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Original research

Can the measurement of amylase in drain after distal pancreatectomy predict post-operative pancreatic fistula?

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ABSTRACT

Introduction: The most frequent reason for performing a distal pancreatectomy is the presence of cystic or neuroendocrine tumors, in which the distal pancreatic stump is often soft and non fibrotic. This parenchymal consistence represents the main risk factor for post-operative pancreatic fistula. In order to identify the fistula and assessing its severity postoperative monitoring of amylase from intraperitoneal drains is important.
Methods: From a retrospective multicentric database analysis were included 33 patients who underwent distal pancreatectomy for pancreatic neoplastic disease.
Results: Postoperative pancreatic fistula occurred in four cases. One patient had a ductal adenocarcinoma, two presented with pancreatic endocrine neoplasms and the last one had an intraductal papillary mucinous neoplasia. Two patients underwent open, the other two laparoscopic distal pancreatectomy.
Discussion: Postoperative pancreatic fistulas after distal pancreatectomy worsen the quality of life, prolong the post-operative stay and delay further adjuvant therapy. In patients who underwent distal pancreatectomy literature exposed some advantages deriving from the placement of abdominal drainages only in selected cases and from their early removal. Patients presenting a high risk of pancreatic fistula had higher amylase levels of drainage fluid in the first postoperative day.
Conclusion: POPF is the most frequently complication after pancreatectomy. In our analysis DFA1 > 5000 can be considered as a predictive factor for pancreatic fistula. For this reason, the systematic measurement of amylase in drain fluid in first-postoperative day can be considered a good clinical practice.

1. Introduction

The most frequent reason for performing a distal pancreatectomy is the presence of cystic [1] or neuroendocrine [2,3] tumors, in which the distal pancreatic stump is often soft and non fibrotic [4]. Indeed pancreatic parenchyma consistency is reduced in those diseases which don't cause an obstruction of the Wirsung and are not usually related to the onset of chronic pancreatitis which is a consequence of the obstruction of the pancreatic duct [5].

After pancreatectomy the soft pancreatic stump represents the main risk factor for post-operative pancreatic fistula (POPF) [6,7], infact POPF is the most frequent complication of

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pancreaticoduodenectomy [8] and distal pancreatectomy (20–40%) [9–12]. From these fistulas can develop abdominal fluid collections and abscesses [13]. For these reasons numerous surgical techniques [14], mininvasive surgery [15–17], new drugs [18] and devices have been employed in clinical practice in order to prevent the onset of pancreatic fistula [19].

So it is very important to identify the fistula and assessing its severity; the presence and grade of POPF were determined using the consensus guidelines from the International Study Group on Pancreatic Fistula (ISGPF) [20]:

- Grade A fistulas: don't need any surgical intervention and overall hospital stay is usually longer
- Grade B fistulas: require a prolongation of postoperatory stay, the permanence of abdominal drains, the evenience to positioning other abdominal drains under radiological guide, administration of antibiotics and parenteral or enteral nutrition
- Grade C fistulas: a reintervention is needed in order to resolve the complication

In order to decrease severity of complications after distal pancreatectomy it is very important the postoperative monitoring of amylase from intraperitoneal drains. As a matter of fact when levels of amylase in the first postoperative day rise over 4000 [21,22] or 5000 UI/L [23] the risk of fistula formation is significantly increased. If amylase levels are under the previously mentioned threshold intraperitoneal drains should be immediately removed in order to reduce the risk of infections [24,25].

In our trial PF is diagnosed when any drain output with an amylase content more than 3 times the upper limit of the normal serum amylase fluid level (>300 IU/L) at postoperative day 3 or later [26].

2. Material and methods

A retrospective analysis of prospective databases from the participant centers has been performed resulting in 33 patients who underwent distal pancreatectomy for pancreatic neoplastic disease.

Mean age was 55 years (range 34–78 years) and male–female ratio was 13:20; the indications for surgery from the most frequent one were:

- ductal adenocarcinoma (14 pts.)
- pancreatic endocrine neoplasms (8 pts.)
- Intraductal Papillary Mucinous Neoplasia IPMN (5 pts.)
- mucinous cystic neoplasms (3 pts.)
- serous cystic neoplasms (2 pts.)
- solid pseudopapillary neoplasm (1 pts.)

All operations were performed by a surgical team experienced in pancreatic surgery.

Twelve patients underwent a spleen preserving pancreaticoduodenectomy (PD).

The interventions were performed by robotic surgery, laparoscopy and open surgery respectively in 6, 11 and 16 patients.

Intraoperative assessment of pancreatic parenchyma consistence, performed by palpation of the pancreatic remnant in open surgery or by direct vision in minimally invasive surgery, resulted in soft and medium–hard pancreatic texture respectively in 16 and in 17 patients.

