Total pancreatectomy as an alternative to high-risk pancreatojejunostomy after pancreatoduodenectomy: a propensity score analysis on surgical outcome and quality of life

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Abstract

Background: Total pancreatectomy (TP) is mentioned as alternative to pancreatoduodenectomy (PD) with high-risk pancreatojejunostomy (PJ) to avoid severe pancreatic fistula-related complications, but its benefit is controversial and comparative studies are scarce.

Methods: Cross-sectional single-center study among patients after PD with high-risk PJ versus patients after single-stage elective TP for any indication (2015–2017), using propensity scores to evaluate surgical outcomes and long-term quality of life (QoL) in three risk strata. EORTC QLQ-C30 and EQ-5D-5L were used for QoL assessment.

Results: Overall, 77 patients after TP (68.8%) and 102 patients after high-risk PD (34.5%) were included. Major morbidity (29.9% vs. 41.2%; p = 0.119) and 90-day mortality (5.2% vs. 8.8%; p = 0.354) did not differ significantly between TP and high-risk PD. Interventions for intra-abdominal fluid collections (9.1% vs. 23.5%; p = 0.011) and postpancreatectomy haemorrhage (6.5% vs. 18.6%; p = 0.018) were more often required after high-risk PD, but these differences did not remain after stratification. QoL was comparable after TP and high-risk PD (75% vs. 83%; p = 0.720), even after stratification.

Conclusions: TP seems not to be inferior to high-risk PD regarding surgical outcomes and QoL. TP could be considered as an alternative to a very high-risk PD, but reluctance persists since TP does not appear to reduce mortality.

Received 12 May 2021; accepted 27 December 2021

This study was presented at the Kirurgveckan (i.e. Swedish Surgical Society Conference), 20/8/2019, Norrköping, Sweden. The TP population is part of previous analyses on surgical outcomes and the impact of endocrine and exocrine insufficiency on quality of life, published in Annals of Surgical Oncology.

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Introduction

Postoperative pancreatic fistula (POPF) remains the most challenging complication after pancreatoduodenectomy (PD).1 POPF requiring change of patient management occurs in approximately 19% of patients2 and up to 29% in case of high-risk PD.3
risk conditions. Although POPF can mostly be managed with percutaneous drainage, the most severe fistulas are still associated with significant morbidity and mortality in up to 72% and 18%, respectively. Additionally, POPF is associated with a delayed postoperative recovery and, therefore, delay or even renunciation of adjuvant therapy in approximately half of these patients.

Given these data, it is not surprising that total pancreatectomy (TP) is mentioned as an alternative to PD in case of high-risk intraoperative conditions, especially in frail patients or those in need of arterial resection. Nevertheless, this indication for TP is mainly based on personal experience and general reluctance exists because of the resulting lifelong endocrine and exocrine insufficiency. Yet, the management of these insufficiencies has improved in recent years. Several studies demonstrated comparable perioperative outcomes between TP and PD, whereas some conclude otherwise. Three studies specified this comparison to PD with high-risk conditions, noticing the potential of TP to improve perioperative outcomes. Quality of life (QoL) was investigated by only one of them, revealing comparable outcomes.

This study aims to investigate the clinical value of TP as an alternative to PD with a high-risk PJ to reduce short-term morbidity and mortality, thereby investigating the impact on long-term QoL.

Methods

This study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Study population and design

Consecutive adult patients (age ≥18 years) who underwent TP (with or without the presence of intraoperative risk factors for a high-risk PJ) or PD with an intraoperatively defined high-risk PJ between January 1, 2015 and October 31, 2017 at Karolinska University Hospital were included. Non-elective procedures and patients with a history of pancreatic surgery were excluded, as well as patients with unavailable variables used to calculate the propensity scores. TP combined with extended arterial resection was excluded to create comparability with the PD population. Also high-risk PDs who were combined with extended arterial resection by exception were excluded.

All patients undergoing PD received two surgical drains as part of the standard management. Somatostatin analogues were not routinely used peri-operatively. In selected cases with persisting POPF, octreotide was administered subcutaneously.

