

An ongoing dispute in the management of severe pancreatic fistula: Pancreatosplenectomy or not?

Dionysios Dellaportas, Aliko Tympa, Constantinos Nastos, Vasiliki Psychogiou, Andreas Karakatsanis, Andreas Polydorou, George Fragulidis, Ioannis Vassiliou, Vassilios Smyrniotis

Dionysios Dellaportas, Constantinos Nastos, Vasiliki Psychogiou, Andreas Karakatsanis, Andreas Polydorou, George Fragulidis, Ioannis Vassiliou, Second Department of Surgery, Athens Medical School, Aretaieion Hospital, 76 Vassilissis Sofias Avenue, 11528 Athens, Greece

Aliko Tympa, Vassilios Smyrniotis, Fifth Department of Surgery, Athens Medical School, Aretaieion Hospital, 76 Vassilissis Sofias Avenue, 11528 Athens, Greece

Author contributions: Dellaportas D performed research and wrote the paper; Tympa A and Nastos C analyzed the data; Psychogiou V and Karakatsanis A designed the tables and structure of the article; Polydorou A, Fragulidis G and Vassiliou I revised the article; Smyrniotis V gave the final approval of the version to be published.

Correspondence to: Dionysios Dellaportas, MD, Second Department of Surgery, Athens Medical School, Aretaieio Hospital, 76 Vassilissis Sofias Ave., 11528 Athens, Greece. dellapdio@gmail.com

Telephone: +30-210-1004177 Fax: +30-210-7286128

Received: June 1, 2010 Revised: September 18, 2010

Accepted: September 26, 2010

Published online: November 27, 2010

Abstract

The aim of this manuscript is to review controversies in managing severe pancreatic fistula after pancreatic surgery. Significant progress in surgical technique and perioperative care has reduced the mortality rate of pancreatic surgery. However, leakage of the pancreatic stump still accounts for the majority of surgical complications after pancreatic resection. Various strategies have been employed in order to manage pancreatic fistula. Nonetheless high grade pancreatic fistula evokes controversy in relation to the choice of treatment. A Medline search was performed, with regard to conservative treatment options versus completion pancreatectomy for the management of pancreatic fistula grade C. Pancreatic fistula rates remain unchanged with an incidence ranging from 5%-20% and this is considered as the most important cause of postoperative death. Many authors claim that

completion pancreatectomy has probably lost its role in favour of interventional radiology procedures, while others believe that completion pancreatectomy continues to have a place in the management of patients with severe clinical deterioration after pancreatic fistula who do not respond to non-surgical interventions. There is no agreement on the best clinical management of severe pancreatic fistula after pancreatic surgery. Completion pancreatectomy is reserved for patients not improving with conventional measures.

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Key words: Pancreatic fistula; Pancreatoduodenectomy; Pancreatosplenectomy; Completion pancreatectomy; Percutaneous drainage

Peer reviewers: Giulio A Santoro, Professor, Pelvic Floor Unit and Colorectal Unit, Department of Surgery, Regional Hospital, Treviso 31000, Italy; Uwe Klinge, MD, Professor, Institute for Applied Medical Engineering AME, Helmholtz Institute, RWTH Aachen Pauwelsstrabe 30, Aachen 52074, Germany

Dellaportas D, Tympa A, Nastos C, Psychogiou V, Karakatsanis A, Polydorou A, Fragulidis G, Vassiliou I, Smyrniotis V. An ongoing dispute in the management of severe pancreatic fistula: Pancreatosplenectomy or not? *World J Gastrointest Surg* 2010; 2(11): 381-384 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v2/i11/381.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v2.i11.381>

INTRODUCTION

Pancreatic surgery has improved dramatically during the past two decades. Mortality rates after Whipple's procedure in the 1980s exceeded 20%, but nowadays mortality has been reduced to less than 5% in high volume centers^[1]. At present the single most important cause of morbidity and mortality after pancreatoduodenectomy (PD) is

pancreatic leakage and fistula (PF)^[2]. Some authors have named pancreatic anastomosis the “Achilles heel” of pancreatic surgery because it has the highest rate of surgical complications among all abdominal anastomoses^[3]. Also PF can lead to prolonged hospital stay and increase the cost of treatment. Various strategies have been employed in order to prevent and manage PF, but when severe grade PF occurs controversy exists about the treatment of choice. Many authors insist that completion pancreatectomy (CP) continues to have a place in patients with severe septicemia and clinical deterioration, while others suggest that CP has lost its role and conservative management is the treatment of choice even for grade C PF. The aim of this study is to highlight the most effective strategy in the management of grade C PF.

DEFINITIONS

There are many different definitions of pancreatic fistula in the literature, based on a multitude of parameters and this renders comparison between studies difficult. A valuable clinical definition was published in 2005 by Bassi *et al*^[1] and the International Study Group for postoperative Pancreatic Fistula. A pancreatic fistula represents a failure in healing of the pancreato-enteric anastomosis or a parenchymal leak not directly related to an anastomosis. Three different grades of PF (grades A, B, C) are defined according to the clinical impact on the patient’s clinical course (Table 1). In terms of measures, PF is a drain output of any measurable volume of fluid on or after postoperative day 3, with an amylase content greater than 3 times the serum amylase activity.

