgery carries a high risk of fistula formation, principally because of the presence of corrosive exocrine secretions. Due to the high rate of pancreatic fistulae, overall complications, anastomotic leaks, and

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**Table 5** Incidence of postoperative fistulae in patients undergoing surgery of the oesophagus and/or stomach

<table>
<thead>
<tr>
<th>Organ</th>
<th>Procedure</th>
<th>Complications (%)</th>
<th>Fistula/leak (%)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oesophagus</td>
<td>Resection</td>
<td>10%</td>
<td>5%</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td>Subtotal oesophagectomy</td>
<td>14%</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td>Transhiatal oesophagectomy</td>
<td>33% (23–62%)</td>
<td>11% (0–15%)</td>
<td>8% (6–16%)</td>
</tr>
<tr>
<td></td>
<td>Oesophagectomy</td>
<td>44%</td>
<td>3%</td>
<td>0%</td>
</tr>
<tr>
<td>Oesophagus/stomach</td>
<td>Oesophagectomy</td>
<td>41% (37–61%)</td>
<td>8% (6–11%)</td>
<td>7% (5–22%)</td>
</tr>
<tr>
<td></td>
<td>Total gastrectomy</td>
<td>35% (24–72%)</td>
<td>12% (0–28%)</td>
<td>6% (0–10%)</td>
</tr>
<tr>
<td></td>
<td>Subtotal gastrectomy</td>
<td>23% (8–90%)</td>
<td>ND</td>
<td>30%</td>
</tr>
<tr>
<td></td>
<td>Distal gastrectomy</td>
<td>18% (5–36%)</td>
<td>5% (0–6%)</td>
<td>4% (0–5%)</td>
</tr>
<tr>
<td></td>
<td>Distal gastrectomy</td>
<td>37%</td>
<td>ND</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>General</td>
<td>17% (4–58%)</td>
<td>5% (0–12%)</td>
<td>3% (0–11%)</td>
</tr>
<tr>
<td></td>
<td>Left upper abdominal exenteration plus Appleby’s method</td>
<td>57%</td>
<td>40%</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td>Omental patch closure</td>
<td>68%</td>
<td>ND</td>
<td>36%</td>
</tr>
<tr>
<td></td>
<td>Antrectomy</td>
<td>11%</td>
<td>2%</td>
<td>2%</td>
</tr>
</tbody>
</table>

*High risk patients with perforated ulcer.

ND, no data.
other fistulae were not included. However, mortality among patients who did develop fistulae was examined in addition to mortality as a result of surgery (table 8). The rate of pancreatic fistulae varied from 3% to 36% in these studies, and fistula mortality from 0% to 22%. Overall mortality was fairly constant in all studies (0–8%).

Due to the high incidence of fistulae following pancreatic surgery, this procedure will be examined in more detail. Tables 9 and 10 show the incidence of fistulae, fistula mortality, and overall mortality according to pancreatic stump management and underlying disease, respectively. The incidence of fistulae varied widely in the different studies, from 0% up to 33% (table 9) and therefore any effect of technique is probably suppressed by variations in study design, surgeon experience, patients, etc.

The effect of underlying disease on fistula incidence is also unclear (table 10). However, it would appear that patients with periampullary carcinoma who develop a postoperative pancreatic fistula are more likely to have a fatal outcome. Overall mortality also seems to be increased in patients with carcinoma of the pancreas or periampullary carcinoma.

BARTOLI ET AL META-ANALYSIS
A meta-analysis carried out during 1975–1989 examined the effects of stump management and underlying pathology on pancreatic fistula and mortality rates following pancreaticoduodenectomy (Whipple’s procedure) in 2684 patients.

The results of this analysis provide some interesting information and will therefore be included here.
A chronically inflamed pancreas is fibrotic and is therefore a particular change in the consistency of the pancreatic tissue. The widely used Wirsung-jejunal end to side anastomosis, the pancreaticojejunal end to side anastomosis, and the pancreaticojejunal end to end anastomosis were associated with fistula formation rates of 11–16% (table 11). However, the now obsolete ligation procedure was associated with a much higher incidence of fistulae (59%) (table 11).

When comparing outcomes of pancreaticoduodenectomy for cancer or for a benign disease such as chronic pancreatitis, the structural alterations present in the pancreas greatly affect the incidence of fistulae. Significantly fewer pancreatic fistulae form after surgery for chronic pancreatitis than for cancer (5% vs 9%, respectively; p=0.001) (table 12) as pancreatitis causes a particular change in the consistency of the pancreatic tissue. A chronically inflamed pancreas is fibrotic and is therefore usually easier to suture whereas the soft normal tissue after tumour resection gives rise to less stable anastomoses. The location of the cancer also affects the incidence of fistulae. Bile duct cancer does not obstruct the pancreatic duct system and therefore anastomosis with the remaining pancreas is much easier to perform. Therefore, pancreaticoduodenectomies for bile duct cancer are associated with a significantly higher incidence of fistulae than for ampullary (p=0.002) or pancreatic (p=0.003) cancer (table 12).

