Diagnosis and management of pancreatic fistulae resulting in pancreatic ascites or pleural effusions in the era of helical CT and magnetic resonance imaging

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SUMMARY

Objectives — Diagnosis of internal pancreatic fistulae (IPF) resulting in ascites or pleural effusions may be facilitated by multislice helical CT-scan and MR-pancreatography (MRP). Conservative treatment with parenteral nutrition and somatostatin analogues (± pancreatic stenting) yields varying results. We aimed to evaluate the usefulness of helical CT and MRP in the diagnosis of IPF. The outcome of patients when the following stepwise treatment algorithm is applied is also described: i) conservative (enteral nutrition and somatostatin analogues); ii) endoscopic stenting; iii) surgery.

Methods — Sixteen consecutive patients (13 M; median age 42 (14-54) yrs) with chronic pancreatitis (alcoholic 15, hereditary 1) and an IPF were prospectively included between March 01 to December 03. All serous effusions (ascites, N=10; pleural effusion, N=6) contained high lipase [median: 7800 (506-59000) U/mL]. Patients with fistulae communicating with pancreatic pseudocysts were not included.

Results — The diagnosis of IPF and its site were determined in 12/16 patients by CT and 14/15 patients by MRP (site of rupture: head: N=5; isthmus: N=5; body-tail: N=6) and confirmed by ERCP or surgery in 9. Localized atrophy of pancreatic parenchyma adjacent to pancreatic duct rupture was observed in 12 patients (75%). The median follow-up was 30 months (18-51). Early surgery was required in 4 of 6 patients, was successful in closing the IPF in 2; — surgery was required in the 4 remaining patients. Preoperative localization of the rupture site was possible in all patients using non-invasive imaging thus guiding elective intervention in all patients requiring surgery.

Conclusion — Helical CT scan and MRP are useful in localizing MPD rupture sites and fistulae and may obviate the need for pancreatic opacification. A systematic treatment algorithm can be safely used starting with medical strategies (enteral nutrition safely replacing the parenteral route) progressing to endoscopy and finally surgery. Overall about 44% of patients require surgery initially or at follow-up.

RÉSUMÉ

Les fistules pancréatiques au cours de la pancréatite chronique : diagnostic non invasif et stratégie thérapeutique

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Objectifs — Le diagnostic de fistule pancréatique (FP) pourrait être facilité par les nouvelles techniques d’imagerie non invasives (scanner en coupes fines [TDM], pancréato-IRM). Les résultats du traitement conservateur (nutrition entérale et analogues de la somatostatine), complété en cas d’échec par la pose endoscopique d’une prothèse pancréatique, sont mal connus. Le but de cette étude était d’évaluer : a) les performances de la TDM et de la pancréato-IRM pour le diagnostic de FP ; b) les résultats d’un algorithme de traitement instauré de manière progressive — traitement conservateur, endoscopique allant jusqu’à la chirurgie.

Malades et méthodes — Seize malades consécutifs (13 H ; âge médian 42 (14-54) ans) ayant une pancréatite chronique (alcoolique : 15, héréditaire : 1) et une FP persistante étaient inclus de mars 2001 à décembre 2003. La FP se traduisait soit par une ascite (N = 9) soit par un épanchement pleural (N = 6) riche en lipase (médiane : 7 800 [506 à 59 000] U/mL). Des malades ayant une FP communiquant avec un pseudo-kyste ont été exclus.

Résultats — Le diagnostic de FP et de son siège était effectué respectivement chez 12/16 malades par la TDM et 14/15 malades par la pancréato-IRM (siège céphalique : N = 5 ; isthmique : N = 5 ; corpéo-caudal : N = 6) et confirmé par la pancréatographie rétrograde ou la chirurgie chez 9 malades. Il existait une atrophie parenchymateuse localisée en regard de la rupture chez 12 malades (75 %). Le traitement de la FP après un suivi médian de 30 mois (18-51) était le suivant : 3 malades étaient opérés d’emblée (dont 2 pour surinfection du liquide à la ponction initiale). Chez 7 des 13 malades restants, le traitement conservateur simple (nutrition entérale associée à l’injection sous-cutanée de dérivés retand de somatostatine) était efficace. Une prothèse transpapillaire, posée avec succès chez 4 des 6 autres malades, était efficace chez 2 malades : les 4 autres malades ont nécessité une chirurgie. La localisation de la fistule avec des méthodes non invasives, possible chez tous les malades, a guidé le type de chirurgie : pancréatectomie régulée (N = 3) ou dérivation (N = 4).