TP for each indication and PD with high-risk PJ were defined according to the World Health Organization definitions. Surgical major morbidity was defined as Clavien–Dindo > II. In-hospital major morbidity was defined as Dindo > II.28 Postoperative outcomes were prospectively collected and then retrospectively controlled and classified. Patients who were still alive at least six months postoperatively, not in terminal care, and able to speak Swedish were considered eligible for assessment of QoL. The minimum of six months was chosen to give patients time to recover from surgery and adapt to their insufficiencies, thus improving the homogeneity of this cohort.

Included PD patients who later underwent an elective completion distal pancreatectomy with non-complication related indications (e.g. premalignant disease, local disease recurrence) were excluded from QoL analyses since the apancratic state could have influenced the comparison in favour of TP unfairly.

Questionnaires

Patients who met the inclusion criteria for QoL assessment were contacted by phone by one of the authors (E.B.). Those who agreed received the following documents by mail or at the outpatient clinic: patient information sheet, informed consent, questionnaire and an additional envelope to return all documents (free return).

The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) (version 3.0) and the EQ-5D-5L questionnaires were used to investigate general well-being, functioning, and symptoms. In the EORTC QLQ-C30 questionnaire, high scores of global health status and functioning suggest good QoL, whereas high symptom scores indicate poor outcomes. The EQ VAS score from the EQ-5D-5L questionnaire represents the feeling of healthiness on the day that the questionnaire was completed on a scale from 0 to 100; a higher score indicates a higher degree of experienced healthiness.

Definitions

TP and PD were defined in accordance with the International Study Group of Pancreatic Surgery (ISGPS). High-risk PJ was defined as the intraoperative presence of soft pancreatic tissue and/or a pancreatic duct size ≤3 mm in diameter. Additional defined risk factors for POPF such as high-risk pathology and intraoperative blood loss were not taken into account since definitive pathology is unavailable during surgery and blood loss is biased by technical issues.

Comorbidity was defined according to the criteria of the Charlson Comorbidity Index (CCI), calculated by: https://www.mdcalc.com/charlson-comorbidity-index-cci (accessed at April 2019). Adenocarcinomas, intraductal papillary mucinous neoplasms (IPMN) and neuroendocrine tumours (NET) were defined according to the World Health Organization definitions.

In-hospital major morbidity was defined as Clavien–Dindo > II. Surgical major morbidity was defined as complication directly related to surgery, such as delayed gastric emptying, postpancreatectomy haemorrhages (PHH), etc.
anastomotic leakage, peripancreatic collections, and wound dehiscence. In addition, delayed gastric emptying, PPH, bile leakage, and POPF were classified in accordance with the ISGAPS and the International Study Group for Liver Surgery (ISGLS); only grade B and C were considered as clinically relevant.  

Ethics
This study is approved by the local Ethical Committee of Stockholm with the registration numbers 2016/2542-31/1 (retrospective data collection) and 2017/1977-32/1 (contacting patients for assessment of QoL). Informed consent was obtained from all patients included for QoL analysis.

Statistical analyses
Data analyses were performed with IBM SPSS for Windows version 26 (IBM Corp., Orchard Road Armonk, New York, US). Categorical data are presented as frequencies and proportions. Categorical variables are compared with the Pearson's chi square test or the Fisher's exact test when appropriate. Continuous data are compared with the student t test, whereas the Mann–Whitney U test is used in case of non-normally distributed data. EORTC QLQ-C30 scores were converted to a scale from 0 to 100 by linear transformation and presented as medians and interquartile ranges (IQR). If the medians of a parameter in comparative groups were identical while statistical significance was reached, the mean values were added to nuance the outcome. Besides statistical significance, subjective significance was tested with the method of Osoba et al.: <5% 'no difference', 5–10% 'little difference', 10–20% 'moderate difference' and >20% 'very much difference'. The EQ-5D-5L dimensions (i.e. mobility, self-care, usual activity, pain/discomfort, and anxiety/depression) are analysed with dichotomized data because of the small sample sizes, comparing level 1 (i.e. no problems) with level 2 up to level 5 (i.e. any degree of problems).

