



Long Standing Pancreatic Fistula

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Introduction

Post Operative Pancreatic Fistula (POPF) remains the most common major complication after partial pancreatic resection and is the principal matter of concern among pancreatic surgeons. In practice, most POPFs resolve spontaneously under conservative treatment. The majority of patients with POPF manifest with immediately obvious presentations after the index operation. However, a subgroup of patients presents with latent POPF. As pointed out by Pratt et al. [1] latent fistulae differ in that they lack an amylase-rich fluid on initial measurement, yet ultimately exhibit (either acutely or sub acutely) the clinical and radiologic findings indicative of fistula. Based on the International Study Group of Pancreatic Fistula (ISGPF) definition, radiologic documentation is neither mandatory nor necessarily recommended for POPF diagnosis. Cross-sectional imaging is widely used in case of a deviation from the normal course, especially for interventional purposes [2]. Recent, multicenter, multinational report of >4,000 pancreatoduodenectomies indicated an overall POPF rate of 19.2%, of which 42.3% were grade A; clinical relevant (CR)-POPFs occurred in 11.1% of all cases [3].

Definition

The consensus definition of POPF, emanated in 2005 by the ISGPF, has been since employed in most of the studies investigating outcome measures in pancreatic surgery, thereby allowing a reliable comparison among different experiences. In 2016, the ISGPF standardized, and refined, the definition for CR-POPF, which broadly includes any clinically relevant squealed, associated with an increased drain fluid amylase that necessitates an alteration of the expected postoperative course [4]. The main novelty has been represented by the introduction of the concept that the fistula must be a clinically relevant condition. The Revised 2016 ISGPS documented the checklist for clinical use [4]. The grade A was removed from the classification and a new category named Biochemical Leak "BL" has been introduced. The "BL" describes a condition in which an increased amylase level is detected from drain fluid, without impacting on the postoperative clinical outcomes and is therefore excluded from the POPF definition. The second substantial change in the 2016 update is represented by a more accurate distinction between the grades B and C [5].

Clinical Implication

Using the 2005 ISGPF, some investigators were unclear whether the use of Interventional Drainage (ID) should shift a grade B POPF into the category of a grade C POPF. In the original 2005 ISGPF classification, a grade B POPF "may require repositioning of the drains," but "if an invasive procedure is needed, the grade B POPF will shift up to a grade C." As such, patients requiring ID for POPF-related collections have been categorized differently into B and C grades in the literature [5]. In validation study, as a result of this new definition, the actual overall POPF rate of our surgical series decreased from 33.7% to 26.7%. Among the entire cohort, grade B POPF increased from 11.5% to 22.1%, whereas grade C decreased from 15.2% to 4.6% [5]. When compared with patients who did not develop a POPF, no differences were detected in term of major surgical complications, reoperations, readmissions rate, 90-day mortality, and length of stay. No differences in terms of morbidity and mortality between BL patients and those with normal amylase drain values were detected, confirming that BL alone does not impact on the final clinical outcome. Whenever an increased amylase activity is found in the fluid from an operatively placed drain, which does not impacted on the clinical outcome of the patient, no fistula should be reported [5]. Surgical reoperation was associated with a significantly higher 90-day mortality rate. The restriction to surgical reoperation as the only invasive procedure able to define a grade C POPF is therefore justified by the significantly worse postoperative outcome related to this condition. The second criterion used in 2016 to segregate POPF grade B from C was the development of organ failure (OF) during the postoperative course. Finally, patients developing OF were more frequently surgically

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explored and had a 50% mortality rate, whereas in the cohort without OF, mortality was nil ($P < 0.001$). OF after POPF has been defined as the need of reintubation, hemodialysis, and/or inotropic agents more than 24 hr for a respiratory, renal, or cardiac insufficiency. ISGPF study revealed aggressive clinical management for POPFs did not improve or worsen 90-day mortality [6]. Postpancreatectomy death might occur as unrelated to the POPF and no grade C should be assigned.

Risk Factors

Vollmer et al. [7] demonstrated the Fistula risk score "FRS" (0 to 10 points) which can be calculated at the time of pancreatic anastigmatic reconstruction on the basis of the weighted influence of 4 risk factors: (i) soft pancreatic parenchyma, (ii) high risk disease pathology (iii) small pancreatic duct size, and (iv) elevated intraoperative blood loss. Subsequently, the Fistula Risk Score (FRS) has been introduced as a highly predictive tool for the development of CR-POPF [8-11]. The best way to prevent pancreatic fistula after pancreatic surgery remains still controversial. Yamaue et al. reviewed RCTs to compare pancreaticogastrostomy (PG) with pancreaticojejunostomy (PJ) during PD, the impact of pancreatic duct stent during PD, and somatostatin analogues after pancreatic surgery to reduce pancreatic fistula [12]. A single randomized trial showed that enteral nutrition is superior to TPN [13]. Pooled data of randomized trials failed to show any advantage of somatostatin analogs for accelerating POPF closure [14]. In 9 multicenter Dutch study, 309 fistula underwent procedure from 2196 PD. There was no tendency observed toward catheter drainage as the first intervention for severe pancreatic fistula over the years of Inclusion [15]. Indications to relaparotomy are not uniform across different studies and depend on institutional expertise and patient's preoperative conditions. The management of life threatening POPF is still subject to debate. This is particularly true now that low mortality rates can be expected in centers dedicated to pancreatic surgery. Accordingly, surgeons must be aware of the available techniques when surgical management is mandatory in difficult situations [16]. 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 [17]. The FRS identifies a distinct high-risk cohort (FRS 7 to 10), which occurs in about 10% of all PDs and demonstrates substantially worse clinical outcomes, including a CR-POPF rate approaching 30% [3,18]. There were 167 (32%) patients who received this strategy; these patients experienced significantly fewer CR-POPFs than when these 2 strategies were not conjointly utilized [18].

Left Sided Pancreatectomy

The incidence of POPF after DP has been reported to range from 18.6% to 64.9% [19-21]. Although various techniques have been attempted to prevent the development POPF after DP, no consensus has been established on the precautionary measures against POPF. Further investigation is necessary to develop a reliable strategy for preventing POPF and to improve the outcomes of DP [22].

Conclusion

POPF is a complex, multivariable phenomenon that continues to challenge pancreatic surgeons. The management strategy is driven by the patient's condition and local expertise and is based on poor evidence. The continuous development of specialist, high-volume units with appropriate resources and multidisciplinary experience in

complication management might further improve the evidence and the outcomes.

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