Conclusion — La TDM et la pancréato-IRM permettent la localisation de la rupture pancréatique et du trajet fistuleux, guidant ainsi le geste endoscopique ou chirurgical. Il est licite d’adopter un algorithme de traitement allant de manière progressive et débutant par un traitement conservateur (nutrition entérale ± analogues de la somatostatine). La chirurgie reste indiquée pour 44 % des malades.
Introduction

Clinical features of ruptured main pancreatic duct (MPD) include an external pancreatic-cutaneous fistula (rare) or an internal fistula with a deep-seated organ (colon, intestine, stomach or bile duct...), an encapsulated collection (pseudocyst) or a serous collection resulting in pancreatic ascites or pleural effusion. The majority of cases of MPD rupture resulting in serous effusions occur in patients with underlying pancreatic disorders but especially chronic alcoholic pancreatitis [1-3]. The diagnosis of pancreatic serous effusions is confirmed by the demonstration of repeatedly high levels of pancreatic enzymes in either paracentetic or pleural effusions [1]. Certain authors have also noted that high levels of albumin may corroborate the diagnosis [2-4]. While the diagnosis of pancreatic serous effusions remains relatively straightforward, patient management remains difficult and surgery is frequently required [5]. These patients are frequently malnourished and are not good candidates for early surgical interventions which comprise either pancreatectomy or drainage procedures [6-8]. Conservative measures comprising bowel rest with parenteral nutrition in conjunction with somatostatin analogues have been efficacious in between 17 to 50% in closing fistulae [1, 2, 9-13] with sometimes an important death rate (up to 17%) [2]. Planning of invasive therapeutic strategies (endoscopy and surgery) requires accurate localization of the MPD rupture site or level of the fistula [10, 14]. Previously, localisation of the rupture site was performed using peroperative pancreatography [1, 4]; this has largely been superseded by endoscopic retrograde pancreatography (ERP) [2, 10, 14, 15]. As well as allowing for accurate localisation of the site of rupture, ERP offers the potential advantage of treatment of the MPD rupture with stent insertion. However, this remains an invasive procedure and cannulation with stent insertion is not always possible due to the presence of fibrous stenosis or calcifications. Successful outcomes following stent insertion occurs in about half of patients [16]. Recent improvements in imaging using thin multislice helical CT and magnetic resonance [17, 18] may offer an alternative in the detection of breaches in the MPD. The accurate localization of pancreatic duct rupture using non-invasive methods would offer an obvious advantage in patients prior to planning surgery or even ERP.

The aims of this study were to: 1) analyse the usefulness of helical multislice helical CT-scan and pancreatic-MR and magnetic resonance pancreatography (MRP) in the detection of pancreatic duct disruptions and fistulas in patients with internal pancreatic fistulæ and serous effusions; 2) prospectively evaluate the outcome in consecutive patients presenting with pancreatic ascites or pleural effusions by applying a systematic treatment algorithm going from conservative measures (using a combination of enteral nutrition and somatostatin analogues) and if required to endoscopic and eventually surgical treatment.

Patients and methods

All consecutive patients attending the medical-surgical unit of Beaujon hospital between March 1st 2001 and December 31st 2003 with serous effusions (either pancreatic ascites or pancreatic pleural effusions) were recruited into the study. The serous effusion was deemed persistent when at least 3 repeated paracentesis or pleural taps within one week were required with recurrent effusions. The serous effusion was defined to be of pancreatic origin in the presence of repeatedly elevated pancreatic enzymes in the aspirated fluid [11]. Patients with pseudocysts were excluded.

General demographic data were recorded such as age, sex, and cause of pancreatitis (alcoholic or other). An episode of acute pancreatitis in the three months preceding the diagnosis of a serous effusion was also recorded. The types of effusion — ascites, pleural effusion or both — as well as biological profile of the effusion (cell count, protein level, presence of germs, and pancreatic enzymes) were noted.