TP and PD were compared using propensity score stratification analysis, aiming to minimize the impact of treatment allocation bias (inter-patient and baseline variability). Propensity scores were calculated by the following (imbalanced) variables: age (continuous), gender (male yes/no), body mass index (BMI) (continuous), neoadjuvant therapy (yes/no), CCI (continuous), postoperative histological diagnosis (malignancy yes/no), and extended resection (yes/no), using multivariable logistic regression analysis. Based on individual propensity scores, patients were divided into three strata (i.e. stratum I, stratum II, and stratum III) to compare TP and PD since propensity score stratification intends to create comparability between both groups in each stratum. A two-tailed value of $p < 0.050$ was considered statistically significant.

Results
Overall, 112 TP and 296 PD were performed during the study period. Excluded were 35 patients after TP (31.3%) because of concomitant arterial resection ($n = 15$, 13.4%) or a history of partial pancreatectomy ($n = 20$, 17.9%) and 194 patients after PD (65.5%) because of the absence of a high-risk PJ ($n = 192$, 64.9%), non-elective surgery ($n = 1$, 0.3%), or concomitant arterial resection despite high-risk conditions ($n = 1$, 0.3%). The final cohort consisted of 77 patients after TP and 102 patients after high-risk PD.

Clinicopathological characteristics
The median age in the TP and PD groups were 70 (IQR 61–74) and 69 years (IQR 62–74) ($p = 0.998$), respectively. The most common indication for TP and PD was adenocarcinoma ($n = 46$, 59.7% vs. $n = 65$, 63.7%; $p = 0.587$) among which 26.0% ($n = 20$) and 2.9% ($n = 3$) originated from IPMN ($p < 0.001$), respectively. Non-invasive IPMN was the most common non-malignant indication ($n = 14$, 18.2% vs. $n = 15$, 14.7%; $p = 0.532$). See Table 1 for the baseline characteristics.

Surgical details
All patients were operated via mid-line laparotomy, except for one laparoscopy-assisted PD and one initial laparoscopic PD that was converted to TP by laparotomy. Concomitant resection of adjacent organs and/or vasculature were performed in 41 TP (53.2%) and 19 PD (18.6%) ($p < 0.001$), particularly portomesenteric venous resection ($n = 36$, 46.8% vs. $n = 14$, 13.7%; $p < 0.001$) and (sub)total gastrectomy ($n = 15$, 19.5% vs. $n = 2$, 2.0%; $p < 0.001$). TP with islet-autotransplantation was not performed.

In the TP group, operation time was longer (439 min [IQR 369–480] vs. 360 min [IQR 320–401]; $p = 0.003$) and intraoperative blood loss was higher (400 ml [IQR 250–813] vs. 200 ml [IQR 118–300]; $p < 0.001$), as compared to high-risk PD. In the high-risk PD group, 76 patients (74.5%) patients had both a small pancreatic duct (≤3 mm) and soft pancreatic tissue while 18 patients (17.6%) had only a small pancreatic duct and 8 patients (7.8%) had only soft pancreatic parenchyma.
and relatively fewer patients were diagnosed with malignancy in stratum II (n = 16, 66.7% vs. n = 17, 47.2%; p = 0.138).

### Postoperative outcomes

#### Full cohort

Overall major morbidity did not differ significantly between TP and high-risk PD (n = 23, 29.9% vs. n = 42, 41.2%; p = 0.119). Surgical major morbidity was significantly higher after PD (n = 17, 22.1% vs. n = 41, 40.2%; p = 0.010), especially as a consequence of intra-abdominal fluid collections (n = 7, 9.1% vs. n = 24, 23.5%; p = 0.011), including drainage of collections (n = 5, 6.5% vs. n = 21, 20.6%; p = 0.008) and intervention for PPH (n = 5, 6.5% vs. n = 19, 18.6%; p = 0.018). The rate of PPH grade B (n = 8, 10.4% vs. n = 9, 8.8%; p = 0.723) was similar in both groups, whereas grade C (n = 2, 2.6% vs. n = 11, 10.8%; p = 0.037) occurred more frequently after PD. High-risk PD was associated with POPF grade B in 21.6% (n = 22) and grade C in 7.8% (n = 8); rescue pancreatectomy was required in 7 patients (6.9%). See Table 2 for the postoperative outcomes.

