



Liver, Pancreas and Biliary Tract

Diabetic control after total pancreatectomy

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Abstract

Background. Diabetes after total pancreatectomy is commonly described as ‘brittle’ with most series reporting outcomes after resection for pancreatitis alone. The aim of this study was to determine glycaemic control in patients resected for benign and malignant disease.

Methods. A retrospective analysis of all patients undergoing total pancreatectomy (1989–2003) from a single institution was done. Data of diabetic control were obtained from case notes, general practitioners and telephonic consultation. Comparison was made against a matched type 1 diabetic population.

Results. Forty-seven patients with a median age of 59 years (range 17–85 years) and median follow-up of 50 months (range 5–136 months) were identified. Thirty-five underwent primary resection with 11 receiving completion procedures. Thirty were for malignancy (19 deceased) and 17 for benign/indeterminate histology (2 deceased). Thirty-three patients were available for detailed follow-up. There was no significant difference between median HbA_{1c} of the study group and the control (8.2% versus 8.1%). The majority of patients reported diabetic control and daily performance as excellent or good. Resection for pancreatitis gave poorer subjective control ($p < 0.05$) than those resected for malignancy. Two patients required in-patient treatment for diabetic complications, with no deaths related to diabetes observed.

Conclusion. Diabetes after total pancreatectomy is not necessarily associated with poor glycaemic control and in the majority results in equivalent biochemical control compared to a normal type 1 diabetic population.

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1. Introduction

Total pancreatectomy (TP) can be curative for selected patients with chronic pancreatitis (CP) [1], for premalignant disease and for well-localised neoplasms such as multifocal islet cell tumours but is less commonly performed for common malignancies such as adenocarcinoma. The invariable insulin-dependent diabetes has traditionally been regarded as a significant cause of morbidity and, especially in those with suspected malignancy, great effort is undertaken to preserve functional pancreatic tissue. Whilst in most cases, supplementation of exocrine insufficiency is relatively straightforward and successful after TP, those patients with pancreatogenic diabetes have long been characterised as having an

unstable ‘brittle’ form of the disease with inherently labile control and a high risk of hypoglycaemia [2–5].

Besides the absence of insulin, the endocrine abnormalities accompanying TP include both glucagon and pancreatic polypeptide (PP) deficiency. This totally deficient diabetic state has been labelled ‘pancreatogenic’ diabetes and is considered to be different from conventional type 1 and 2 diabetes. The absence of glucagon renders the patient vulnerable to episodes of severe hypoglycaemia, resistant to ketosis and is associated with high plasma levels of gluconeogenic precursors including lactate and alanine [6,7]. The consequences of lack of PP are yet to be fully understood, but it has been suggested that PP, produced mainly in the pancreatic head, plays a key role in the induction of hepatic sensitivity to insulin and insulin receptor regulation [8,9] and hence its deficiency may contribute to the increased hepatic insulin resistance seen in pancreatogenic diabetes. After pancreatectomy, insulin receptors are upregulated peripherally,

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rendering patients uniquely sensitive to hormone replacement [10]. Consequently, stable diabetic control for these patients is often problematic and characterised by periodic episodes of both hyper- and hypoglycaemia. Despite this evidence, not all patients who undergo TP report poor glycaemic control (GC) and, moreover, many patients report good performance status with few complications.

The aims of this study were to assess diabetic control and complications following TP and to assess the impact of post-resection GC.

2. Methods

2.1. Patients

All patients treated by TP at a tertiary care hepatobiliary unit between June 1989 and October 2003 were retrospectively identified from a departmental surgical database and medical records. All were National Health Service patients and received no private treatments. Patients were operated upon in a single centre by a specialist team of hepatobiliary/pancreatic surgeons.

The majority of cases were performed as a single operation with an intraoperative decision to perform TP. Postoperatively, all patients were seen by a specialist diabetic nurse liaison and/or consultant diabetologist. Surgical follow-up was done in a single centre with close support from patient's general practitioners.

Data including patient's characteristics, indication for operation, complications, histology, insulin and pancreatic enzyme requirement were obtained from case notes with data regarding the patient's socioeconomic status extracted from patient's hospital records and by telephonic interview. Telephonic interview conducted by the first author (P.J.) with all living patients was used to collect data on patient's insulin requirements, episodes of hypo-/hyperglycaemia and liaison with diabetic services. In addition, patients' own view of their diabetic control, ability to perform daily activities (work, leisure and hobby) and the need for in-patient treatment were established. Diabetic control was assessed as either excellent (no restriction in daily activities), good (mild impairment, <25% restriction of restriction activities), fair (moderate impairment, 25–50% restriction of activities) or poor (significant impairment, >50% restriction of activities). All available glycosylated haemoglobin levels (HbA_{1c}) were obtained after liaison with patient's general practitioners.

Diabetic control in the study group was compared against age-matched type 1 diabetics identified from a separately maintained prospective diabetic database held by the same hospital's endocrinology service. Data were available for duration of disease, most recent HbA_{1c}, age, weight and body mass index (BMI). This database did not contain information regarding readmission and/or diabetic complications.

2.2. Statistics

Variables were compared using the Pearson χ^2 test, Mann–Whitney *U*-test and Pearson rank order correlation. All analyses were performed using statistical software (SPSS v13.0, Chicago, USA). Differences were considered statistically significant at $p < 0.05$.

3. Results

A total of 47 patients (25 male and 22 female) underwent TP during the study period. Median age at operation was 59 years (range 17–85 years).

The indications were as follows:

- Group 1: TP as a single elective operation ($n = 32$);
- Group 2: TP as an emergency procedure ($n = 1$);
- Group 3: emergency TP for secondary haemorrhage after pancreaticoduodenectomy (PPD) ($n = 9$);
- Group 4: completion due to ongoing symptoms ($n = 4$).

In one case, it was not possible to determine the indication for TP from hospital records. Indications for operation and patient histology are given in Table 1.

The 30-day mortality for the entire group was 21.7% ($n = 10$). There were four deaths in the elective TP/completion pancreatectomy (group 1, 11%) with deaths due to multiorgan dysfunction syndrome ($n = 2$), subarachnoid haemorrhage at 5 days ($n = 1$) and large bowel infarction at 21 days ($n = 1$). In group 2, there was one death from necrotising pancreatitis within 24 h of resection due to overwhelming sepsis. In group 3, five of the nine patients (55%) succumbed within 30 days of operation. There were two additional deaths by 60 days: one due to previously occult metastatic disease and the other due to a late catastrophic haemorrhage. Ten of those who died within 60 days had malignant disease, nine of whom had proven lymph node metastasis.

At present, 11 patients out of 30 with malignancy and 15 of 17 with benign and indeterminate histology are still alive (median survival = 24 and 79 months, respectively). No deaths in this series were attributable to diabetic complications or metabolic consequences of pancreatic resection. Two patients with indeterminate malignant potential are still alive with no sign of recurrence (45 and 52 months post-resection). Four patients previously resected for CP (group 4) underwent elective completion pancreatectomy for continuing abdominal pain. Two were lost to follow-up having moved abroad with one patient further untraceable despite liaison with their registered GP. Overall follow-up data were available for 33 patients. Median follow-up was 50 months (IQR = 31 months, range 5–136 months).

Socioeconomic data were assigned using a Weberian stratification [11] accounting for earnings, occupation, education, housing and social grouping categorised. Patients were stratified as follows:

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