Examining the effect of disease on fistula mortality, it was found that subjects with bile duct cancer had the highest mortality rate (70%) followed by patients with pancreatic and ampullary cancer (table 12). The difference in mortality for pancreaticoduodenectomies for cancer versus chronic pancreatitis was significant (21% vs 9%, respectively; p=0.047). Although these mortality rates were higher than would be expected now due to improved patient care, they still give a good indication of the increase in mortality according to the underlying illness.

### Table 9: Pancreatic fistulae, fistula mortality, and overall mortality rates with different pancreatic remnant treatments after pancreaticoduodenectomy

<table>
<thead>
<tr>
<th>Treatment of pancreatic stump</th>
<th>Pancreatic fistula (%)</th>
<th>Fistula mortality (%)</th>
<th>Overall mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreaticojejunostomy end to side anastomosis</td>
<td>12 (2–33)</td>
<td>26 (0–50)</td>
<td>9 (0–50)</td>
</tr>
<tr>
<td>Pancreaticojejunostomy end to end anastomosis</td>
<td>25 (2–45)</td>
<td>10 (0–25)</td>
<td>7 (0–25)</td>
</tr>
<tr>
<td>Pancreaticogastrostomy</td>
<td>9 (0–12)</td>
<td>9 (0–20)</td>
<td>9 (0–20)</td>
</tr>
<tr>
<td>ND, no data.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 10: Pancreatic fistulae, fistula mortality, and overall mortality rates by underlying illness

<table>
<thead>
<tr>
<th>Underlying condition</th>
<th>Pancreatic fistula (%)</th>
<th>Fistula mortality (%)</th>
<th>Overall mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bile duct cancer</td>
<td>18 (2–38)</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Ampullary cancer</td>
<td>18 (2–38)</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Neoplastic disease</td>
<td>10 (2–34)</td>
<td>0 (0–10)</td>
<td>0 (0–10)</td>
</tr>
<tr>
<td>Endocrine tumour</td>
<td>12 (2–34)</td>
<td>0 (0–10)</td>
<td>0 (0–10)</td>
</tr>
<tr>
<td>Chronic pancreatitis/ inflammatory disease</td>
<td>20 (9–34)</td>
<td>0 (0–10)</td>
<td>0 (0–10)</td>
</tr>
<tr>
<td>ND, no data.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 11: Incidence of pancreatic fistulae with different pancreatic remnant treatments after pancreaticoduodenectomy

<table>
<thead>
<tr>
<th>Treatment of pancreatic stump</th>
<th>Fistula (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ligation</td>
<td>59 (5–75)</td>
</tr>
<tr>
<td>Total anastomosis</td>
<td>13 (5–57)</td>
</tr>
<tr>
<td>Pancreaticojejunostomy end to side anastomosis</td>
<td>16 (5–57)</td>
</tr>
<tr>
<td>Pancreaticojejunostomy end to end anastomosis</td>
<td>12 (5–57)</td>
</tr>
<tr>
<td>Wirsung-jejunal end to side anastomosis</td>
<td>11 (5–57)</td>
</tr>
<tr>
<td>Pancreaticogastrostomy</td>
<td></td>
</tr>
<tr>
<td>Occlusion</td>
<td>7 (0–12)</td>
</tr>
<tr>
<td>Closure+anastomosis</td>
<td>8 (0–12)</td>
</tr>
</tbody>
</table>

The relevance of gastrointestinal fistulae in clinical practice
In a later review of patients undergoing Whipple’s procedure, mortality fell from 18% during 1970–1979 (n=2133) to 7% during 1980–1989 (n=1474). Morbidity was also reduced, from 49% (n=1049) to 35% (n=521) during the same time periods. However, these changes cannot be attributed to a reduced fistula rate, as the incidence of pancreaticojejunoanastomosis leak only fell slightly, from 12% (n=1049) to 9% (n=521).

In a more recent study, mortality rates were examined in 312 patients undergoing partial pancreaticoduodenectomy. Hospital mortality decreased from 4.9% during 1983–1992 to 1.4% during 1995–1996. The complication rate also decreased, from 60% to 41%, as did hospital stay, from 24 days to 16 days. These improvements were attributed to better surgical techniques and increased surgeon experience.

CONCLUSION
Gastrointestinal fistulae, the majority of which form after operative procedures, are a major cause of morbidity and mortality. Their effects on the patient are wide ranging—pain, complex wound care, psychological effect on self image and self esteem, reduced quality of life, delayed return to social and work activities, and anxiety about future operative procedures and possible death. Complications such as nutritional problems, abscesses, and sepsis may also occur. Furthermore, a postoperative fistula increases hospital stay which obviously increases hospital costs.

Despite numerous medical advances—improved diagnostic techniques, improved patient care (parenteral nutrition, antibiotics, intensive care, and wound care), peroperative management, and surgical techniques—the overall number of postoperative fistulae has not fallen. This may be because these factors have also led to an increase in the number of operations carried out, particularly in patients at high surgical risk (old, malnourished, or catabolic tumoral patients). Furthermore, improved surgical techniques have led to more complex surgery being performed which again has increased the risk of fistula formation despite improved care.

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