Imaging methods

Helical CT Scan

All patients underwent helical CT scan and all but 1 had pancreatic magnetic resonance (MR) imaging with MRP to identify a pancreatic fistula or MPD rupture site. Thin slice helical tri-phase CT scan of the pancreas and abdomen was performed using a standard protocol as follows: two sequential breath-hold helical acquisitions were performed after intravenous injection of 140 mL of iodinated contrast material at a rate of 2 mL/s; thin section images through the pancreas, 45 s after injection of intravenous contrast material, with section effectively collimated to 2.5 mm at a pitch of 1.5, and thin section through the liver and pancreas, 70 s after initiation of infusion of contrast material, each section effectively collimated to 5 mm at a pitch of 1.5. Water was given as oral contrast to obtain complete filling of the duodenal lumen. In addition, additional thoracic slices were taken in the event of a pancreatic pleural effusion in order to locate and follow a pancreatic fistula.

Magnetic resonance technique

All magnetic resonance images were acquired with a 1.5-T unit (Gyrosan Intera, Philips) with a dedicated phased-array coil and high-performance gradients. Two different pancreatic-MR snapshot techniques were applied: thick-slab single-shot turbo spin-echo T2-weighted sequences and multi-section thin-slab, single-shot turbo spin-echo T2-weighted sequences. Thick-slab sequences were acquired as a single 20-45 mm slice in radiated coronal and oblique orientations with two ranges both on pancreatic head and body, and on pancreatic tail (echo spacing, 8.3 msec; effective TE, 1,000 msec; image matrix, 512 × 512; field of view, 350 mm). Thin-slab MRP sequences were acquired with sequential 3-mm slices in the axial and coronal planes (echo spacing, 4.2 msec; effective TE, 183 msec; image matrix, 272 × 512; field of view, 386 mm). No patient preparation or sedation was required.

Definition of an internal pancreatic fistula

A pancreatic fistula was defined as a tubular tract communicating with the pancreas and the pleural or peritoneal cavity. At CT the rupture was evidenced by a disruption of the MPD with disappearance of pancreatic parenchyma between rupture and abdominal cavity or peripancreatic tissue. A fistula was observed as a hypodense tubular tract communicating with the MPD rupture and pleural or peritoneal cavity, often surrounded by a rim of enhancement. At MR these patterns were highly hyper intense at T2 due to the pancreatic juice, with the same shapes. The following data were recorded for imaging methods: presence or not of fistula and its trajectory, exact site of MPD rupture (pancreatic head, isthmus or body-tail), presence of pancreatic or MPD calcifications, pancreatic atrophy and stigmata of acute pancreatitis. The performance of CT and MR was judged by the clear and unequivocal identification of either a pancreatic fistula or MPD rupture site as attested to by two senior pancreatic radiologists (MP, PV); confirmation was analyzed in the event of follow-up endoscopic retrograde pancreatography (ERP) or surgery.

Treatment strategy

The medical files of all patients were reviewed at a medico-surgical-radiological conference prior to inclusion of all patients. Decisions following failure of one or other treatment were conducted in a similar multidisciplinary manner. All patients were informed of the treatment strategies and gave written informed consent prior to endoscopy or surgery. Following diagnosis of a persistent pancreatic effusion (>1 week), patients were systematically treated using a similar progressive treatment algorithm (figure 1) from least to most aggressive as follows:

1. Conservative medical treatment: comprising nil per os with enteral nutrition using a naso-gastric feeding tube (1,500-2,000 kcal/day) in conjunction with a somatostatin analogue (Octreotide® 100-200 µg tid subcutaneously; the dose was increased from 100 to 200 µg tid after 10 days in the event of persistent fistula output and doses above 600 µg/day were not administered). Medical treatment was judged to have failed if at 3 weeks the patient still required pleural or abdominal drainage for recurrent serous effusions with high pancreatic enzymes.
2. Endoscopic treatment: in the event of failed medical treatment alone, patients underwent ERP with MPD stent insertion by two endoscopists experienced in pancreatic pathology (PP, FM). Patients were treated with broad spectrum iv antibiotics (amoxicillin-clavulanic acid and ciprofloxacin) prior to ERP and for 48 hours after endoscopy. Endoscopic treatment was judged to have failed in the event of technical failure, recurrent serous effusions or complications of stent insertion;

3. Surgery: surgery was reserved for patients with failed medical and endoscopic therapy or in the event of complications such as documented serous effusion super-infection at any stage in the treatment programme. The surgical technique was decided on an individual patient basis according to the MPD rupture site as reviewed at a multidisciplinary meeting with two senior pancreatic surgeons (AS, JB).