Patients with POPF after high-risk PD (n = 30, 29.4%) had higher rates of overall major morbidity (n = 24, 80.0% vs. n = 18, 25.0%; p < 0.001), multiple major morbidity (n = 16, 53.3% vs. n = 6, 8.3%; p < 0.001), and 90-day mortality (n = 6, 20.0% vs. n = 3, 4.2%; p = 0.018) as compared to patients without POPF after high-risk PD (n = 72, 70.6%). See Table 3 for perioperative outcomes in patients after high-risk PD with and without POPF. In-hospital and 90-day mortality in the group of POPF grade C were both 37.5% (n = 3), of whom in-hospital and 90-day mortality rates were 28.6% (n = 2) when rescue pancreatectomy was performed.

#### Strata

After stratification, overall major morbidity rates were similar in stratum I (n = 17, 41.5% vs. n = 7, 38.9%; p = 0.853), whereas outcomes were in favour of TP in stratum II (n = 4, 16.7% vs. n = 15, 41.7%; p = 0.041). No significant differences were seen stratum III (n = 2, 16.7% vs. n = 20, 41.7%; p = 0.180). Differences in major morbidity in stratum II and III were mainly

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**Table 1** Baseline characteristics

<table>
<thead>
<tr>
<th>Patients, n</th>
<th>Full cohort</th>
<th>Stratum I</th>
<th>Stratum II</th>
<th>Stratum III</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TP</td>
<td>PD</td>
<td>TP</td>
<td>PD</td>
</tr>
<tr>
<td></td>
<td>77</td>
<td>102</td>
<td>41</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>23.5%</td>
<td>69 (65–74)</td>
<td>69 (65–74)</td>
</tr>
<tr>
<td>Age (years)a,b</td>
<td>70 (61–74)</td>
<td>69 (62–74)</td>
<td>70 (59–73)</td>
<td>69 (65–74)</td>
</tr>
<tr>
<td>Male sex, n (%)c</td>
<td>44 (57.1)</td>
<td>48 (47.1)</td>
<td>27 (65.9)</td>
<td>10 (55.6)</td>
</tr>
<tr>
<td>BMI (kg/m²)d,e</td>
<td>26 (23–29)</td>
<td>24 (22–28)</td>
<td>26 (25–28)</td>
<td>24 (22–28)</td>
</tr>
<tr>
<td>CCIc</td>
<td>3 (2–5)</td>
<td>3 (2–4)</td>
<td>4 (3–6)</td>
<td>3 (3–5)</td>
</tr>
<tr>
<td>NAT, n (%)d</td>
<td>7 (9.1)</td>
<td>4 (3.9)</td>
<td>4 (9.8)</td>
<td>4 (22.2)</td>
</tr>
<tr>
<td>Operation time (min)b</td>
<td>439 (369–480)</td>
<td>360 (320–401)</td>
<td>453 (391–533)</td>
<td>393 (338–444)</td>
</tr>
<tr>
<td>Intraoperative blood loss (ml)b</td>
<td>400 (250–813)</td>
<td>200 (118–300)</td>
<td>600 (300–1125)</td>
<td>200 (175–525)</td>
</tr>
<tr>
<td>Procedure details, n (%)</td>
<td>15 (19.5)</td>
<td>55 (53.9)c</td>
<td>5 (12.2)</td>
<td>6 (33.3)</td>
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<tr>
<td>Splenectomy</td>
<td>64 (83.1)</td>
<td>–</td>
<td>36 (87.8)</td>
<td>–</td>
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<tr>
<td>Extendedc</td>
<td>41 (53.2)</td>
<td>19 (18.6)c</td>
<td>35 (85.4)</td>
<td>14 (77.8)</td>
</tr>
<tr>
<td>Venous resection</td>
<td>36 (46.8)</td>
<td>15 (14.7)c</td>
<td>30 (73.2)</td>
<td>10 (55.6)</td>
</tr>
<tr>
<td>Multivisceral resection</td>
<td>19 (24.7)</td>
<td>5 (4.9)c</td>
<td>17 (41.5)</td>
<td>5 (27.8)</td>
</tr>
<tr>
<td>Malignant diagnosis, n (%)c</td>
<td>60 (77.9)</td>
<td>73 (71.6)</td>
<td>35 (85.4)</td>
<td>18 (100)</td>
</tr>
</tbody>
</table>

