ORIGINAL ARTICLE

Simultaneous pancreatectomy and liver transplantation: a single-institution experience

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Abstract

Background: There is wide debate among transplant centres regarding the indications for liver transplantation (LT) in malignancy. We report a single-centre experience with simultaneous LT and total pancreatectomy or pancreaticoduodenectomy.

Methods: We performed a retrospective review of a prospectively established database of patients who underwent simultaneous LT and total pancreatectomy or pancreaticoduodenectomy. We analysed demographics, indications, approach and outcomes.

Results: Between 1991 and 2006, 11 patients (four male; median age 51 years) underwent simultaneous LT and total pancreatectomy (n = 4) or pancreaticoduodenectomy (n = 7). Indications included metastatic neuroendocrine tumour (n = 5), hepatocellular carcinoma (n = 2), metastatic periampullary adenocarcinoma (n = 1), periampullary adenocarcinoma with end-stage liver disease (ESLD) (n = 2) and intraductal papillary mucinous neoplasm with ESLD (n = 1). The three patients with ESLD had non-alcoholic steatohepatitis, primary sclerosing cholangitis or cryptogenic cirrhosis. Median postoperative length of stay was 31 days (21–110 days). Overall median survival was 101 months (95% confidence interval 70.6–131.4). One-year survival was 91%, 2-year 90%, 5-year 67% and 10-year 33%. Postoperative complications included: re-operation (n = 4); anastamotic leak (n = 2); abdominal abscess (n = 3), and organ rejection (n = 1).

Conclusions: We report a series of pancreatectomy or pancreaticoduodenectomy and simultaneous LT in patients with extensive malignancy or impending liver failure that prevented pancreatectomy. This series provides evidence that combined pancreatic resection and LT can be a strategy in both radical resections and cases with ESLD that would otherwise preclude operative intervention.

Keywords
Liver transplant, pancreatectomy, malignancy, simultaneous

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Introduction

Liver transplantation (LT) is performed around the world for both end-stage liver disease (ESLD) and malignancy. Although Starzl envisioned a role for LT in primary hepatic malignancy not amenable to conventional resection,1 recurrence rates and the scarce supply of donor organs restrict transplantation to those for whom there is believed to be maximal survival benefit. The indications for transplantation for malignancy in the USA and Europe continue to be debated. Although there are current accepted criteria for LT in hepatocellular carcinoma (HCC), the indications are not well defined in extensive primary and secondary malignancy.

In 1993 Bismuth and colleagues published a study comparing disease-free survival of LT vs. liver resection in HCC. Their results showed overall survival whether treated with transplantation or resection, but subgroup analysis revealed an 83% disease-free 3-year survival after transplant in single and binodular tumours <3 cm in diameter.2 Although the United Network for
Organ Sharing (UNOS) bases its criteria for LT in primary hepatic malignancy on these data, large transplant centres have found some success using broader criteria and have challenged these guidelines.\textsuperscript{3,4} This push for more liberal transplantation criteria in primary liver malignancy is a focus of debate among transplant centres.

There is also considerable debate over the appropriate treatment for metastatic disease that is not amenable to limited resection. Although most centres have reported generally poor results with overall and disease-free survival after radical resection and transplantation for metastatic tumours, some centres have reported favourable results, suggesting that the potential for cure or palliation is patient- and/or disease-specific.\textsuperscript{5–7} Cumulatively, these studies show mixed results, but there have been efforts to find prognostic factors for survival with regard to patient selection, primary disease process and operation. Recently, there has been an accumulation in evidence of prolonged palliation and cure in the slower-growing metastatic neuroendocrine tumours. Multiple centres report survival rates of 50–90\% at 5 years after transplant, usually with significant palliation from tumour burden and endocrine function.\textsuperscript{6–11} Various papers, including a review by Pascher et al. in 2005, have reported single and multi-centre studies of overall survival and disease-free survival after LT for metastatic neuroendocrine tumour, and found that patients aged <50 years, undergoing less extensive operations (i.e. sparing the stomach and pancreas) and with favourable tumour biology (Ki67 and E-Cadherin) may gain the greatest benefit.\textsuperscript{10,12,13}

Although indications for LT in primary and secondary hepatic malignancy are evolving, there is a continued need to report outcomes in the management of specific tumours, as well as the surgical management of a variety of tumours. Here we describe a 15-year experience at a single institution with pancreatectomy or pancreaticoduodenectomy and simultaneous LT for multiple diagnoses in order to better define how management may impact survival.

### Materials and methods

Approval for this study was obtained from our Institutional Review Board. A search for simultaneous pancreatectomy or pancreaticoduodenectomy and LT was performed on a prospective database for all patients who underwent transplantation at the University of Pittsburgh between 1991 and 2006. We analysed patient demographics, indications, operations, complications and survival rates.

