Male gender and increased body mass index independently predicts clinically relevant morbidity after spleen-preserving distal pancreatectomy

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Abstract

AIM
To identify risk factors for clinically relevant complications after spleen-preserving distal pancreatectomy (SPDP). No previous studies explored potential predictors of morbidity after SPDP.

METHODS
The data of 41 patients who underwent a SPDP in a single surgical center between 2000 and 2015 were retrospectively reviewed from a prospectively maintained electronic database established in our Department of Surgery. The database included demographic, clinical, bioumoral, pathological, intraoperative and postoperative parameters. Uni- and multivariate ana-
lyses were performed to assess potential predictors of clinically relevant morbidity. Postoperative morbidity was defined as in-hospital complications and mortality was assessed at 90 d. Clinically relevant morbidity was defined as complication ≥ grade 2 Dindo.

RESULTS
Overall morbidity rate was 34.1% (14 patients): grade I (6 patients, 14.6%), grade II (2 patients, 4.8%), grade IIIa (1 patient, 2.4%), and grade IIIb (5 patients, 12.2%). A number of 5 patients (12.2%) required re-laparotomy for postoperative complications. There was no postoperative mortality. Thus, at least one clinically relevant complication occurred in 8 patients (19.5%). Univariate analysis identified male gender (P = 0.034), increased body mass index (P = 0.002) and neuroendocrine pathology (P = 0.013) as statistically significant risk factors. Multivariate analysis identified male gender [odds ratio (OR): 1.29, 95%CI: 1.07–1.55, P = 0.005] and increased body mass index (OR: 23.18, 95%CI: 1.72–310.96, P = 0.018) as the only independent risk factors of clinically relevant morbidity after SPDP.

CONCLUSION
Male gender and increased body mass index are independently associated with increased risk of clinically relevant morbidity after SPDP. These findings may assist a surgeon in clinical decision-making to better select patients suitable for SPDP.

Key words: Spleen-preserving distal pancreatectomy; Morbidity; Male gender; Body mass index

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Core tip: No previous studies explored potential predictors of morbidity after spleen-preserving distal pancreatectomy (SPDP). The study aims to identify risk factors for clinically relevant complications after SPDP. Data of 41 patients with SPDP were reviewed and univariate and multivariate analyses were performed to assess potential predictors of clinically relevant morbidity, defined as complication ≥ grade II Dindo. The rate of clinically relevant complications was 19.5%. Male gender [odds ratio (OR): 1.29, 95%CI: 1.07–1.55, P = 0.005] and increased body mass index (OR: 23.18, 95%CI: 1.72–310.96, P = 0.018) were found as independent risk factors of clinically relevant morbidity after SPDP. These findings may assist a surgeon in clinical decision-making to better select patients suitable for SPDP.
Table 1 Demographic, clinical, bioumoral, intraoperative and pathology data of 41 patients with spleen-preserving distal pancreatectomy: A comparative analysis between patients with and without clinically relevant postoperative complications