Data statistics and presentation

Demographic data are given in numbers with median values (and range) and percentages where indicated. Success of each treatment was judged in the absence of recurrent effusions and the number of patients requiring surgery following failed medical and/or endoscopic treatment was calculated. Factors potentially predictive of treatment outcome were compared using the Fisher’s Exact test (with P<0.05 as significant).

Results

Sixteen consecutive patients (13 men) with a median age of 42 years (range: 14-54) were included. An underlying pancreatic disorder was present in all patients (alcoholic chronic pancreatitis [N=15] with a median pure alcohol consumption of 100 g/day; hereditary pancreatitis [N=1]). An episode of acute pancreatitis preceded the occurrence (<3 months) of serous pancreatic effusion in 9 patients (56%).

Ten patients had pancreatic ascites alone, six had pleural effusions alone (bilaterial in 3) and no patients had both ascites and pleural effusions. Symptoms at presentation included: abdominal pain of varying intensity (N=7) in those with pancreatic ascites; increasing dyspnoea (N=3) and fever (N=1) for pleural effusions. Three patients with ascites were asymptomatic apart from remarking abdominal distension. Significant weight loss (>15% of total body weight despite effusions) was observed in 9 patients (56%). All serous effusions contained either high amylase or lipase (median values with range of amylase and lipase: 8154 U/mL [323-46000] and 7800 U/mL [504-59000], respectively). The median total protein level was 39 g/L (range: 3-59). All but two initial aspirates were sterile at the outset.

Results of helical CT and MRP

Helical CT was available in all patients and MRP in all but one. Pancreatic calcifications were demonstrated at CT scan in 6 patients (38%). The site of MPD rupture was determined by CT in 8 (50%) patients whereas a fistula was clearly identified in 12/16 (75%). Combined pancreatic MR and MRP localized the MPD rupture site in 10 of 15 patients (67%) and a fistula was observed in 14/15 (93%). When combining both helical CT and/or MRP, the exact site of MPD rupture and fistula was clearly observed in 94% (15/16) and 100% of patients, respectively. Examples of MPD rupture sites and fistulae identification are given in figures 2 and 3. The MPD rupture site was located
in the pancreatic head in 5 patients, isthmus 5, and the body/tail, 6. The site of rupture was confirmed by ERCP or surgery in 9 patients. Localized atrophy of pancreatic parenchyma adjacent to pancreatic duct rupture was observed in 12 patients (75%).

Results of treatment

Of the 16 consecutive patients included, three underwent immediate surgery (due to super-infection of serous fluid aspirate in two patients and a further patient refused to undergo conservative medical or endoscopic treatment as he had previously been treated for pancreatic pseudocysts with prolonged enteral nutrition 18 months prior to diagnosis of pancreatic fistula). The remaining 13 patients were treated according to the defined treatment algorithm (Table I).

Conservative Medical Treatment

Enteral nutritional was well tolerated and an intake of between 1500 to 2000 kcal/day (depending on individual needs) was achieved in all 13 patients treated conservatively. The combination of nil p.o. and enteral nutrition was successful in 7 of 13 patients (54%) with all but one patient responding within 3 weeks; conservative measures were continued in the remaining patient as the number of paracentesis steadily decreased over a 5-week period.

Endoscopic Treatment

Six patients underwent ERP with a view to a drainage procedure. In two patients placement of a stent failed: in one with pancreas divisum and rupture of the dorsal pancreatic duct, it was impossible to catheterize a small minor papilla despite a pre-cut; the ventral duct showed changes compatible with pancreatitis without rupture or fistula (this patient underwent surgery with super-infection of ascites just prior to surgery); in another, stent insertion was impossible due to stones in the distal MPD and he underwent a pancreatico-jejunostomy drainage procedure. Placement of an endoprosthesis was possible in 4 patients resulting in successful drainage of MPD rupture in 2 patients. In the two patients successfully treated with stenting, changing of the stents was performed at 3 months and stents were definitively removed at 6 months. In the remaining 2 patients serous effusion super-infection occurred necessitating surgery.

