Predictive factors of morbidity in distal pancreatic resections

Fatores preditivos de morbidade nas ressecções pancreáticas esquerdas

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ABSTRACT

Objective: To evaluate the postoperative morbidity of distal pancreatic resections and to investigate its predictive factors.

Methods: The study was conducted retrospectively from a prospectively maintained database. From 1994 to 2008, 100 consecutive patients underwent left pancreatic resections. The primary variable of interest was postoperative morbidity, and various other characteristics of the population were simultaneously recorded. Later, for the analysis of predictors of postoperative morbidity, the subgroup of patients who underwent distal pancreatectomy with spleen preservation (n = 65) was separately analyzed with regards to the different techniques of section of the pancreatic parenchyma, as well as to other possible predictors of postoperative morbidity. Results: Considering all left pancreatic resections performed, the occurrence of overall, relevant and serious complications was 55%, 42% and 20%, respectively. The factors predictive of postoperative morbidity after distal pancreatectomy with spleen preservation were the technique employed for section of the pancreatic parenchyma, age, body mass index and the performance of concomitant abdominal operations. Conclusion: The morbidity associated with pancreatic resections to the left of the superior mesenteric vessels was high. According to the stratification adopted based on the severity of complications, some predictive factors have been identified. Future studies with larger cohorts of patients are needed to confirm these results.

Key words: Surgical procedures, operative. Pancreatectomy. Postoperative complications. Morbidity. Pancreatic fistula.

INTRODUCTION

Left pancreatic resections (LPRs) are surgical procedures associated with significant postoperative morbidity, ranging from 4% to 60% in reported series. Different definitions of morbidity have been adopted in these studies, making interpretation of their results difficult. In order to solve this problem, there was a consensus meeting of the International Study Group on Pancreatic Fistula (ISGPF) with the aim of establishing a definition for which this is one of the major complications after pancreatectomy. The technical section of the pancreatic parenchyma during pancreatic resections has been cited by several authors as a potential predictive factors of pancreatic fistula (PF). Several techniques are being used, reflecting lack of knowledge about the superiority of a particular technique over another. This fact is mainly due to methodological limitations of the studies (selection bias and morbidity definitions) or the absence of significant differences between results.

Motivated by this lack of evidence, with the present study the authors aimed to assess the experience of the Institut Mutualiste Montsouris (Paris, France) in performing left pancreatic resections to the superior mesenteric vessels, with a focus on determining postoperative morbidity and its predictors.

METHODS

The study was conducted retrospectively from a prospectively maintained database. From 1994 to 2008, 100 consecutive patients underwent left pancreatic resections. The primary variable of interest was postoperative morbidity. The LPR procedures included splenopancreatectomy (Spl-Pd), distal pancreatectomy with spleen preservation (Pd) and enucleations of lesions located to the left of the superior mesenteric vessels. Due to the heterogeneity of the group, to investigate predictors of postoperative morbidity we studied only the subgroup of patients who underwent Pd (n = 65). We recorded...
postoperative morbidity, as well as patient characteristics and variables related to preoperative and postoperative periods in a database, as summarized in table 1.

We standardized morbidity and complications as synonymous, defined as any intra-abdominal adverse event occurring intra or postoperatively. Pancreatic fistula was defined as any volume of fluid rich in amylase (more than three times the normal concentration of serum amylase), obtained from the percutaneous drain, after the third postoperative day. Pancreatic fistulas were then classified according to the consensus of ISGPF.

Complications were classified as proposed by Dindo and adapted by De Oliveira, where they were divided into five categories according to the severity of events. In this classification, complications types I and II were simple events and did not require invasive treatment; type III were events requiring invasive treatment approaches, where III A required percutaneous drainage under local anesthesia and III B required reoperation; type IV defines the situation where the patient was in poor condition, with involvement of at least one organic system (respiratory, renal, bone marrow, etc.) and generally sent to the ICU; and type V, the events that resulted in death occurred before the 30th day after the first surgical procedure. Aiming to investigate potential predictors of postoperative complications, we qualified these five events (I-V) in three types of complications: non-relevant, relevant, and serious, defined as follows: Event Severity below III A, non-relevant complications (I and II); III-a events: relevant complications; events of gravity higher than III-a (III-B, IV and V): serious complications.

For the section of the pancreatic parenchyma different techniques were applied: ultrasonic scissors (Ultracision™); scissors aided by “rescue” bipolar coagulation (Gyalt bipolar forceps); linear stapler-cutter; and other less common. Regarding the use of staple to approach the pancreatic parenchyma, staple loads used were of vascular type and the “staple line” was reinforced with polydioxanona (PDS) stitches. Three models of staplers have been used in the course of the experiment. Until 2006, Endo-Gia™ 30-45mm and ETS 30/45mm. After 2006, Echelon 60mm replaced the previous models. Regarding the technique involving the use of scissors and “rescue” bipolar coagulation, the pancreatic stump was closed with PDS stitches in a fashion termed as “fish mouth” (splaying the edges of the residual pancreatic stump for better approximation).