**TP**, total pancreatectomy; **PD**, pancreatoduodenectomy; **n**, number of patients; **min**, minutes; **ml**, millilitres; **BMI**, body mass index; **CCI**, Charlson Comorbidity Index; **NAT**, neoadjuvant therapy.

a Used for propensity score stratification analysis.
b Median (interquartile range).
c Indicates significant difference (p < 0.050).
caused by lower rates of surgical complications after TP. However, the significant differences in the incidences of intra-abdominal fluid collections, percutaneous drainage, and intervention for PPH as well as PPH grade C between TP and high-risk PD disappeared after stratification. In stratum I, respiratory major morbidity was non-significantly higher after TP (n = 8, 19.5% vs. n = 0, 0%; p = 0.092), whereas respiratory complications were similar in the other strata. The POPF rates did not differ significantly between the strata. In stratum I, none of the PD patients underwent a rescue pancreactectomy, in contrast to 4/36 patients in stratum II (11.1%) and 3/48 patients in stratum III (6.3%). Postoperative hospital stay and in-hospital and 90-day mortality rates did not differ significantly in each stratum. See Table 2 for the postoperative outcomes.

Quality of life
A total of 39/77 (50.6%) patients after TP and 43/102 (42.2%) patients after high-risk PD were included for QoL assessment at a median of 43 months (IQR 33–49) and 52 months (IQR 41–60) (p < 0.001) postoperatively, respectively. See Fig. 1 for the flow chart of inclusion.

Full cohort
In the full cohort, global health status and overall functioning were comparable between TP and PD. See Table 4 for QoL. Insomnia (33.3%, IQR 0–33.3 vs. 0%, IQR 0–33.3; p = 0.024) and diarrhoea (33.3%, IQR 0–66.7 vs. 0%, IQR 0–33.3; p = 0.040) were more prominent after TP, in contrast to appetite loss (0% [mean = 4.3%], IQR 0–0 vs. 0% [mean = 14.3%], IQR 0–33.3; p = 0.037). See Supplemental digital content 1 and 2 for a detailed comparison of the overall study populations, including a sensitivity analysis to assess the influence of rescue pancreactectomy in the PD group.

Strata
In the three strata, there were no differences in QoL parameters. In stratum I, emotional functioning was non-significantly better after TP (91.7%, IQR 83.3–100 vs. 75.0%, IQR 62.5–91.7; p = 0.067). Appetite loss (0% [mean = 0%], IQR 0–0 vs. 0% [mean = 13.3%], IQR 0–33.3; p = 0.019) and constipation (0% [mean = 0%], IQR 0–0 vs. 0% [mean = 20.0%], IQR 0–50.0; p = 0.019) were worse after PD, whereas no significance was reached as regards diarrhoea (33.3%, IQR 16.7–50.0 vs. 0%, IQR 0–33.3; p = 0.106) in stratum I.

Discussion
This cross-sectional single center study found that TP is not inferior to high-risk PD regarding short-term surgical outcomes and long-term general QoL, with a potential benefit of TP in case of non-extended resections. Given the lower rates of interventions for intra-abdominal collections and haemorrhages,
TP could be considered in very high-risk patients, but this decision has to be weighed carefully since mortality is not lower after TP as compared to high-risk PD.

Over the last two decades, TP has slowly become more popular in the repertoire of pancreatic surgeons. However, indications remain unclear and are mostly based on local expertise, one being TP as an alternative to PD with high-risk PJ to avoid POPF-related morbidity and mortality. This indication is acknowledged and practiced in carefully selected patients at Karolinska University Hospital.