| Parameter                                      | All patients | No complications (33 patients) | Clinically relevant complications (8 patients) | P value |
|------------------------------------------------|--------------|---------------------------------|------------------------------------------------|---------|
| Male gender                                    | 12 (29.3%)   | 7 (21.2%)                       | 5 (62.5%)                                      | 0.031   |
| Age, yr                                        | 41 (18-76)   | 39 (18-76)                      | 51 (34-66)                                     | 0.067   |
| Charlson comorbidity index                     | 0 (0-4)      | 0 (0-4)                         | 1.5 (0-3)                                      | 0.157   |
| Body mass index, kg/m²                         | 25 (19-42)   | 24 (19-37)                      | 34.5 (24-42)                                   | 0.002   |
| Overweight and obesity                         | 22 (53.6%)   | 15 (45.4%)                      | 7 (87.5%)                                      | 0.049   |
| Obesity                                        | 8 (19.5%)    | 7 (21.2%)                       | 1 (12.5%)                                      | 1.012   |
| Diabetes mellitus                              | 1 (2.4%)     | 0                               | 1 (12.5%)                                      | 0.195   |
| Chronic pancreatitis                           | 6 (14.6%)    | 5 (15.1%)                       | 1 (12.5%)                                      | 1.012   |
| Preoperative leucocytes number, /μL            | 7700 (4900-15300) | 7700 (4900-15300) | 7300 (5200-9200) | 0.961   |
| Preoperative neutrophil number, /μL           | 4900 (2800-13200)  | 4900 (2800-13200)  | 4050 (3500-6400) | 0.759   |
| Preoperative lymphocyte number, /μL           | 1800 (1000-3300)  | 1600 (1000-3300)  | 2200 (1100-2900) | 0.291   |
| Preoperative neutrophil-to-lymphocyte ratio   | 2.9 (1.2-8.4) | 2.9 (1.2-8.4)                   | 2.2 (1.6-5.8)                                  | 0.135   |
| Preoperative platelet number, /μL             | 262500 (161000-464000) | 264000 (161000-410000) | 258000 (170000-464000) | 0.735   |
| Preoperative platelet-to-lymphocyte ratio     | 134 (55.4-372.7) | 134 (55.4-372.7)              | 1419 (85-372.7)                                | 0.550   |
| ASA score 3                                    | 6 (14.6%)    | 4 (12.1%)                       | 2 (25%)                                        | 0.577   |
| Minimally invasive approach                    | 6 (14.6%)    | 4 (12.1%)                       | 2 (25%)                                        | 0.577   |
| Soft pancreas texture                          | 35 (85.3%)   | 28 (84.8%)                      | 7 (87.5%)                                      | 1.000   |
| Associated procedures                          | 5 (12.2%)    | 4 (12.1%)                       | 1 (12.5%)                                      | 1.000   |
| Operative time, min                            | 150 (70-330) | 150 (70-320)                    | 185 (120-330)                                  | 0.067   |
| Estimated blood loss, mL                       | 150 (50-600) | 150 (50-600)                    | 175 (50-300)                                   | 0.550   |
| Intraoperative blood transfusions              | 1 (2.4%)     | 1 (2.4%)                        | 0                                              | 1.000   |
| Tumor diameter, cm                             | 3.5 (0.4-14) | 3.0 (0.4-14)                    | 2.75 (0.4-3.5)                                 | 0.060   |
| Length of resected pancreas, cm                | 9 (6-12)     | 9 (6-12)                        | 8.5 (8-12)                                     | 0.784   |
| Malignant pathology                            | 4 (2.4%)     | 3 (9.1%)                        | 1 (12.5%)                                      | 1.000   |
| Neuroendocrine pathology                      | 18           | 11                              | 7                                              | 0.013   |

¹Fisher’s exact test (two-tailed); ²Mann-Whitney test (two-tailed); ³Assessed no more than one week prior to surgery. ASA: American Society of Anesthesiologists.

Postoperative pancreatic fistulae, hemorrhage and delayed gastric emptying were classified according to the International Study Group of Pancreatic Surgery definitions.

The patients were stratified according to the World Health Organization definitions for underweight (BMI < 18.5 kg/m²), normal weight (BMI: 18.5-24.9 kg/m²), overweight (BMI: 25-29.9 kg/m²) and obesity (BMI ≥ 30 kg/m²).

Statistical analysis

Data are expressed as number (percentage) for categorical variables and median (range) for continuous variables. Fisher’s exact test (two-tailed) and Mann-Whitney test (two-tailed) were used to compare categorical and continuous variables, respectively. Potential predictors of clinically relevant morbidity were tested in univariate analysis, and risk factors with P-values < 0.1 were included in a multivariate binary logistic regression model with the forwarding stepwise method.