A series of 11 patients with the above criteria were found (four pancreatectomy, seven pancreaticoduodenectomy). They included seven females and four males, with a median age of 51 years (range 17–67 years). Primary diagnoses were neuroendocrine tumour (\( n = 5 \)), periampullary adenocarcinoma (\( n = 3 \)), HCC (\( n = 2 \)) and intraductal papillary mucinous neoplasm (IPMN) (\( n = 1 \)) (Table 1).

### Results

#### Indications

All 11 patients undergoing pancreatectomy/pancreaticoduodenectomy and LT had a malignant or premalignant condition as the primary indication for operation. Liver transplantation was undertaken for extensive primary liver tumour (\( n = 2 \)), malignancy metastatic to the liver (\( n = 6 \)), or localized non-hepatic malignancy in the setting of ESLD (\( n = 3 \)). Five patients had metastatic disease from a pancreatic neuroendocrine tumour and one patient had metastatic disease from a pancreatic adenocarcinoma. Two patients had primary liver malignancy (HCC) which extended into the duodenum. Three patients had limited periampullary adenocarcinoma or IPMN with pre-existing ESLD that met UNOS criteria for LT. In these three patients the cause of ESLD included well-compensated primary sclerosing cholangitis (PSC), decompensated non-alcoholic steatohepatitis (NASH), and decompensated cryptoge-

### Table 1 Patient demographics, including primary diagnosis and length of stay, for patients undergoing simultaneous pancreatectomy or pancreaticoduodenectomy and liver transplantation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age, years</th>
<th>Postoperative LOS, days</th>
<th>Primary tumour diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>17</td>
<td>31</td>
<td>Duodenal carcinoïd</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>60</td>
<td>25</td>
<td>IPMN</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>46</td>
<td>110</td>
<td>Periampullary adenocarcinoma</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>67</td>
<td>49</td>
<td>Periampullary adenocarcinoma</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>33</td>
<td>31</td>
<td>Neuroendocrine tumour</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>53</td>
<td>21</td>
<td>Neuroendocrine tumour</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>44</td>
<td>26</td>
<td>Neuroendocrine tumour</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>52</td>
<td>67</td>
<td>Neuroendocrine tumour</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>51</td>
<td>73</td>
<td>HCC</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>21</td>
<td>30</td>
<td>HCC (fibrolamellar)</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>52</td>
<td>33</td>
<td>Periampullary adenocarcinoma</td>
</tr>
</tbody>
</table>

LOS, length of stay; F, female; M, male; IPMN, intraductal papillary mucinous neoplasm; HCC, hepatocellular carcinoma
nic cirrhosis with severe portal hypertension and failed transjugular intrahepatic portosystemic shunt (TIPS).

**Operations**

In all patients, the extent of the disease was known prior to operation. All 11 patients in this series underwent pancreatectomy/pancreaticoduodenectomy and cadaveric LT during the same operation, although the order of resection and transplantation varied. Five patients underwent only pancreaticoduodenectomy and LT. Of these five, three had localized non-hepatic malignancy with ESLD and underwent transplantation prior to pancreaticoduodenectomy, one had duodenal carcinoid metastatic to the liver and also underwent transplantation prior to pancreaticoduodenectomy, and the remaining patient had HCC with retroduodenal extension and underwent initial pancreaticoduodenectomy immediately followed by LT.

The other six cases required more extensive resections, which included colectomy and total pancreatectomy (Table 2). All of them underwent resection prior to LT. Two patients had pancreaticoduodenectomy and colectomy for extensive HCC and metastatic neuroendocrine tumour, respectively. Four others underwent total pancreatectomy, three of them for metastatic neuroendocrine tumour and one for extensive periampullary adenocarcinoma.

It is of note that no patients received liver-directed chemotherapy or embolization prior to resection as this was not standard practice at this institution at that time. In addition, patient records showed no note of neoadjuvant or adjuvant chemotherapy. Unfortunately, longterm follow-up data for degree of diabetes and insulin requirements after pancreatectomy were not available in these patients.

**Complications**

Four patients required re-operation. One patient required three re-operations during the primary hospitalization for a pancreatic anastamotic leak and subsequent abscesses and a second patient underwent laparotomy for abscess drainage. Another patient in the group underwent an exploratory laparotomy and ‘washout’ for suspected intra-abdominal sepsis. The final re-operative case had two revisions of the pancreatic anastomosis and died on hospital day 50 from multisystem organ failure. Non-operative complications included one patient with thrombosis of the right hepatic artery, one patient who suffered from graft vs. host disease, and one with a postoperative myocardial infarction (Table 2).

**Survival**

There was only one death during the initial hospitalization, and 10 of 11 patients lived for ≥ 1 year. At the time of analysis, five of the 11 subjects were alive, with a median survival of 11 years (range 1–16 years). Overall median survival was 101 months (95% confidence interval 70.6–131.4). One-year survival was 91%, 5-year 67% and 10-year 33% (Table 3).

**Discussion**

Liver transplantation in malignancy is a highly controversial topic. Because of the current limitations of available organs, the most widely accepted practice is to follow guidelines which seemingly optimize survival after transplantation. Recent studies of primary and secondary hepatic malignancy have shown that important criteria for prolonged survival or palliation include tumour type, tumour biology, patient age and the extent of operation.

