

## ORIGINAL ARTICLE

# Changing indications for a total pancreatectomy: perspectives over a quarter of a century

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## Abstract

**Introduction:** The indications for a total pancreatectomy (TP), its peri-operative management, provision of pancreatic surgical services and medical treatment of the inherent exo- and endocrine deficient states have all changed considerably over recent decades. The effects of these upon the incidence, indications for and outcomes of TP are unclear. Patients undergoing TP at a single institution over a quarter of a century were reviewed to try to address these issues.

**Methods:** Data on patients who underwent elective (el-) and emergency TP (em-TP) between 1987 and 2013 were reviewed. Patient demographics, indications, intra-operative details, peri-operative management and long-term outcomes were analysed. Absolute numbers of TP were reported relative to partial pancreatectomy rates.

**Results:** In total, 136 patients underwent TP [98 (72.1%) el-TP; 38 (27.9%) em-TP]. There was a significant change in indication for el-TP with it increasingly performed for (an intraductal papillary mucinous neoplasm (IPMN) and renal cell metastases whereas there was a decrease in the number of el-TP performed for chronic pancreatitis ( $P = 0.025$ ). The relative rates of el-TP, however, did not change significantly across the study period ( $P = 0.225$ ). The median length of stay after el-TP decreased from 19 days pre-1997 to 12 days post-1997 ( $P = 0.009$ ). The relative use of em-TP declined by 0.28 percentage points per year [ $P = 0.018$ ; 95% confidence interval (CI): 0.04–0.41].

**Conclusions:** The indications for el-TP have changed; it is being performed more frequently although the proportion relative to other pancreatic resections has not changed. A decrease in the rate of em-TP is likely to reflect improved peri-operative management of a pancreatic fistula and its complications after a pancreaticoduodenectomy.

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## Introduction

Enthusiasm for a total pancreatectomy (TP) has varied with time. Early interest in elective TP (el-TP) as a potential solution to the high rates of tumour recurrence after a partial pancreatectomy waned with a clearer understanding of the tumour biology of pancreatic adenocarcinoma.<sup>1</sup> More recently, however, interest in el-TP has been replaced by alternative indications for the procedure, with increasing recognition of multifocal parenchymal

diseases including intraductal papillary mucinous neoplasms (IPMNs), multifocal renal cell metastases, multifocal neuroendocrine tumours (NET) and inherited neoplastic diseases, including multiple endocrine neoplasia (MEN)<sup>1</sup>, prompting clinicians to re-evaluate the role of el-TP.<sup>2,3</sup> A further indication for TP is in the emergency setting (em-TP), where a completion pancreatectomy can be performed as a method of sepsis control in cases of a post-operative pancreatic fistula (POPF) after a partial pancreatectomy. Improvements in

cross-sectional radiology and the ability to perform percutaneous drainage of intra-abdominal collections, however, have provided alternative methods of sepsis control in this setting.

The post operative exo- and endocrine deficient states have always tempered enthusiasm for TP. The diabetic state has been considered so severe it has been termed 'brittle diabetes'. However, in recent years, improvements in insulin regimens and specialist nurse-led diabetic care have dramatically improved diabetic outcomes post TP.<sup>4-8</sup> There is now debate over the actual severity of the diabetic state, with several groups reporting equivalent HbA1c levels between type 1 diabetics and TP patients.<sup>4-8</sup>

The development of high-quality enzyme replacement formulations has also improved morbidity from exocrine insufficiency.

Given the changing indications for elective surgery, an evolution in the understanding of POPF and sepsis control and medical management of the inherent exo- and endocrine deficient states after TP, the present study aimed to review indications and trends in both el-TP and em-TP at a single institution with a dedicated pancreatic surgical service over a quarter of a century.

## Patients and methods

This study considers two distinct scenarios, el-TP and em-TP. Both indications are considered in this study to contrast potential enthusiasm for differing indications for TP within the same institution over a prolonged period to review trends in managing various pancreatic diseases and complications.

