Pancreatoduodenectomy with Venous Resection or Palliative Therapy? A Meta-Analysis

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ABSTRACT

This review evaluated the risks and survival benefits of pancreatoduodenectomy associated with venous resection compared with palliative surgery. A systematic review with meta-analysis was performed. Higher overall survival was observed in the pancreatic resection group (HR = 4.000; 95% CI 2.800 to 5.200). However, the palliative group had fewer complications (RD = 0.170; 95% CI -0.260 to 0.070). There was no significant difference in the mortality rates (RD = 0.000; 95% CI -0.030 to 0.030). In centres with experience in pancreatic surgery, resection may be considered for locally advanced cancer and major venous invasion. Pancreatoduodenectomy with vascular resection may improve survival for periampullary tumours compared with palliation therapy. However, pancreaticoduodenectomy with major venous resection has potentially higher morbidity than palliation therapy.

Key Words: Pancreatoduodenectomy, Pancreatic neoplasms, Vascular surgical procedures.


INTRODUCTION

The incidence of ductal adenocarcinoma of the pancreas is increasing, and this type of tumour may become one of the main causes of malignancy-related death in the next decade.¹ This high mortality rate is due to its usual advanced presentation. Half of the patients have distant metastasis at the diagnosis, and only a minority of the tumours are considered resectable.² Pancreatic cancers present high biological aggressiveness, with early hematogenous dissemination.³

At present, the only curative option for periampullary tumours is the R0 surgical resection.⁴ However, pancreatoduodenectomy for cancer is a technically complex procedure with a high risk for morbidity and mortality, especially when the tumour also involves the superior mesenteric/portal vein.⁵ In high-volume institutions, the postoperative complications rates range from 35 to 44%,⁶,7 and mortality rates range from 2.5 to 6%.⁶,13,14 Even with curative-intent resection, the long-term survival is low.⁵,15,16

Although systemic dissemination remains an absolute contra-indication to surgery, neoplasms with vascular involvement may benefit from vascular resection, offering a chance of cure given that the R0 surgery is achieved.¹⁷,¹⁸

Many authors have proposed venous vascular resections in patients with periampullary neoplasms with an associated invasion of the portomesenteric venous axis.¹⁹-²² However, the morbidity, mortality, and long-term survival outcomes for venous vascular resection are significantly worse than the standard pancreatoduodenectomy.¹⁶ Nevertheless, the survival gain of periampullary neoplasms associated with major venous resection compared with palliation therapy is still unknown.

This review aimed to compare the pancreatoduodenectomy associated with venous resection and palliative therapy (no resection) for treating patients with periampullary neoplasms.

METHODOLOGY

A systematic search was performed on Lilacs, Embase, Cochrane, Medline, Cochrane, and gray literature up to June 2022. The strategy comprised a combination of keywords and MeSH terms including mesenteric vein, vascular resection, portal vein, portal system, vein resection, vascular reconstruction, vein reconstruction, pancreas, pancreatic, neoplasm, cancer, adenocarcinoma, pancreaticoduodenectomy and duodenopancreatectomy. The protocol of this study was previously in a public database (PROSPERO: CRD42021292488).

Two independent authors performed literature search and screening. A third author resolved any disagreement. Any controlled observational or experimental study was considered for inclusion. Conference proceedings, editorials, animal models, letters, reviews, and case reports were excluded. There was no restriction for the search period and language. Inclusion criteria were studies comparing palliation therapy with pancreatoduodenectomy with major venous resection.
(superior mesenteric vein, portal vein, or portomesenteric confluence) for periampullary tumour. Combined arterial resection was excluded. Robins-I was used to assess the bias and GRADEpro for certainty.

The outcomes studied were overall survival, postoperative mortality, postoperative complications, bleeding, pancreatic leak, reoperation, and length of hospital stay.

The software STATA was used for statistical analysis. Categorical variables were described as risk difference (RD), and continuous variables were expressed as mean difference (MD). The hazard ratio (HR) was used for the evaluation of overall survival. If the HR was not informed, HR was estimated using previously published methods. A fixed or random-effects analysis model was applied according to the I² statistics. The level of significance was set at 0.05.

RESULTS

Initially, 1,487 papers were retrieved using the search criteria. After screening and applying eligibility criteria, ten studies were selected for the meta-analysis (Figure 1). Only one study was a randomised prospective trial. The evaluation of the risk of bias is presented in Table I, and the certainty assessment is shown in Table II.

![Figure 1: Selection flow diagram.](image)

![Figure 2: Overall survival.](image)
Pancreatic neoplasm and vein resection

Figure 3: Postoperative outcomes. (a) Postoperative mortality; (b) Postoperative complications; (c) Need for a blood transfusion; (d) Pancreatic leak; (e) Reoperative procedures; (f) Length of hospital stay.

Table I: Analysis of the risk of bias (Robins-I).