This study defined 35% of the PD population as having a high-risk PJ. The proportion is substantially larger in comparison to the 10% (Fistula Risk Score 7–10) reported in a previous multicenter study. Whereas the adhered definition in our study probably includes Fistula Risk Score 3–6 as well, POPF grade B (22% vs. 22%) and POPF grade C (8% vs. 8%) rates are equal, also strengthened by the POPF grade B/C rates in the moderate to high-risk Fistula Risk Score study group from Senda and colleagues. In contrast, Adrianello et al. revealed a higher POPF incidence (39%) in case of Fistula Risk Score 7–10, but without any grade C fistulas. Major morbidity (41% vs. 22–36%) and 90-day mortality (9% vs. 5–6%) were worse in the current study, compared to similar cohorts. A plausible explanation is the higher number of concomitant vascular and multivisceral resections, but this assumption is contradicted by the more or less consistent outcomes after PD between the three strata. The Dutch Pancreatic Cancer Group has provided insight on the nationwide management of severe pancreatic fistulas. The results revealed worrisome in-hospital mortality that nearly equals our population (17% vs. 18%). Smits et al. suggest a beneficial effect of catheter drainage instead of primary relaparotomy on morbidity and mortality; a plea for a step-up approach for severe pancreatic fistulas. However, even in a step-up approach, relaparotomy with eventual rescue pancreatectomy will be unavoidable in some patients and delay of surgery could even work counterproductive in frail patients. This philosophy may explain the 6.9% rescue pancreatectomy rate in this selective, high-risk PD cohort. Differences in the rate of patients with high-risk PD between cohorts may also partly explain the worldwide variety in the use of rescue pancreatectomy.

To our knowledge, this is only the second series that conducted a comparative analysis including QoL evaluation between TP and PD with high-risk PJ. Several retrospective studies compared general outcomes after TP and PD. The national database from the American College of Surgeons revealed higher major morbidity and a doubled 30-day mortality rate (6% vs. 3%) after TP in comparison to PD. In contrast, others demonstrated comparability in major morbidity (19–30% vs. 26–37%) and perioperative mortality (0–7% vs. 0–5%) from which four studies matched both groups. One single-center study compared TP versus PD with high-risk PJ (Fistula Risk Score 7–10), revealing no differences in major morbidity, whereas Luu et al. compared TP indicated for high-risk pancreatic remnant versus high-risk PD, demonstrating comparable major morbidity and mortality. Marchegiani et al. compared intraoperatively converted PD to TP for any indication versus high-risk PD (alternative Fistula Risk Score), demonstrating a trend to significantly lower major morbidity (19% vs. 31%) after TP as consequence of lower rates of peripancreatic collections, intra-abdominal abscesses, sepsis, and haemorrhages among others. However, 90-day mortality rates were similar. Current propensity score stratification analysis confirmed the non-inferiority of TP; major morbidity and mortality were similar in patients with mostly extended surgery for malignancy, whereas major morbidity seemed to be better after TP in a population predominantly characterized by standard procedures.

In contrast to popular belief, general long-term QoL after TP seems to be comparable with those who underwent PD, even after propensity score stratification. In the past, several series have compared QoL between TP and PD. The main conclusion concerns comparable overall QoL, while...
physical, mental, and social functioning are commonly more affected after TP.15,42–44 A similar tendency was observed in this study. In contrast, Marchegiani et al. revealed almost comparable outcomes of global health status, functioning, and symptom scores with neither statistical nor clinically relevant differences.19 One can assume that functioning is influenced by the daily

Table 4 Quality of life

<table>
<thead>
<tr>
<th>Patients, n (%)</th>
<th>Full cohort</th>
<th>Stratum I</th>
<th>Stratum II</th>
<th>Stratum III</th>
</tr>
</thead>
<tbody>
<tr>
<td>TP</td>
<td>39/77 (50.6)</td>
<td>13/41 (31.7)</td>
<td>16/24 (66.7)</td>
<td>10/12 (83.3)</td>
</tr>
<tr>
<td>PD</td>
<td>43/102 (42.2)</td>
<td>5/18 (27.8)</td>
<td>18/36 (50.0)</td>
<td>20/48 (41.7)</td>
</tr>
</tbody>
</table>

Follow-up (months)c 43 (33–49) 50 (42–62) 41 (24–53) 50 (41–58) 45 (32–49) 58 (43–64)

EORTC QLQ-C30

<table>
<thead>
<tr>
<th>Global health statusc</th>
<th>75 (67–83)</th>
<th>67 (50–83)</th>
<th>67 (50–83)</th>
<th>67 (50–83)</th>
<th>75 (58–83)</th>
<th>75 (74–83)</th>
<th>79 (74–83)</th>
<th>83 (70–96)</th>
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<td>Overall functioning scorec</td>
<td>80 (73–89)</td>
<td>78 (67–94)</td>
<td>79 (74–83)</td>
<td>83 (70–96)</td>
<td>88 (72–94)</td>
<td>93 (81–96)</td>
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EQ-5D-5L