Surgery

The overall number of patients requiring surgery on an intent-to-treat basis was 7 of 16 (44%). According to patients entering the treatment algorithm, 4 of 13 patients (31%) required surgery. In all patients undergoing surgery, pre-operative localization of the MPD rupture site at CT or MRP facilitated the planned procedure which included: MPD bypass procedures (N=3); pancreatico-gastric or -jejunostomy, 2 and 1, respectively), distal pancreatectomy with splenectomy (N=3) and pancreaticoduodenectomy (N=1). No significant complication was observed following surgery.

In the 13 patients entering the treatment algorithm 4 of 7 patients responding to conservative measures had no definable abnormality of the MPD compared to 1 of 6 patients where such treatment failed; this difference was not however statistically significant. In addition, other factors predictive of treatment success/failure (site of MPD rupture, presence of stenosis or pancreas divisum, dilatation of MPD) were not found. Treatment response was not correlated with type of serous effusion as conservative medical treatment and endoscopy were effective in 3 and 1 patients with pleural effusions and in 4 and 1 with ascites, respectively.
Table I. – Patient characteristics with pancreatic duct abnormalities and treatment outcome according to the applied treatment algorithm (except for patients n°14, 15 and 16).

<table>
<thead>
<tr>
<th>Cause of pancreatic pathology</th>
<th>Rupture Localization</th>
<th>Main pancreatic duct anatomical abnormalities (at MRPD1 or ERCP2)</th>
<th>Conservative Treatment</th>
<th>ERCP</th>
<th>Surgery</th>
<th>Follow-up, months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Stenosis/Dilatation</td>
<td>Other</td>
<td>Yes/No</td>
<td>Outcome</td>
<td></td>
</tr>
<tr>
<td>1 Alcohol</td>
<td>Isthmus</td>
<td>Short stenosis (head) with proximal dilatation (7 mm)1</td>
<td>+ success</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>2 Alcohol</td>
<td>Head</td>
<td>None1</td>
<td>+ success</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>3 Alcohol</td>
<td>Body-Tail</td>
<td>Diffuse dilatation (10 mm) without stenosis1</td>
<td>+ success</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4 Alcohol</td>
<td>Isthmus</td>
<td>Short stenosis (head) with proximal dilatation (10 mm)1</td>
<td>+ success</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>5 Alcohol</td>
<td>Isthmus</td>
<td>None1</td>
<td>+ success</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>6 Alcohol</td>
<td>Body-Tail</td>
<td>None1</td>
<td>divum</td>
<td>+</td>
<td>success</td>
<td>—</td>
</tr>
<tr>
<td>7 Alcohol</td>
<td>Body-Tail</td>
<td>None1</td>
<td>+ success</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>8 Hereditary</td>
<td>Head</td>
<td>Long stenosis (head) with long proximal dilatation1, 2</td>
<td>+ failure</td>
<td>Failed stent insertion</td>
<td>—</td>
<td>By-pass PJ</td>
</tr>
<tr>
<td>9 Alcohol</td>
<td>Body-Tail</td>
<td>Short stenosis (body) with no dilatation1, 2</td>
<td>+ failure</td>
<td>Dilatation + stent</td>
<td>success</td>
<td>—</td>
</tr>
<tr>
<td>10 Alcohol</td>
<td>Tail</td>
<td>None1, 2</td>
<td>+ failure</td>
<td>Stent</td>
<td>failure</td>
<td>DP &amp; S</td>
</tr>
<tr>
<td>11 Alcohol</td>
<td>Isthmus</td>
<td>Short stenosis head with no proximal dilatation1, 2</td>
<td>+ failure</td>
<td>Dilatation + stent</td>
<td>success</td>
<td>—</td>
</tr>
<tr>
<td>12 Alcohol</td>
<td>Head</td>
<td>No stenosis &amp; diffusely dilated dorsal duct (7 mm)1</td>
<td>+ failure</td>
<td>Failure to catheterize</td>
<td>—</td>
<td>By-pass PG</td>
</tr>
<tr>
<td>13 Alcohol</td>
<td>Head</td>
<td>Short stenosis head with no proximal dilatation1, 2</td>
<td>+ failure</td>
<td>Dilatation + stent</td>
<td>failure</td>
<td>DP &amp; S</td>
</tr>
<tr>
<td>14 Alcohol</td>
<td>Body</td>
<td>Short stenosis (head) with proximal dilatation (8 mm)1</td>
<td>Noa</td>
<td>—</td>
<td>—</td>
<td>By-pass PG</td>
</tr>
<tr>
<td>15 Alcohol</td>
<td>Head</td>
<td>Short stenosis (head) with proximal dilatation (4 mm)1</td>
<td>Nob</td>
<td>—</td>
<td>—</td>
<td>PD</td>
</tr>
<tr>
<td>16 Alcohol</td>
<td>Isthmus</td>
<td>None1</td>
<td>Noe</td>
<td>—</td>
<td>—</td>
<td>DP &amp; S</td>
</tr>
</tbody>
</table>