The most of pancreatic resections were performed by means of mechanical stapler (23 pts.), in the remnant patients the proximal stump was sutured by single loose suture (8 pts.). Only in three patients an absorbable fibrin sealant patch was employed (TachoSil). Two drainage tubes connected to a collection bag were placed in the left subphrenic cavity and near the pancreatic stump in the patients who had undergone distal pancreatectomy and splenectomy, only a perianastomotic peritoneal drain in those patients who underwent spleen preserving distal pancreatectomy. Amylase concentration in the peritoneal drainage fluid was measured on the first postoperative day and on the fifth postoperative day. We define a high risk of POPF when the dosage of amylase in drain is over 5000 IU/L in the first postoperative day, independent of the volume produced, and we suspected a POPF when the dosage of amylase in drain is over 200 IU/L in the fifth postoperative day, independent of the volume produced.

3. Results

Seven patients (21.2%) had amylase drain >5000 IU/L in the first postoperative day, and 5 of them (15.1%) had a dosage of amylase in drain over 200 IU/L in the fifth postoperative day.

Postoperative pancreatic fistula occurred in four cases (12.1%).

Demographics of patients with fistula were the following:

- 59 years (range, 44–78 years)
- male–female ratio 1:1
- indications for surgery: 1 pt. with ductal adenocarcinoma, 2 pts. with pancreatic endocrine neoplasms and 1 pt. with IPMN.

The pancreatic texture was soft in three cases and medium–hard in 1 case. Two patients underwent open, the other two laparoscopic distal pancreatectomy. Only in one patient an absorbable fibrin sealant patch was used (TachoSil).

These pancreatic fistulas were classified using ISGPF criteria in different grades of severity: two were Grade A, one was Grade B, and one was Grade C.

The Grade A patients did not undergo any treatment but they required a longer hospitalization.

The Grade B patient underwent total parenteral nutrition and somatostatine and then antibiotic treatment.

The Grade C patient underwent a second operation for fluid peripancreatic collection.

4. Discussion

The most frequent postoperative morbidity after distal pancreatectomy consists in pancreatic fistula [27–30]; the incidence of this complication is still invariate in the reports from high volume centers [31,32]. POPF (postoperative pancreatic fistula) after distal pancreatectomy differ from those after DCP because the former are not cause of important post-operatory complications [33], but they worsen the quality of life, prolong the post-operatory stay and they delay the start of further adjuvant therapy [34]. Despite this, in order to reduce the incidence of pancreatic fistulas after distal pancreatectomy new surgical techniques, new drugs and devices have been proposed:

- pancreatic stapler transection with bare metal staples [35–37] or with reinforced staple loads [38].
- the Finnish [39].
- stump radiofrequency closure [40].
- use of pancreatic duct stent [41,42].
- application of a biological sealing agent over the pancreatic stump [43,44], coverage of the pancreatic remnant with falciform ligament [45].

None of these techniques significatively reduced the incidence of the POPF. In the past the routine employment of intraperitoneal

peripancreatic drains was the gold standard since they could prevent the build-up of peritoneal fluid collections, as well monitoring pancreatic leaks and hemorrhage [46]; but at the moment it is not proved that the routine placement of drains doesn't reduce morbidity related to POPF [47,48] and, on the contrary, it increases the risk of complications [49]. In patients who underwent distal pancreatectomy literature has exposed some advantages deriving from the placement of abdominal drainages only in selected cases [50] and from their early removal in patients presenting at low risk of POPF [51].

In order to achieve an early removal of the abdominal drainages is mandatory to stratify patients in terms of risk of development of pancreatic fistulas. Indeed patients who presented a high risk to develop a POPF were those who had higher amylase levels of drainage fluid in the first postoperative day [52].

Predictive values for DFA1 (first postoperative day drain amylase values) are very variable in the literature, ranging from DFA1 > 90 U/L [53], DFA1 > 100 U/L [54], DFA1 $\geq$ 350 U/L [55], to 5000 U/L [56].

5. Conclusions

POPF is the most frequently complication after pancreatectomy. In our analysis DFA1 > 5000 can be considered as a predictive factor of the presence of pancreatic fistula. For this reason, the systematic measurement of amylase in drain fluid in first-postoperative day can be considered a good clinical practice.

Ethical approval

None required.

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None.

Author contribution

Roberto Cirocchi, Luigina Graziosi, Andrea Polistena, Claudio Renzi, Jacopo Desiderio, Masahiko Hirota: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data; also participated substantially in the drafting and editing of the manuscript.

Alessandro Sanguinetti, Carlo Boselli, Giuseppe Noya, Amilcare Parisi, Annibale Donini, Nicola Avenia: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data, edited and approved the final version of the manuscript.

Conflicts of interest

None.

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