

Complications after pancreaticoduodenectomy: the problem of current definitions

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Abstract

Pancreaticoduodenectomy nowadays represents a complex procedure and a challenge for the surgeon. Even though mortality is reported to be below 5% for experienced surgeons, morbidity is still around 30%–50%, often leading to prolongation of hospital stay, demanding postoperative investigations and procedures, and outpatient monitoring of the patients with complications. In the literature there is no agreement on the definitions of postoperative complications following pancreaticoduodenectomy, leading to a wide range of complication rates in different specialist units, particularly regarding the source of every complication, postoperative pancreatic fistula, and others such as delayed gastric emptying. Some authors have demonstrated that applying different definitions in homogeneous, single-center series, the incidence of a complication varied with statistical significance, implying the impossibility of correctly comparing different experiences. It seems essential to organize a Consensus Meeting among expert surgeons to prepare world-wide accepted definitions. The aim of this article is to review the current controversial definitions and to suggest a new clinical-based approach to the problem of the feasibility and reliability of the definitions themselves.

Key words Pancreaticoduodenectomy · Complications · Definitions · Pancreatic fistula · Delayed gastric emptying

Introduction

Pancreaticoduodenectomy (PD) is a complex surgical procedure associated with a still significant mortality of just below 5% and morbidity of 30%–50%.^{1–23} The major surgical complications are postoperative pancreatic fistula (POPF), hemorrhage, abscess, and delayed gastric emptying (DGE), which can lead to a

substantial modification in the postoperative management with prolonged hospital stay, repeat operations, and mortality.

The problem of the current definition of complications is strictly correlated with the determination of their incidence, as was well demonstrated in a recent paper published by Bassi et al.¹ concerning pancreatic fistula (PF); it is clear that the more disagreement there is between specialists about the definitions, the more likely there will be different experiences of incidence of complications.

The problem with definitions arises not only in questions of terminology and anatomically or physiopathologically correct descriptions of a postoperative event but also from different interpretations of patient outcomes. This problem also has consequences in terms of evaluation of techniques and procedures in performing an operation as complex as PD in which almost every phase is the target of experimental trials carried out by experts.

In the 1990s the focus of the majority of pancreatic surgeons was on demonstrating the feasibility of PD with an acceptable mortality rate, at least in high-volume centers, and fighting against many clinicians' skepticism of resection for ductal carcinomas.^{2,3} As observed by the authors themselves,⁴ postoperative morbidity was more difficult to quantify because definitions of specific complications varied from unit to unit also in multicentre studies.^{5,6}

In contrast, at the same time, some authors used definitions of complications of PD such as POPF based on definite biochemical and demonstrably quantifiable parameters, focusing on the need to strictly identify an epiphenomenon rather than to weigh the real clinical impact of a postoperative event.^{7,8}

In the twenty-first century, having won the battle with the skeptics and learnt a lot about pancreatic secretion and its pharmacological inhibition, of which the identification and management of a POPF was major part, we

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now need clinically based definitions of complications accepted worldwide to compare the different experiences of different centers with the aim of optimizing the management for each complication.

Postoperative pancreatic fistula

POPF is still the most common and dangerous severe complication after PD, the incidence of which ranges widely in reported series from 2%⁹ to more than 20%,^{10–22} also the result of the application of different definitions. Because of our own daily arguments about patient outcome and uncertainty in determining whether drained fluid did or did not indicate a POPF, we did a Medline search to identify the definitions of PF among expert pancreatic surgeons in the series reported and found in a 10-year period (1991–2000) 26 different definitions.¹ The relevant observation was that the incidence of POPF was significantly different (from 10% to 28.5% $P < 0.00001$) in the same group of 242 patients who underwent resections performed by the same surgical team in our center depending upon the definition applied.

The parameters considered should identify those patients in whom a postoperative event has modified the outcome of the operation and should be as objective as possible, such as monitoring the daily output of amylase-rich fluid over a specific time frame. The various definitions in use are not the only reason for the basic need to better stratify the postoperative course between minor events and catastrophic clinical situations. Even in our series published in 2001,²³ among patients with specific surgical complications, the range of hospital stay was wide, between 10 and 69 days, leading us to believe that the definitions applied sometimes do not accurately reflect the clinical impact of events.

So far it seems that a simple, reliable, and easy-to-apply definition has the intrinsic limitation of generating many false-negative or false-positive results in terms of a complication's incidence and may not realistically give a good picture of what really happened to a patient during the postoperative hospital stay, as shown in Table 1.^{7–9,11,23–36} We have to consider the length of the hospital stay and also the resources used in terms of radiology, laboratory tests, or further interventional procedures. Furthermore we need to determine whether the discharged patient is able to reestablish a normal daily routine or needs to attend a daily outpatient clinic for dressing changes and monitoring of the in-situ drain, thus incurring a further social cost. As regard a definition of POPF, it is important to determine the grading of a postoperative event based on the aforementioned parameters.

