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Review

Pancreatectomy for metastatic disease: A systematic review

H. Adler*, C.E. Redmond, H.M. Heneghan, N. Swan, D. Maguire, O. Traynor, E. Hoti, J.G. Geoghegan, K.C. Conlon

National Surgical Centre for Pancreatic Cancer, St Vincent's University Hospital, Elm Park, Dublin, Ireland

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Abstract

Aim: Tumours rarely metastasise to the pancreas. While surgical resection of such metastases is believed to confer a survival benefit, there is limited data to support such management. We present a systematic review of case series of pancreatic metastasectomy and analysis of survival outcomes.

Methods: A literature search was performed using the PubMed and Cochrane databases and the reference lists of relevant articles, searching for sizeable case series of pancreatic metastasectomy with curative intent. Data extracted included basic demographics, histological primary tumour, presentation, operative management, complications and survival, while the MINORS index was used to assess study quality.

Results: 18 studies were found which met our inclusion criteria, involving 399 patients. Renal cell carcinoma (RCC) was the commonest malignancy metastasising to the pancreas, responsible for 62.6% of cases, followed by sarcoma (7.2%) and colorectal carcinoma (6.2%). While survival data was not uniformly reported, the median survival post-metastasectomy was 50.2 months, with a one-year survival of 86.81% and five-year survival of 50.02%. Median survival for RCC was 71.7 months with 70.4% five-year survival. Median survival was similar in patients with synchronous and metachronous pancreatic metastases, but patients with additional extrapancreatic metastases had a significantly shorter survival than patients with isolated pancreatic metastases (26 versus 45 months). Study quality was poor, with a median MINORS score of 10/16.

Conclusions: Within the limitations of a review of non-randomised case series, it would appear that pancreatic metastasectomy confers a survival benefit in selected patients. Better evidence is required, but may prove difficult to acquire.

Keywords: Pancreatic metastasis; Metastasectomy; Pancreatectomy; Metastatic renal cell cancer

Introduction

Metastatic tumours of the pancreas are extremely rare, accounting for less than 5% of pancreatic malignancies diagnosed in living patients.[1] Pancreatic metastases are found more frequently at autopsy, being identified in up to 15% of patients with malignant disease.[2] While resection of metastatic lesions to liver and lung has been well described and is generally accepted to improve survival, the optimal management of pancreatic metastases is ill-defined. Surgical resection of these metastases is believed to confer a survival benefit, although evidence supporting this theory is weak and based solely on case reports and small retrospective case series. The aim of this study was to perform a systematic review of the literature to better define the outcomes after pancreatic metastasectomy.

Methods

This review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[3]

Search strategy for identification of studies

A systematic literature search of the Cochrane and PubMed databases was performed. For the PubMed database search, the keywords were used as both text words and Medical Search Headings (MeSH terms). The

* Corresponding author. Tel.: +353 87 212 3429.
E-mail address: hugh.adler@gmail.com (H. Adler).

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keywords were combined using Boolean operators as follows: (pancreas AND (metastasis OR metastases) AND (surgery OR surgical OR resection OR pancreatectomy OR metastasectomy)). There was no restriction on the date of publication. In addition to the primary electronic search we reviewed all 'related citations' linked to each relevant abstract in PubMed and manually reviewed the bibliographies of selected articles and relevant review papers to identify other studies for inclusion.

Study selection

Inclusion criteria for this systematic review were case series with at least ten patients, published in the English language before 24 October 2013, reporting survival data after pancreatic resection for secondary malignancies. Exclusion criteria were: case reports, review articles, studies reporting on surgical technique only and studies reporting resections for lymphoma or en-bloc resections involving the pancreas. Potentially relevant manuscripts were retrieved in full and assessed based on inclusion and exclusion criteria. When two publications were believed to involve potentially duplicated or overlapping patient populations (based on authors, institutions and study years), only the larger cohort was included in this review to avoid double-counting of patients. Series focusing on the palliative management of pancreatic metastases were excluded. Series of secondary malignancies of the pancreas in which some were managed medically were included if the survival data for patients who underwent resection could be extracted separately.

Data collection and statistical analysis

Data extracted from selected studies included (but was not limited to) the year of publication, authors' institution and country, number of patients and their demographics, histology of primary tumour, presentation (symptomatic or incidental finding), timing (synchronous or metachronous with the primary tumour), presence or absence of extrapancreatic metastases, operation performed, operative mortality and morbidity and survival data. Given the paucity of data on this topic, any measure of survival (median, one, two or five-year survival) was extracted. Statistical analyses were performed only on extracted summarised data from the selected studies. Basic descriptive statistics (percentages and weighted means) were used to summarize the patient, study, and outcomes data. Weighted means were calculated for oncological outcomes across all studies, with the unpaired *t*-test used to compare survival outcomes. Statistical analysis was performed using GraphPad software (GraphPad Software Inc, California, 2013).

We assessed the methodological quality of the selected studies using the Methodological Index for Non-Randomised Studies (MINORS) criteria.[4] This tool, validated by its original authors, assesses eight items (12 items in controlled studies), each of which is assigned a score of 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate).

Results

Search yields & data retrieval

Our initial literature search yielded 3405 citations. After an initial screening of titles and abstracts, 34 articles were reviewed in full to determine whether they met the inclusion criteria. Of these, 4 featured patient populations that overlapped with subsequent, larger studies, and 12 were rejected because they did not fulfil the inclusion criteria. The remaining 18 studies met the above criteria to merit inclusion in the extractable and analysable dataset.[5–23] The search strategy and outcomes are summarised in Fig. 1.

Study characteristics

The dataset consisted of 18 original studies, involving 399 patients who had undergone resection of pancreatic metastases. All studies were retrospective single-institution case series, although 7 relied on prospectively-maintained databases. Mean cohort size was 27, median 18 patients per study (range 10–70). The majority of studies were from Europe ($n = 12$), followed by series from the USA ($n = 4$), Canada ($n = 1$) and Korea ($n = 1$).

Patient characteristics

Of the 399 patients investigated in the 18 studies, 42% were female. At the time pancreatic metastases were discovered, the mean age of the patients was 61.7 years. Disease free interval (DFI, time from resection of primary tumour to diagnosis of pancreatic secondary lesions) was not consistently reported, however among studies which reported mean DFI the weighted mean was 65.9 months (data not shown). Demographic characteristics are summarised in Table 1.

RCC was the commonest malignancy metastasising to the pancreas, accounting for 62.6% of all primary tumours ($n = 250$); six articles focused entirely on RCC. Sarcomas were the second commonest primary tumour ($n = 29$, 7.2%), followed by colorectal carcinoma ($n = 25$, 6.2%), ovarian carcinoma ($n = 19$, 4.7%) and melanoma ($n = 16$, 4%) (Fig. 2).

Most centres performed standard procedures for resection of a pancreatic lesion—distal pancreatectomy ($n = 174$, 43.6%), pancreaticoduodenectomy ($n = 144$, 36.1%), and total pancreatectomy ($n = 52$, 13.0%). Some units performed variants of the standard procedures such as simple enucleation ($n = 20$, 5.0%), middle pancreatectomy ($n = 6$, 1.5%) and duodenum-preserving pancreatic head resection ($n = 3$, 0.7%).