Grade A PF is the most common grade and has no major clinical impact. It is managed with gradual removal of the drains that were placed intraoperatively.

Grade B PF is a clinically relevant fistula and it may be associated with abdominal pain, fever, leukocytosis. In most cases the patient is supported with total parenteral nutrition (TPN) or enteral nutrition. The drains should be left in place and if there is any evidence of abdominal collections on CT scan or US, further drainage is required. Also, antibiotics and somatostatin analogues are sometimes employed.

Grade C PF is the most severe, with a high mortality rate. When grade C PF occurs it usually presents with abscesses, peritonitis, sepsis and hemorrhage. These patients require major interventions. Treatment of this life-threatening condition can be conventional, with image-guided or operative drainage, or more aggressive with completion pancreato-splenectomy.

MANAGEMENT OF PANCREATIC FISTULA GRADE C IN SEVERAL STUDIES

Pancreatic fistula incidence varies among different centers between 2%-30% depending also upon the definition used^[2-4] (Table 2).

Cullen *et al*^[5] studied 375 patients who underwent PD for a variety of indications. They reported that 66 patients

Table 1 Classification of pancreatic fistula (from Bassi *et al*^[1])

	Grade A	Grade B	Grade C
Clinical conditions	Well	Often well	Ill, appearing bad
Specific treatment ¹	No	Yes/no	Yes
US/CT	Negative	Negative/positive	Positive
Persistent drainage after 3 wk ²	No	No	Yes
Re-operation	No	No	Yes
Death related to PF	No	No	Possibly yes
Signs of infection	No	Yes	Yes
Sepsis	No	No	Yes
Readmission	No	Yes/no	Yes/no

¹Partial or total parenteral nutrition, antibiotics, enteral nutrition, somatostatin analogue, and/or minimal invasive drainage; ²With or without a drain *in situ*. PF: Pancreatic fistula; US: Ultrasonography; CT: Computed tomography scan.

(18%) had pancreatic leakage, of whom only 18 (27%) could be graded as grade C. Completion pancreatectomy was performed in 7 patients with a high degree of destruction and inflammation in the retroperitoneum. The authors concluded that although CP had a very high mortality rate in the treatment of a dehiscence pancreato-jejunal anastomosis, it may be the only option available to salvage the patient, and lesser procedures could have proved ineffective in controlling the leak.

High rates of mortality and morbidity after CP have also been reported by Farley *et al*^[6] (24% and 41% respectively). Their study was conducted on 458 patients who underwent CP after various severe complications following Whipple’s procedures, including PF. The authors concluded that re-evaluation and a decision to use CP is crucial and can be life-saving, when conventional measures have failed, and it should be performed early in the course of clinical deterioration of the patient. Another interesting study was published by van Berge Henegouwen *et al*^[7] comparing drainage versus CP after pancreatic leakage. The authors claim that among 269 patients undergoing PD, 29 (11%) developed severe and persistent leakage of the anastomosis. They suggested that early CP is the treatment of choice, since they reported no mortality after this treatment option, in contrast with previous studies^[5,6], while mortality was seen after managing PF with conventional measures. However, the grade of the PF in this study cannot be clearly defined as the definitions from Bassi were given after their study was published and it is possible that patients without severe deterioration were surgically managed without any resulting mortality.

In order to determine risk factors for PF grade C, Fuks *et al*^[8] studied 680 patients who underwent PD in 5 digestive surgery departments in the northwest region of France. PF was defined according to the Bassi definition. The incidence of PF was 111 patients (16.3%) and PF grade C occurred in 36 patients (32 % of PF). The overall mortality rate due to PF grade C was 38.8%. The mortality rate for CP was one in two patients (50%). Mortality for operative drainage was reportedly 55%. No data were given for percutaneous drainage.

Table 2 Incidence and management of pancreatic fistula in different studies *n* (%)

Authors	<i>n</i>	Incidence of PF/ grade C PF	Treatment		Mortality rate	
			Conservative or surgical drainage	CP	Conservative	CP
Cullen <i>et al</i> ^[5] , 1994	375	66 (18)/18 (4.8)	11 (61)	7 (39)	5 (8)	
Farley <i>et al</i> ^[6] , 1996	458	NA	NA	17	NA	4 (24)
van Berge Henegouwen <i>et al</i> ^[7] , 1997	269	29 (11)/NA	21	8	8 (38)	0
Fuks <i>et al</i> ^[8] , 2009	680	111 (16.3)/36 (5.2)	34 (95)	2 (5)	14 (38.8)	
de Castro <i>et al</i> ^[9] , 2005	459	41 (8.9)/27 (10.2)	18 (67)	9 (33)	6 (15)	0
Büchler <i>et al</i> ^[10] , 2003	617	20 (3.2)/NA	NA	0	0	0
Haddad <i>et al</i> ^[11] , 2009	117	35 (30)/14 (12)	9 (65)	5 (35)	2 (22)	3 (60)

PF: Pancreatic fistula; CP: Completion pancreatectomy; NA: Not available.