There is a general consensus that resection and transplantation for neuroendocrine tumours may yield longterm palliation and survival as a result of the slow-growing nature of these tumours. Because of the relative success of surgical treatment of these tumours, more extensive studies regarding the tumour biology and patient factors associated with survival have been carried out. Such studies have revealed that age, extent of operation and molecular markers Ki67 and E-cadherin may be useful in predicting survival.10,14 Additionally, there have been reports of success.
with radical resection in multiple types of cancer, but these are few and have not been duplicated across multiple transplant centres.\textsuperscript{6,7,13–17} Indications for LT are evolving, and it is of crucial importance that centres accurately report their outcomes so that organ utilization is optimized and perhaps indications expanded. Selection criteria for type of tumour, extent of tumour and biological properties are changing, but there are limited reports on how the extent of operation can impact survival.\textsuperscript{13,18} Most reports discuss ‘extensive’ vs. ‘limited’ operations, which can vary from multistage resection and transplantation to cluster resections and multivisceral transplants. There are no studies specifically addressing simultaneous LT and pancreatectomy or pancreaticoduodenectomy in cancer and/or ESLD.

Here, we report a series of 11 patients operated over a period of 16 years who underwent LT with simultaneous pancreatic operations for locally advanced malignancy or confined malignancy in the setting of ESLD. We found only one in-hospital death and a median post-transplant survival of 101 months. Our practice has evolved over this period and the indications for radical resection with LT have changed to accommodate better understanding of tumour biology and advances such as directed chemoembolization. In the early part of our series we found that the decision for radical resection or transplantation was driven by attempts at curative resection for a variety of malignancies that originated from or spread to the liver in an era when the biology of disease following transplantation was largely unknown. The later part of our series demonstrates a shift towards performing transplantation or resection in patients with ESLD that would otherwise preclude these patients from undergoing well established procedures for their given pathology. Although these operations presented obvious technical challenges, we believe that our practice of performing LT prior to oncological resection and ensuring that it was accomplished with good preliminary function made a vital contribution to their general success. No cases were approached and abandoned as a result of complications with the LT.

Table 3 Patient demographics showing year of operation, primary tumour, end-stage liver disease at time of operation, years survival since operation and cause of death

<table>
<thead>
<tr>
<th>Patient</th>
<th>Year of operation</th>
<th>Primary tumour diagnosis</th>
<th>ESLD</th>
<th>Survival</th>
<th>Cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2006</td>
<td>Duodenal carcinoid</td>
<td>No</td>
<td>1 year</td>
<td>Alive</td>
</tr>
<tr>
<td>2</td>
<td>2005</td>
<td>IPMN</td>
<td>Yes</td>
<td>2 years</td>
<td>Alive</td>
</tr>
<tr>
<td>3</td>
<td>1996</td>
<td>Periampullary adenocarcinoma</td>
<td>Yes</td>
<td>11 years</td>
<td>Alive</td>
</tr>
<tr>
<td>4</td>
<td>1995</td>
<td>Periampullary adenocarcinoma</td>
<td>Yes</td>
<td>50 days</td>
<td>Sepsis (perioperative)</td>
</tr>
<tr>
<td>5</td>
<td>1992</td>
<td>Neuroendocrine tumour</td>
<td>No</td>
<td>2 years</td>
<td>Recurrence</td>
</tr>
<tr>
<td>6</td>
<td>1991</td>
<td>Neuroendocrine tumour</td>
<td>No</td>
<td>8 years</td>
<td>Lost to follow-up</td>
</tr>
<tr>
<td>7</td>
<td>1991</td>
<td>Neuroendocrine tumour</td>
<td>No</td>
<td>16 years</td>
<td>Alive</td>
</tr>
<tr>
<td>8</td>
<td>1991</td>
<td>Neuroendocrine tumour</td>
<td>No</td>
<td>3 years</td>
<td>Sepsis</td>
</tr>
<tr>
<td>9</td>
<td>1991</td>
<td>HCC</td>
<td>No</td>
<td>8 years</td>
<td>Lost to follow-up</td>
</tr>
<tr>
<td>10</td>
<td>1991</td>
<td>HCC (fibrolamellar)</td>
<td>No</td>
<td>16 years</td>
<td>Alive</td>
</tr>
<tr>
<td>11</td>
<td>1990</td>
<td>Periampullary adenocarcinoma</td>
<td>No</td>
<td>9 years</td>
<td>Recurrence</td>
</tr>
</tbody>
</table>

ESLD, end-stage liver disease; IPMN, intraductal papillary mucinous neoplasm; HCC, hepatocellular carcinoma

Although this series does not allow us to derive prognostic indicators for longerterm survival, it does demonstrate that LT combined with pancreaticoduodenectomy or pancreatectomy can result in prolonged survival. Although many of the studies that led to the current standards in LT were small, retrospective series, they have been crucial in determining how to best allocate organs that are in scarce supply.

Conflicts of interest
None declared.

References