* : patient refused to enter treatment algorithm as had previously undergone 2 successful endoscopic drainage procedures for pseudocysts and opted for surgery; a : superinfection of pancreatic ascites treated at the outset surgically with pancreaticoduodenectomy (PD); b : superinfection of pancreatic ascites treated surgically with distal pancreatectomy (DP) and splenectomy (S).

Follow-up

The median follow-up after start of treatment was 30 months (range: 22-51) and no deaths occurred. No patient successfully treated with conservative medical treatment relapsed in the follow-up period. All patients but one remained alcohol-free at follow-up. In the two patients in whom MPD stents were successful no relapse has occurred. Similarly, no recurrence has been noted in patients treated surgically.

Discussion

Internal pancreatic fistulae resulting in either pancreatic ascites or pleural effusions are rare and few recent data pertaining to either diagnostic or management strategies are available. The accumulation of free pancreatic fluid in the peritoneal cavity results from either anterior disruption of the MPD or rupture of a pseudocyst [1, 2]. Pancreatic pleural effusions occur from fistulous connections between the pancreas and the pleural spaces directly via the diaphragm or via a retroperitoneal route to the mediastinum [1, 19, 20]. Internal fistulae resulting in serous effusions stem from large ruptures or fistulae usually resulting in significant fluid accumulation and necessitating repeated pleuro- or paracentesis. In accordance with published data, we found that patients with a history of chronic pancreatitis (alcoholic in 94%) presenting with pancreatic ascites had few specific symptoms while dyspnoea was present in 50% of those with pleural effusions [2, 9, 21]. An episode of documented acute pancreatitis within the year preceding the diagnosis of internal pancreatic fistula was observed in about half of patients (56%) which is within the range of older series (3.6 to 50%) [2, 5, 13, 21].

Accurate localisation of the MPD rupture site is imperative in planning treatment especially surgery in patients with serous pancreatic effusions [10, 14]. Formerly, precise localisation of the rupture entailed either peroperative [1, 4] or endoscopic
pancreatography [2, 10, 14, 15]. Lack of preoperative identifi-
cation of the point of leakage can lead to a 50% surgical failure rate
due to inadequate surgical planning while the failure rates
to fall to 12-18% in patients in whom the rupture site was found at
preoperative ERP [10]. Demonstration of the rupture site by non
invasive imaging methods offers several advantages especially
in planning pre-surgical management strategies in an elective
manner. Opacification via ERP, requiring sedation and/or
anesthesia, carries inherent risks but especially super-infection
of serous collection (as was the case for two of our patients)
[13, 22]. A novel aspect in the current series was the use of both
helical CT and pancreatic MR combined with MRP in studying
the pancreas and the adjacent surrounding tissues in an effort to
identify the MPD rupture site and fistula. Although the MPD
rupture site was demonstrated by CT and MRP in 50 and 67%
of patients, respectively the site of disruption was clearly identified
in all but one patient when both techniques were combined. The
excellent performance of magnetic resonance was observed by
the identification of a fistula communicating with the MPD in
14 of 15 (93%) patients using MRP. Identification of a fluid-
containing fistula using CT scan is well established [18] however
its performance in localizing the site of ductal rupture appears
poorer. Initial promising results have been suggested using pan-
creatic MR and MRP [17, 18]. The advantage of MR is the com-
bined possibility of studying both pancreatic parenchymal and
ductal changes as well as allowing indentification of a T2 hyper-
intense fistulous tract. Using two ranges of radiated thick slices
and particularly one studying the tail of the pancreas seems to be
mandatory. The current study clearly confirms the initial promis-
ing results of pancreatic MR, combined with MPR, which should
be proposed as the imaging method of choice in these patients.