P-values < 0.05 were considered statistically significant. Statistical analyses were performed with SPSS (Statistical Packages for Social Sciences) version 20.0 software (SPSS Inc., Chicago, IL, United States).

RESULTS

Morbidity

Overall morbidity rate was 34.1% (14 patients): grade I (6 patients, 14.6%), grade II (2 patients, 4.8%), grade IIIa (1 patient, 2.4%), and grade IIIb (5 patients, 12.2%). A number of 5 patients (12.2%) required re-laparotomy for postoperative complications. There was no postoperative mortality. Thus, 8 patients (19.5%) developed clinically significant morbidity.

Postoperative pancreatic fistula was observed in 13 patients (31.7%): grade A (6 patients, 14.6%), grade B (5 patients, 12.2%), and grade C (2 patients, 4.8%).

Postoperative delayed gastric emptying was observed in 5 patients (12.2%): grade A (2 patients, 4.8%), grade B (2 patients, 4.8%), and grade C (1 patient, 2.4%).

Postoperative hemorrhage was observed in 5 patients (12.2%): grade B (1 patient, 2.4%), and grade C (4 patients, 10%).

Other complications included intra-abdominal abscess, wound infection and splenic vessels thrombosis (one patient each, 2.4%).

Patients who developed clinically significant postoperative complications required postoperative blood transfusion in high percent (6 patients, 75%), while no patients from the group without complications needed a blood transfusion (P < 0.001).

Overall median hospital stay was 8 d (5-45 d) and was significantly higher for patients with clinically significant morbidity (25 d, range 8-45 d), compared with patients without complications (7 d, range 5-24 d).
Uni- and multivariate analysis of predictors of clinically relevant morbidity after SPDP

Univariate analysis identified male gender ($P = 0.034$), increased BMI ($P = 0.002$) and neuroendocrine pathology ($P = 0.013$) as statistically significant risk factors. Furthermore, the multivariate analysis also included age, operative time and tumor diameter ($P$-values $< 0.1$) (Table 1).

Multivariate analysis identified male gender [odds ratio (OR): $1.29$, 95%CI: $1.07$-$1.55$, $P = 0.005$] and increased BMI (OR: $23.18$, 95%CI: $1.72$-$310.96$, $P = 0.018$) as the only independent risk factors.

DISCUSSION

Morbidity rates after SPDP without splenic vessels removal vary between $18\%$ and $71\%$[7,12-14,17,19,20,22,26] and pancreatic fistula represents the most frequent complication: $7.6\%$-$40\%$[28]. Furthermore, pancreatic fistula is considered a risk factor for compromised patency of spleen vessels after SPDP and late complications such left portal hypertension[29].

Severe or clinically relevant complications after SPDP occur in $11.6\%$-$18\%$ of patients[2,6,14,16,20-22,26] and pancreatic fistula rates were $34.1\%$, $19.5\%$, and $31.7\%$, respectively.

Male gender[3,15,21] or increased BMI[3,14,15,18,24] were previously found independent risk factors of overall morbidity or pancreatic fistulae in few studies including all together DP with and without splenectomy. However, most studies failed to demonstrate any correlation of male gender[2,6,8,14,16,20-22,26] or increased BMI[2,3,6,16,17,19,21-23,25,26] with morbidity after DP. In the present study, male gender and increased BMI was found the only independent risk factors for overall clinically relevant morbidity after SPDP.

Age[2,6,8,13,15,18,20,22,25,26], diabetes[2,6,8,13,16,19,23,25,26], chronic pancreatitis[2,6,15,16,19,26], American Society of Anesthesiologists (ASA) score[2,13,14,16,18,20,22,24], blood loss[7,12-14,17,19,20,22,26], operative time[2,3,12,13,15,19,21,22,26], soft pancreas texture[14,22,23], pathology[3,6,8,13,15,18,21-26] and type of approach (open or minimally invasive)[14,15] does not appear to be independent risk factors of overall morbidity or pancreatic fistulae after DP in most published studies, as it was the case in the present study.