The splenic preservation was prioritized, even when there was impairment of the splenic artery. Regarding EN, evaluation by intraoperative ultrasonography was routinely performed in order to estimate the proximity of the lesion with the pancreatic duct. The administration of anti-secretion medication (somatostatin derivatives) was not a routine. At the end of the procedures a chest tube with light suction (Haemovac®-type) was usually positioned near the edge of the residual pancreatic stump. This drain was maintained during the first seven days. After this period, a computed tomography (CT) was routinely performed to exclude the presence of residual fluid collections.

In the statistical analysis, overall, serious and relevant complications were used as independent outcomes in univariate and multivariate analysis of predictive factors. For univariate analyzes, we used the chi-square and Fisher tests for qualitative variables. For multivariate analyzes, we used the logistic regression model. To test the independence (confirm) of predictive factors, variables that showed trends toward significance in univariate analyzes were included in the logistic regression models. Some of the variables that entered in the univariate analyzes were: surgical approach (laparotomy vs. laparoscopic); malignancy vs. benign disease; tumor size; gender; age; BMI; duration of surgery; administration of somatostatin derivatives; intraoperative drain placement; splenic preservation; periods in which surgical procedures were performed (1994-2001 vs. 2002-2008); concomitant abdominal operation; elective pancreatic duct ligation; ASA score; and section techniques of the pancreatic parenchyma.

All tests were two-tailed; p value <0.05 was considered significant.

This study was approved by the Ethics in Research Institutions and the source of origin of data and of the researcher (Protocol 134/08 - CEP-HUCFF).

RESULTS

As for postoperative morbidity, considering LPRs (n = 100), the incidence of overall, non-relevant, relevant and severe complications was 55%, 13%, 42% and 20%, respectively. Considering only Pds (n = 65), the incidence of overall, non-relevant, relevant and severe complications was 59%, 17%, 42% and 18%, respectively. With respect specifically to PF, these incidences were 24%, 4.5%, 4.5% and 20%, respectively. Complications included, in addition to PF, bleeding in 9%, collections in 15% and abscesses in 16%. No deaths intraoperative occurred.

In univariate analysis, age and BMI were predictive for the occurrence of overall complications. In multivariate analysis, these two variables remained as such (p <0.05). The median age was 53 years in those with complications (SD = 15.4) and 61 years in those without complications (SD = 12.8). Likewise, the median BMI was 24kg/m² in those complications (SD = 3.8) and 20kg/m² in those with no complications (SD = 2.6).

According to the adopted complications stratification, non-relevant complications occurred in only 16.7% of the procedures. Because they are rare and of no clinical relevance, a more detailed analysis was not performed. For relevant complications univariate analysis results showed greater morbidity when comparing the use
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of ultrasonic scissors to the use of bipolar scissors \( (p=0.01 – OR=13 ; 95\% CI : 1.3-125) \). These results were confirmed by multivariate analysis \( (p=0.03 – OR=13, 95\% CI : 1.2-140) \). Although the surgical approach (laparoscopic versus laparotomy) has shown borderline statistical significance in univariate analysis, this was not confirmed by multivariate analysis.

In relation to serious complications, univariate analysis suggests a significantly higher morbidity when using stapler compared to bipolar scissors \( (p=0.01 – 40\% \text{ and } 5.5\%, \text{ respectively}) \). These results were confirmed by multivariate analysis \( (p=0.01 – OR=10.9 ; 95\% CI : 1.72 \text{ to } 69.2) \).

The same occurred with the variable “concomitant abdominal operation”, whose results also suggest higher morbidity when these procedures were performed, comparing to when they were not performed \( (p=0.03 – 50\% \text{ and } 14\%, \text{ respectively}) \), which also was confirmed by multivariate analysis \( (p=0.04 – OR=7.6; 95\% CI : 1.05-54.7) \).

Other variables analyzed included surgical approach (laparotomy vs. Laparoscopic) and time of interventions (1994-2001 versus 2002-2008). Although both variables have shown borderline significance in univariate analysis, this was not confirmed by multivariate analysis.

**DISCUSSION**

The LPR procedures are considered safe, with a mortality rate close to zero in specialized centers\(^{13,7,11,24-29}\), hampering the studies of predictors of postoperative mortality. Nonetheless, there is important associated postoperative morbidity, especially pancreatic fistulas\(^{7,17,28}\).
LPRs, such results would be hampered by the heterogeneity of predictive factors, we believe that if we included all the subgroup of patients undergoing Pd procedures for analysis the case of fistulas. As justification for the choice of the percutaneous drainage in 70% of cases, reaching 80% in respectively. The handling of these events was limited to including severe fistulas, occurred in only 20% and 6%, procedures have resulted in complications, serious events, definitions of morbidity).