Another novel aspect pertaining to the current study is the
application, in a prospective manner with meaningful follow-up
(30 months), of a uniform treatment strategy going from least
to most aggressive in a step-wise fashion. Success with conservative
treatment measures have been documented for many years with
rates ranging from 17 to 50% [1, 2, 9-13] however, the inconsis-
tent use of in-dwelling chest or abdominal drains, the varying
doses of somatostatin analogues, enteral versus parenteral nutri-
tion and discrepancies in patient selection for medical or surgical
therapies makes for critical appraisal difficult. In the current study
we wished to analyze a step-wise treatment approach with pro-
spective consecutive recruitment of all patients with internal pan-
creatic fistulae and high-output serous effusions (requiring repeat
aspirations) undergoing a homogeneous therapeutic approach.
Seven of 13 patients (54%) entering the treatment algorithm were
successfully managed with a combination of exclusive enteral
nutrition and somatostatin analogues, the majority within
3 weeks (no indwelling drains were used in these patients). No
relapse has been observed with a median follow-up of
30 months (range: 22 to 51). While previous series reported
high mortality in conservatively managed patients (up to 17% in
old series predating 1975) [2, 23] improvement in general med-
cal care ensures that initial conservative strategies can be safely
commenced with careful monitoring. A recent series reported
success in only 1 of 6 patients treated conservatively with internal
pancreatic fistulae and pancreatic serous effusions [12]. It has
been suggested that patients with advanced pancreatic disease
should be selected for early surgery [24] however, this approach
has never been formerly tested. Indeed, early surgery is not
always possible and imposes inherent risks in patients with
serous pancreatic effusions who present severe weight loss due to
combined pancreatic disease and alcoholism (56% here). Conser-
vative measures with adequate nutritional support to correct
catabolism [9] may not only heal the fistula or MPD rupture but
may lessen the risk of general anesthesis for subsequent by-pass
or pancreatic resection if required. While older nutritional meth-
ods using total parenteral nutrition continues to be employed [13]
in this setting, the current study demonstrates that enteral nutrition
can be successfully used thus avoiding complications, which are
occasionally fatal [13], of in-dwelling venous catheters. The
enteral route was chosen given its efficacy in patients with severe
acute pancreatitis where equivalence with parenteral nutrition
has been observed [25, 26]. Even recent series lack data on a
conservative management approach; only 41% of patients with
MPD duct disruption (resulting in either pseudocyst or serous
pancreatic effusions) were initially managed with parenteral
nutrition by Varadarajulu et al. [16]. Somatostatin analogues
have not been proven to be more effective that placebo in
decreasing output and closing external fistulae [27]. While it has
been suggested that somatostatin analogues are beneficial in
closing high-output fistulae [28] use of this therapy was not
found at univariate analyses to be related to this favorable outcome
[5]. Difficulties in interpretation of data arise from the small
number of patients, the variability in doses used and heterogene-
ity of patients (internal vs external fistulae and failures as a result
of serous fluid superinfection or concurrent pathologies) [5].

The choice of 3 weeks as a cut-off for failed conservative
treatment is arbitrary and is based upon previous personnel and
published data; indeed, other groups have chosen between 2 to
4 weeks [8, 21, 29, 30]. A cut-off of 3 weeks appears appropri-
ate and ensures: 1) progressive nutritional increase (individual
objectives may be slow to achieve) and 2) adequate duration of
somatostatin analogue therapy. If the delay is shorter, there is a
risk of erroneously attributing the lack of efficacy to conservative
measures; it also appears illogical that to extend the delay is
longer than 3 weeks given the efficacy of efficacious invasive
endoscopic or surgical measures.