Hepaticojejunal fistula

Hepaticojejunal fistula is not a common major complication after PD, with an incidence ranging from 2% to 4% in high-volume centers,^{23,37,38} but it is often associated with a POPF when it occurs in patients who have undergone a pancreaticojejunostomy reconstruction. The low and homogeneous reported incidence demonstrates that there is substantial agreement on the definition, and in most cases, the problem of the clinical impact of the fistula has to be correlated to the course of the associated POPF. It is essential to distinguish an early postoperative biliary leakage revealed by bile-stained fluid coming from the drain, which often resolves in few days as soon as bowel activity returns to normal, from a persistent high-volume output leading to a modification of the clinical postoperative course as a result of biliary fluid collection or abscess; the relevant clinical impact in the latter case should be graded when a biliary fistula is reported. When the biliary leakage persists longer than 5 postoperative days, a radiological imaging, conventional fistulography, or a computed tomography-guided contrast scan is needed to plan adequate treatment.²³

Delayed gastric emptying

The incidence of delayed gastric emptying (DGE) after pancreaticoduodenectomy differs greatly among different centers, ranging from 4% to 57%.^{9,18,23,39–42} As for POPF, there is no single, universally accepted definition, but reported definitions vary from the need for a nasogastric tube 10 days after operation and^{9,23} nasogastric drainage of 10 days' duration or more or the delay of regular diet beyond 14 days postoperatively⁴¹ to the inability to consume a regular diet.⁴³ Riediger et al.⁴² applied to the same group of 204 resected patients the three different definitions reported with the results that the incidence of DGE varied from 5.9% to 14.7%.

Another observation concerns the association between DGE and other surgical complications well established in the vast majority of reports. In severe complicated postoperative courses, patients are often kept nil by mouth and sometimes with nasogastric drainage or with total enteral nutrition for a considerable period, leading to the impossibility of determining whether they experienced DGE. It is necessary to substratify the population, giving the incidence of DGE in the subgroup without other abdominal complications,⁴² to identify the patients to review for further medical approaches to the physiopathology of the duodenum–jejunum reconstruction after pylorus-preserving pancreaticoduodenectomy.

Table 1. Definition of pancreatic fistula in recently reported series

Author	Definition
Buchler 1992 ⁷	Concentration of amylase and lipase in the drainage fluid more than 3 days postoperatively of more than three times the serum concentration and a drainage volume of more than 10ml/24h at the same time
Ihse 1994 ²⁴	Amylase-rich output >25 ml daily for more than 2 weeks
Pederzoli 1994 ⁸	Drain output of fluid with amylase content more than three times the maximum normal value exceeding 10ml per 24h for at least 4 days from day 4 after operation
Yeo 1995 ²⁵	Drainage of greater than 50ml of amylase-rich fluid on or after postoperative day 10
Parviainen 1996 ²⁶	Drain output of fluid with amylase content more than three times the upper normal value and more than 50ml daily on the 7th postoperative day or later
Andivot 1996 ²⁷	More than 100ml/day after postoperative day 3 or intra-abdominal abscess with amylase level more than 1000 U/l
Chew 1997 ²⁸	Persistently high output (>50 ml) of amylase-rich fluid from the peripancreatic drains after postoperative day 10 or a leak that was demonstrated roentgenographically
Howard 1998 ¹¹	More than 10ml/day of drainage fluid with an amylase and lipase concentration more than 3 times the serum concentration more than 5 days after the procedure
Park 1998 ²⁹	Daily drainage of greater than 50ml of amylase-rich fluid on or after postoperative day 7
Heslin 1998 ³⁰	Persistent pancreatic fluid drainage that continued at a rate of 30ml or more per day and did not resolve by postoperative day 7
Slim 1999 ³¹	More than 10ml/day after postoperative day 3 of amylase rich (>3 times n.v.) drainage fluid or intra-abdominal fluid collection adjacent to pancreatic anastomosis or reoperation showing an anastomotic dehiscence
Buchler 2000 ⁹	Secretion of 30ml or more of amylase-rich drainage fluid (more than 5000 units) per day for more than 10 days
Bassi 2001 ²³	Amylase-rich output of 30ml/24h or greater for at least 7 days beyond the 4th postoperative day. Confirmed by fistulography
Peng 2003 ³²	A significant increase in the volume or a change in the nature of the effluent from the surgical drain, or the persistence of amylase-rich drainage output in excess of 50ml/day and amylase levels of more than 1000 IU/l
Shan 2003 ³³	Amylase-rich fluid (above threefold serum amylase) from the drain 10ml/day for longer than 7 days
Popiela 2004 ³⁴	Drainage of at least 10ml of amylase-rich fluid detected in abdominal drains after 3rd postoperative day
Sutton 2004 ³⁵	Recovery of fluid from peripancreatic drains with an amylase content 5 times greater than normal
Munoz-Bongrand 2004 ³⁶	An amylase-rich surgical drainage fluid (above fivefold serum amylase) after postoperative day 5, or by the presence on computed tomography scan of a fluid collection located close to the anastomosis or containing amylase-rich fluid, or by operative findings in case of reoperation.

Intra-abdominal abscess

The incidence of intra-abdominal abscess ranges between 1.2% and 7.8% in the recent literature.^{9,22,38,42,44} There is wide agreement on the etiology of the abscess as a consequence of a poorly drained POPF or hepaticojejunum leakage. On the other hand, we observed a correlation between a low incidence of POPF and surprisingly high rates of fluid collection or abscesses leading to several repeat operations.^{13,45,46} As observed recently by Munoz-Bongrand,³⁶ the measurement of the amylase content of peripancreatic fluid collection and abscesses is mandatory and leads to the definition of such fluid collection as a POPF. In this case, the terminology should be as exact as possible to avoid underestimation of postoperative complications. We recommend adherence to the Atlanta Classification,⁴⁷ in which there is a distinction between acute fluid collection appearing early and lacking any wall and pancreatic abscess with a wall of granulation tissue. If the

drainage of a symptomatic acute fluid collection gives an amylase-rich fluid, it is best to define this complication as a POPF. Furthermore, our suggestion is to avoid the generic terminology of “abscess” because this usage leads to great confusion in the interpretation of data and comparison of different experiences.

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