### Data collection

All patients undergoing a partial or total pancreatic resection [TP, distal pancreatectomy (DP) and pancreaticoduodenectomy (PD)] between January 1987 and December 2013 were identified from a prospectively maintained institutional database. El-TP included single-stage planned elective or single-stage unplanned elective TP where an intra-operative decision to perform TP and not a partial pancreatectomy was made. Patients who had previously undergone a partial pancreatectomy with a subsequent elective completion pancreatectomy were also included in the el-TP group. Em-TP was defined as a completion pancreatectomy performed after a previous partial pancreatectomy in order to control or treat sepsis. The rates of partial pancreatic resection were observed and compared with the rates of el-TP and em-TP to understand changes in the proportion of these operations over time.

Data on patient demographics, indications for surgery, pathology, peri-operative complications and long-term outcomes were retrieved from the database for all TP patients. Data accuracy was confirmed by retrospective review of patient records.

Follow-up of patients consisted of clinical review every 4–6 months for 2 years with at least an annual follow-up until 5 years. Follow-up aimed to assess evidence of tumour recurrence and survival. Sequelae of endocrine insufficiency and post-operative quality of life have been reported elsewhere.<sup>9</sup>

### Statistical analysis

The relationships between pre-surgical factors, and the outcomes of overall survival, complication rates and lengths of hospital stay were assessed separately for patients undergoing el- and em-TP.

Survival analysis was performed using Kaplan–Meier survival curves, with Log-Rank significance tests. Complication rates were compared across factors using Fisher's exact test. As the distribution of lengths of hospital stay was highly skewed, a non-parametric approach to analysis was employed. The Mann–Whitney and Kruskal–Wallis tests were used, depending on the number of groups to be compared, and data were summarized using medians and quartiles.

The trends over time in frequency and relative rates of pancreatic resection were then compared using linear regression models. The year number was included as the independent variable, and either the number of operations, or relative proportion of operations entered as the dependent variable. When working with proportions, the denominator was set as a weighting variable, in order to give greater influence to percentages based on a greater number of patients. The resulting coefficients represented the year-on-year increase in operations or the percentage point change in proportions, respectively.

All analyses were performed using IBM SPSS 19 (IBM Corp., Armonk, NY, USA), with  $P < 0.05$  indicative of statistical significance. A medical statistician (J.H.) provided advice on study design and with data analysis.

## Results

### Study population

Some 1609 pancreatic resections were performed comprising of 1232 PD (76.5%), 241 DP (15.0%) and 136 TP (8.4%). Of the TP group 98 were el-TP (72.1%) and 38 em-TP (27.9%).

### Elective TP

In total, 80 (82%) patients underwent a single-stage planned el-TP, 11 (11%) a single-stage unplanned el-TP, and a 7 (7%) elective completion pancreatectomy. An intra-operative decision was made to convert from a PD to a TP in 11 patients owing to evidence of tumour deposits (macroscopic or microscopic) beyond the neck of the pancreas (6), need for extensive venous reconstruction (3), inadvertent arterial damage (1), or findings of a soft pancreas deemed unsuitable for anastomosis (1).

The median age of patients undergoing el-TP was 63 years (range 18–84) and 53/98 (54.1%) were male. El-TP was performed for adenocarcinoma (45; 46%), NET (8; 8%), chronic pancreatitis (18; 18%), trauma (1; 1%), IPMN (12; 12%), renal cell metastases (10; 10%), benign lesions (3; 3%) and other malignant lesions (1; 1%).

The median follow-up was 8.4 years, and at last follow-up, 61 (62.2%) patients had died. Post-operative mortality did not change significantly over time ( $P = 0.763$ ). A total of 12 patients (KM estimate 12.5%) died within 90 days of surgery owing to abdominal sepsis (4), pneumonia (4), myocardial infarction (1),

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