<table>
<thead>
<tr>
<th>Mobility (problems), n (%)b</th>
<th>11 (28.2)</th>
<th>3 (23.1)</th>
<th>3 (60.0)</th>
<th>5 (31.3)</th>
<th>3 (30.0)</th>
<th>3 (15.0)</th>
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<tr>
<td>Self-care (problems), n (%)b</td>
<td>3 (7.7)</td>
<td>1 (7.7)</td>
<td>0 (0)</td>
<td>2 (12.5)</td>
<td>1 (5.6)</td>
<td>0 (0)</td>
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<tr>
<td>Usual activity (problems), n (%)b</td>
<td>17 (43.6)</td>
<td>4 (30.8)</td>
<td>8 (50.0)</td>
<td>7 (38.9)</td>
<td>5 (50.0)</td>
<td>5 (25.0)</td>
</tr>
<tr>
<td>Pain/discomfort (problems), n (%)b</td>
<td>23 (59.0)</td>
<td>3 (60.0)</td>
<td>10 (62.5)</td>
<td>10 (55.6)</td>
<td>5 (50.0)</td>
<td>12 (60.0)</td>
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<td>Anxiety/depression (problems), n (%)b</td>
<td>14 (35.9)</td>
<td>2 (15.4)</td>
<td>3 (60.0)</td>
<td>8 (50.0)</td>
<td>6 (33.3)</td>
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<td>EQ VASc</td>
<td>80 (70–90)</td>
<td>75 (65–90)</td>
<td>80 (65–88)</td>
<td>75 (50–88)</td>
<td>75 (50–90)</td>
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</tbody>
</table>

All values are on a scale from 0 to 100%, presented as median (IQR); TP, total pancreatectomy; PD, pancreatoduodenectomy; n, number of patients. a Indicates significant difference (p < 0.050). b Dichotomized to level 1 (i.e. no problems) and level 2–5 (i.e. no problems). c Median (interquartile range).
impact of metabolic insufficiency, while differences in symptoms are not always evidently quantified by small sample sizes. It is likely that the limited differences do not represent the real burden of metabolic insufficiencies after TP per se. Patients adjust their standards over time, which could clarify the comparable QoL in the present and previous series. Particularly patients who underwent pancreatic surgery for malignancies are capable to accept the challenges of pancreateogenic diabetes as it outweighs the (potential) oncological benefit in contrast to those who are resected for non-malignant indications. On the other hand, Hartwig et al. suggested that these differences are just temporary.

Although the precise indications for TP as alternative to PD with high-risk PJ remain dependent on the preferences of individual surgeons, TP seems to be an option in carefully selected patients at high-volume centers with substantial experience in TP. TP can be selectively used in patients with a relative short life expectancy that need quick recovery (e.g. pancreatic cancer); extremely challenging conditions for PJ reconstruction (e.g. fatty replaced pancreas parenchyma) and the presence of comorbidities that could influence the postoperative risk on POPF (e.g. renal failure). On the other hand, pancreatic cancer patients rarely have a high-risk pancreas in comparison with the population of premalignant or periampullary neoplasms. Nevertheless, TP should probably be avoided in these latter indications. Interestingly, other clinicians suggest that TP with islet-autotransplantation could be considered in case of non-malignant indications. TP .

In conclusion, surgical outcomes and general QoL are not worse after TP as compared to high-risk PD, especially in cases of non-extended surgery, but reluctance for TP should persist since TP does not reduce postoperative mortality. TP could be considered as an alternative to a very high-risk PD in carefully selected patients with need for quick recovery and who are capable of managing the associated metabolic consequences of TP.

Financial disclosure/Conflicts of interest

(1) Marco Del Chiaro has been awarded with an industry grant (Haemonetics, Inc) to conduct a multicenter study to evaluate the prognostic implications of TEG in pancreatic cancer. (2) Marco Del Chiaro is co-principal investigator of a Boston Scientific sponsored international multicenter study on the use of intraoperative pancreatoscopy of patients with IPMN.

References


Appendix A. Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.hpb.2021.12.018.