However, few studies identified age[14,19,23], chronic pancreatitis[13], ASA score[13], increased operative time[13,23], blood loss[18,21,22,25], soft pancreas texture[18], neuroendocrine pathology[14] and laparoscopic approach[20] as independent risk factor for postoperative complications after DP.

It is worth mentioning that a meta-analysis has shown that laparoscopic DP has been associated with significantly decreased morbidity rates, compared with the open approach[30].

Several studies have associated neuroendocrine pathology with an increased risk of postoperative complications (including pancreatic fistulae) after pancreatic resections[14,18,31]. In the present study patients with neuroendocrine pathology have had increased risk of clinically relevant complications only in univariate analysis.

Nevertheless, a recent meta-analysis has shown that soft pancreas texture, increased BMI, blood loss or operative time are high-risk factors for pancreatic fistulae occurrence after DP[32].

The present study also explored the potential predictive value of surrogates of inflammatory markers such as the neutrophil-to-lymphocyte ratio or platelet-to-lymphocyte ratio for morbidity after SPDP but failed to identify any correlation. These inflammatory markers were previously demonstrated to predict morbidity after major surgery such as liver resections[33] but not for pancreatic resections[34].

The results of the present study should be regarded with caution because there are a limited number of patients.

In conclusion, male gender and increased body mass index are independently associated with increased risk of clinically relevant morbidity after SPDP. Thus, the results of the present study may assist a surgeon in clinical decision-making to better select patients suitable for SPDP.

ARTICLE HIGHLIGHTS

Research background

Many studies have explored potential predictors of morbidity after distal pancreatectomy. All the reported studies included both patients with and without spleen preservation. Some studies have suggested that there might be some differences in outcomes between the patients with distal pancreatectomy, with and without spleen preservation. To date, there is no study to explore potential predictors of postoperative morbidity in a group of patients with only spleen-preserving distal pancreatectomy. The aim of the study is to identify risk factors for clinically relevant morbidity after spleen-preserving distal pancreatectomy in a single surgical center experience.

Research motivation

Morbidity after spleen-preserving distal pancreatectomy remains a significant concern and preservation of the spleen during distal pancreatectomy might sometimes be technically challenging. Thus, identification of potential predictors of clinically relevant morbidity in patients with spleen-preserving distal pancreatectomy would be of interest for clinical practice to better select the patients for this type of surgical procedure.

Research objectives

The primary objective of the study was to explore potential predictors of clinically relevant morbidity after spleen-preserving distal pancreatectomy in a single surgical center experience.

Research methods

It was a retrospective analysis reviewing the data of 41 consecutive patients who underwent spleen-preserving distal pancreatectomy with spleen vessel preservation between 2000 and 2015 in our Department of Surgery. Appropriate statistical tests were used to compare potential risk factors between the groups.
of patients with and without clinically relevant morbidity after spleen-preserving distal pancreatectomy, in uni- and multivariate analyses.

**Research results**
To the best of our knowledge, this is the first study exploring potential predictors of clinically relevant morbidity in patients with spleen-preserving distal pancreatectomy. The study found male gender and increased body mass index as independent predictors of clinically relevant morbidity after spleen-preserving distal pancreatectomy.

**Research conclusions**
This is the first study that identifies male gender and increased body mass index as risk factors of clinically relevant morbidity in a group of patients with only spleen-preserving distal pancreatectomy. Patient-related factors such as gender and body mass index should be taken into consideration when a spleen-preserving distal pancreatectomy is proposed. The data provided in the present study can be used for clinical decision-making, particularly when preservation of the spleen during distal pancreatectomy is technically demanding.

**Research perspectives**
Preoperative evaluation of patients suitable for a spleen-preserving distal pancreatectomy is of utmost importance. The impact of male gender and body mass index on postoperative outcome after spleen-preserving distal pancreatectomy remains to be explored in future studies including more substantial number of patients.

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