Conservative treatment failed in 6 patients who commenced
the step-wise programme all of whom underwent ERP with the
intention of transpapillary stenting. Intraductal stenting is thought
to decompress a high-pressure pancreatic ductal system but may
also bypass an adjacent stricture and partially occlude the rup-
ture site. Endoscopic therapy, when feasible, achieves good
results in the treatment of communicating pseudocysts and in
decompressing upstream dilatation in cases of MPD stenosis in
chronic pancreatitis [16, 31, 32]. However, treatment failure
may occur in 33-50% of patients [16]. The treatment of MPD
ruptures with high output pancreatic serous effusions may be dif-
ficult. Success of endoscopic treatment in patients with serous
effusions depends largely on two difficulties: 1) the ability to
transgress a stricture (fibrotic or calcified) downstream to the rup-
ture site and 2) the placement of the stent in the pancreatic duct
upstream to the site of duct disruption. On the contrary, in
patients with communicating pseudocysts, endoscopic measures
are easier as the stents can be placed directly into the pseudocyst
trough rupture site. In the current study, a stenosis distal to the
site of MPD disruption was documented in 8 patients (50%) using
MRP and confirmed in four who underwent direct opacification.
Technical success with stent insertion was achieved in 4 patients
with successful drainage in 2 (50%). Bracher et al. successfully
used an endoscopic stenting approach in 7 of 8 patients with
pancreatic ascites with a success rate of 88% within 6 weeks
[22]. However, interpretation is again difficult due to the retro-
spective nature of the study and perhaps selection bias and the
inclusion of two patients with leaky pseudocysts [22] (the treat-
ment of communicating pseudocysts in patients with chronic
pancreatitis is probably different and deserves to be dealt with
separately). The good results using transpapillary stenting
reported by Kozarek et al. [33] in all 4 patients following failed
medical therapy are also hard to analyze given the additional
therapeutic measures employed (large volume paracentesis or
use of percutaneous drains). An individualized approach based
on findings usually related to the pancreatic ductal anatomy was also
recently described [13] as follows: conservative treatment in cases of simple MPD
dilatation; endoscopy and stent insertion for those with partial

striction or duct disruption; and surgery in case of complete duct obstruction or disruption. Endoscopic stenting was successful in all four patients treated on the basis of a retrospective treatment programme [13] and application of such ductal changes to treatment, while interesting, requires prospective analysis. It cannot be excluded that patients with moderate duct changes would have responded to simple conservative treatment. In the present study 4 of 7 patients responding to conservative measures had no demonstrable abnormalities of the MPD however this was not statistically significant and anatomical factors predicting treatment outcome were not identified but this may be due to the relatively small number of patients compared on an intent-to-treat basis (N=13). Finally, endoscopic treatment carries a risk of exacerbating matters with infection of ascitic fluid [13, 22] as was the case in 2 of our patients. When endoscopic treatment fails, surgery should be employed rapidly to avoid complications especially superinfection of serous fluid.

Although we confirmed the good results obtained using conservative management strategies in patients with internal pancreatic fistulae and serous effusions, surgery retains an important role in these patients. Seven of 16 patients underwent surgery on an intent-to-treat basis. The three patients not entering the treatment algorithm underwent early surgery due to serous effusion superinfection in two and refusal of conservative treatment in one patient. The MPD rupture was accurately located by MRP in all of these patients and guided elective surgery (pancreaticoduodenectomy, distal pancreatectomy with splenectomy and MPD by-pass, respectively). In the remaining 13 patients, 31% required surgery following failed conservative and endoscopic treatment. In the event of failed medical and/or endoscopic methods surgery should be performed [2, 5, 8]. Main pancreatic duct decompression with pancreato-jejunostomy should be preferred [6, 7] and pancreatic resection should be limited to avoid pancreatic dysfunction [8, 34]. The overall success of surgery approaches 80% [2, 6, 7, 9, 35-37] and no relapse was observed in the current series after a median of 30 months.

In conclusion, new imaging methods with helical CT scan and especially pancreatic MR and MRP are useful in diagnosis of MPD rupture sites and fistulae in patients with internal pancreatic fistulae resulting in pancreatic ascites and pleural effusions. In addition, these non-invasive methods help to accurately guide therapeutic measures and obviate the need for diagnostic endoscopic pancreatic opacification. Application of a systematic treatment algorithm can be safely used starting with medical strategies, where enteral nutrition can safely replace the parenteral route, progressing to endoscopy and finally surgery. Conservative treatment will result in closure of high output fistulae in more than half of patients. Transapillary endoscopic stenting is also useful in some patients however, surgical therapy remains necessary in about 40% of cases.

**REFERENCES**