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Nevertheless, these results were influenced by the inclusion of small studies and other methodological limitations of the study (selection bias and heterogeneous definitions of morbidity).

Regarding the method of parenchymal section, various techniques are described, two of which stand out for being the most frequently used: the stapling (cutting and stapling with mechanical stapler) and cold blade section (scalpel or scissors). Kleef et al. showed that the adoption of stapler section as a predictive factor for PF (p = 0.003). These authors reported an incidence of PF after using staplers of approximately twice as the ones with scalp blade section (OR=2.56 ; 95% CI: 1.18-5.93)21. However, their definition of PF was more selective than the one of ISGPF15. Conversely, a meta-analysis showed results in favor of the stapling technique (lower PF incidence) as compared to the scalpel17. Nevertheless, these results were influenced by the inclusion of small studies and other methodological limitations of the study (selection bias and heterogeneous definitions of morbidity).

In the present study, although 55% of the procedures have resulted in complications, serious events, including severe fistulas, occurred in only 20% and 6%, respectively. The handling of these events was limited to percutaneous drainage in 70% of cases, reaching 80% in the case of fistulas. As justification for the choice of the subgroup of patients undergoing Pd procedures for analysis of predictive factors, we believe that if we included all the LPRs, such results would be hampered by the heterogeneity of surgical procedures and other related confounders. In addition, the Pd group proved to be representative of the LPR total group (Table 1).

Regarding the predictive factors identified, BMI and the performance of concomitant abdominal operation were confirmed as predictors of overall and severe complications, similar to the result reported by Ferrone et al.11.

The results of this study also suggest that the use of ultrasonic scissors correlated with incidence almost ten times greater of complications (general morbidity) than the use of a cold blade. The same is true when comparing the use of the stapler with the use of cold blade in relation to the outcome serious complications. Additionally, performing other abdominal operation resulted in an incidence almost eight times higher of serious complications when compared to only pancreatectomy.

To explain these results, some details of the studied cohort of patients should be mentioned (Table 1): approximately half of the procedures were performed laparoscopically; spleen preservation was obtained in about 80% of LPRs (n = 80); 95% of Pds (n = 62) and, when the splenic artery was preserved, in 58.5% of Pds (n = 38). Malignant tumors accounted for approximately 65% of the lesions operated, demonstrating the position of authors in favor of a laparoscopic approach for resection also of malignant pancreatic tumors9,13. This attitude contrasts with most of the other published series, in which the laparoscopic approach has rarely prevailed1,2,11,12,14,21,27-33; there is a lower rate of splenic preservation and malignant tumors do not predominate9,13.

Regarding study limitations, the retrospective nature inevitably incurs in a selection bias. The small study population prevents identification of small differences in the multivariate analysis (type 2 error). Such error could only be avoided when designing a controlled clinical trial.

Based on the results of this study, it can be concluded that age, BMI and concomitant abdominal operation proved to be predictors of morbidity after distal pancreatectomy with spleen preservation. In addition, the method of section of the pancreatic parenchyma was a relevant predictive factor for serious complications, which allows authors to prefer the use of blade over other techniques. Due to its design methodology, this study should be considered a pilot study, and the analysis of larger, multicenter cohorts should be encouraged to confirm the directions toward which the results of this study point.
RESUMO

Objetivo: Avaliar a morbidade pós-operatória e investigar a existência de seus fatores preditivos. Métodos: O estudo foi realizado de forma retrospectiva, a partir de uma base de dados mantida de forma prospectiva. De 1994 a 2008, 100 pacientes consecutivos foram submetidos à ressecções pancreáticas esquerdas. A principal variável de interesse foi a morbidade pós-operatória, tendo diversas outras características da população sido registradas simultaneamente. Posteriormente, para a análise de fatores preditivos de morbidade pós-operatória o subgrupo de pacientes que foi submetido aos procedimentos de pancreatectomia distal com preservação do baço (n=65) foi analisado separadamente quanto à relevância das diferentes técnicas de seção do parênquima pancreático, assim como, outros possíveis fatores preditivos à ocorrência de morbidade pós-operatória. Resultados: Considerando-se juntamente todas as ressecções pancreáticas esquerdas realizadas, a ocorrência de complicações globais, de complicações relevantes e graves foi 55%, 42% e 20%, respectivamente. Os fatores que se mostraram preditivos à ocorrência de morbidade pós-operatória após pancreatectomia distal com preservação do baço foram a técnica de seção do parênquima pancreático, idade, índice de massa corporal e a realização de operação abdominal concomitante. Conclusão: A morbidade associada às ressecções pancreáticas, à esquerda dos vasos mesentéricos superiores, foi importante. De acordo com a estratificação adotada baseada na gravidade das complicações, alguns fatores preditivos foram identificados. Estudos futuros com coortes maiores de pacientes são necessários para confirmar tais resultados.


REFERENCES


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