Additionally, de Castro *et al*^[9] studied the optimal management of PF after PD. He used a different definition for PF. PF was defined as high amylase level in drain fluid (> 3 times serum level), or leakage proven by CT or US or re-laparotomy in combination with clinical deterioration of the patient. PF presented at 41 patients (8.9%). Non-surgical drainage was performed in 14 of them. Drains placed intra-operatively were maintained in 7 of these patients and percutaneous drainage was conducted in the rest. The mortality rate was 15% (6 patients died). One of them underwent surgical drainage and three underwent surgical exploration and disconnection of the pancreatic-jejunal anastomosis, with preservation of a pancreatic remnant. No patient died of those who needed CP. Of the seven patients who survived after re-laparotomy and preservation of a pancreatic remnant, most were re-admitted suffering from necrosis, pseudocysts and fistulas. This strategy prevented diabetes mellitus, the major concern in the CP group, in approximately half of the patients although at the cost of an increased risk of postoperative death. This study concluded that CP continues to have a place in the management of patients with severe septicemia after PF, who do not respond to non-surgical drainage procedures. However the PFs included in this study were not restricted to grade C as the Bassi definitions did not exist at the time of the study. Grade B fistulas were certainly included in the PFs that were managed in the study.

On the other hand, there are authors who do not support CP due to the mortality, morbidity and other consequences. Büchler *et al*^[10] claimed that CP should no longer be considered in patients with a PF. They studied 617 patients who underwent pancreatectomy. The overall incidence of PF in this study was 3.2% (20 patients) with no mortality reported after PF. However no data are given concerning the severity of these PF cases. Seventeen of the 20 patients who developed this complication healed with conservative treatment, two underwent interventional drainage procedure after developing a low-output PF and a simultaneous peri-anastomotic abscess and only one required reoperation in order to deal with a high-output PF (> 200 mL/d). No patient underwent CP. The authors conclude that CP has probably lost its role in PF management. However, the data from this study cannot be compared with other studies as there is no correlation of the impact of PF with the patient overall status. As a result

there is no way to exclude grade A and B PF cases which would have a better prognosis and would not require major interventions.

Haddad *et al*^[11] published an article about the treatment of choice for PF after PD. In their study 121 patients underwent PD of which 35 (30%) developed PF. Of these 20 were managed conservatively and 14 were re-operated. Five underwent CP and overall mortality in the re-operated patients was 60% (3 patients). Nine patients underwent surgical debridement and drainage with 22% mortality (2 patients). This study suggests that CP should be performed only in patients with peritonitis and severe inflammation of the retroperitoneal space. Additionally, radiological or conservative surgical treatment of PF should be the preferred option, because extensive drainage and CP are procedures which have high mortality and morbidity rates. The authors also give emphasis on postoperative CP endocrine insufficiency and the associated morbidity.

MANAGEMENT CONTROVERSIES

Despite the extensive experience with pancreatic resection procedures and the decrease in overall complication rates and hospital stay, pancreatic leak rates remain unchanged^[12]. Rates of postoperative mortality, wound infection, cardiac complications, intra-abdominal abscess, bile leak, hemorrhage from the rupture of a pseudo-aneurysm and frequency of re-operation are significantly greater in patients with PF. Consequently, prevention and effective management of these patients is a major concern for pancreatic surgeons^[13]. Obviously the management of complications associated with PF requires a multidisciplinary approach involving the pancreatic surgeon, intensive care team and interventional radiologists^[14]. PF grade A and B are well managed conservatively with TPN, somatostatin analogues, slow removal of the drains placed intra-operatively and percutaneous drainage of abdominal collections, if needed^[4]. On the other hand PF grade C is a life-threatening condition and may require operative intervention when there is evidence of sepsis and/or organ dysfunction. The overall re-laparotomy rate has decreased, indicating that many complications can be managed by non-operative means. Once the operative approach is decided the degree of destruction and inflammation in the retro-peritoneum probably plays the major role in determining the operative

procedure for correcting the leaking pancreaticojejunal anastomosis. At the present time, the use of CP is under debate whereas conservative management is thought to be as a salvage solution equally efficient to CP. Although CP has high mortality rates, but lesser procedures may be ineffective in controlling the leak. This aggressive approach achieves sterilization of the infection source and has a decreased need for re-operation. However, it is a technically demanding procedure with major pitfalls as it leads, in most cases to splenectomy and, moreover, to endocrine insufficiency with potential lethal severe hypoglycaemia.

The preferred management strategy remains a matter of debate and generally depends on the severity of the leak and the surgeon's preference.

CONCLUSION

The operating skills of the surgeon and the clinical assessment of the patient are crucial in deciding on surgical intervention through completion pancreatectomy patients with PF grade C who do not clinically improve under conventional measures. Future studies should be designed according to strict and uniform criteria concerning the severity and degree of PF in order to evaluate the place of each therapeutic intervention for the management of this complication.

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S- Editor Wang JL L- Editor Hughes D E- Editor Lin YP