<table>
<thead>
<tr>
<th>Author</th>
<th>Bias due to confounding</th>
<th>Bias in selection of participants into the study</th>
<th>Bias in classification of interventions</th>
<th>Bias due to deviations from intended interventions</th>
<th>Bias due to missing data</th>
<th>Bias in measurement of outcomes</th>
<th>Bias in selection of the reported results</th>
<th>Overall bias</th>
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<tbody>
<tr>
<td>Cheung</td>
<td>Low</td>
<td>Serious</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
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<tr>
<td>Wang et al.</td>
<td>Low</td>
<td>Serious</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
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<td>Ravikumar et al.</td>
<td>Low</td>
<td>Serious</td>
<td>Low</td>
<td>Low</td>
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<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Podda et al.</td>
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<td>Serious</td>
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<td>Low</td>
<td>Moderate</td>
<td>Moderate</td>
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<td>Moderate</td>
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<tr>
<td>Barnes et al.</td>
<td>Low</td>
<td>Serious</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
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<tr>
<td>McClaine et al.</td>
<td>Low</td>
<td>Serious</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
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<td>Moderate</td>
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<td>Boggi et al.</td>
<td>Low</td>
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<td>Low</td>
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<tr>
<td>Norero et al.</td>
<td>Low</td>
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<td>Low</td>
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<tr>
<td>Lygidakis et al.</td>
<td>Low</td>
<td>Serious</td>
<td>Low</td>
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<tr>
<td>Vladoev et al.</td>
<td>Low</td>
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<td>Low</td>
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<td>Moderate</td>
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</table>

Table II: Certainty assessment (GRADEpro).

<table>
<thead>
<tr>
<th>Certainty assessment</th>
<th>Studies</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Publication bias</th>
<th>Overall certainty of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall survival</td>
<td>8 studies</td>
<td>Serious¹</td>
<td>Serious³</td>
<td>Not serious</td>
<td>Not serious</td>
<td>None</td>
<td>☒ Low</td>
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<tr>
<td>Postoperative mortality</td>
<td>3 studies</td>
<td>Serious¹</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Serious¹</td>
<td>None</td>
<td>☒ Low</td>
</tr>
<tr>
<td>Postoperative complications</td>
<td>2 studies</td>
<td>Serious¹</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Serious¹</td>
<td>None</td>
<td>☒ Low</td>
</tr>
<tr>
<td>Bleeding</td>
<td>3 studies</td>
<td>Serious¹</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Serious¹</td>
<td>None</td>
<td>☒ Low</td>
</tr>
<tr>
<td>Pancreatic leak</td>
<td>3 studies</td>
<td>Serious¹</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Serious¹</td>
<td>None</td>
<td>☒ Low</td>
</tr>
<tr>
<td>Reoperation</td>
<td>2 studies</td>
<td>Serious¹</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Serious¹</td>
<td>None</td>
<td>☒ Very low</td>
</tr>
<tr>
<td>Length of hospital stay</td>
<td>2 studies</td>
<td>Serious¹</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Serious¹</td>
<td>None</td>
<td>☒ Low</td>
</tr>
</tbody>
</table>

(¹) Risk for selection bias; (³) Statistical heterogeneity I² > 50%; (²) Low-pooled sample size.
DISCUSSION

This systematic review showed that pancreatic resection increased survival in patients with locally advanced periampullary cancer as compared to palliative surgery. However, more extensive resection implied more significant morbidity, extended hospital stays, bleeding, and higher postoperative complications, including pancreatic leaks.

A previous meta-analysis showed that pancreaticoduodenectomy with major vein resection was associated with a higher perioperative morbimortality and worse long-term results than without vascular procedures.16 These findings raise the question whether pancreaticoduodenectomy with major vein resection is the treatment of choice for local advanced periampullary neoplasms or whether palliation therapy should be applied; the results of the present systematic review have implications for decision-making. The higher long-term survival rate in the resection group compared with the palliation implies that pancreaticoduodenectomy with vein resection should be the first-line therapy. However, knowing the higher perioperative morbidity of surgical resection, choosing between resection or palliation therapy should be based on an insightful patient clinical evaluation. Patient selection criteria should rely on age, performance status, and comorbidities, among other surgical risk variables.

In addition to evaluating surgical risk variables, the potential benefits and risks of performing resection or palliation therapy for advanced peripapillary cancer should be shared with the patient and family. Shared decision-making (SDM) is a collaborative approach that involves the patient and their family, as well as the healthcare team, in the decision-making process. In SDM, the team provides the patient with information about their condition, the available treatment options, and the associated risks and benefits. The patient and their family are encouraged to ask questions and provide their preferences and concerns. In the context of complex conditions, such as locally advanced peripapillary neoplasms, SDM can help ensure that the patient is well-informed about their options and is an active participant in the decision-making. The healthcare team can provide information about the surgical procedure, including the risks and benefits, and can discuss alternative treatment options, such as palliation therapy. The patient’s preferences and values should be considered when making a decision. SDM can help to build trust between the patient and the healthcare team. When the patient feels heard and valued, there is a higher chance that the patient will be satisfied with the short and long-term surgical outcomes.37
The great gain in long-term survival with pancreatic and major venous resection is probably possible only when R0 resection is feasible. These procedures are complex and should only be performed in experienced centres so that the chance for R0 resection with low morbidity can be achieved.\(^{38-45}\)

The resection of periampullary tumours with associated venous invasion of the portomesenteric axis has a high risk of overall morbidity, reoperations, and postoperative bleeding.\(^6\) The mean operative mortality is 4%.\(^6\) This high morbidity could justify the augmented length of hospital stay in the resection group, which was observed in this study's results.

The present review also showed that the pancreatic leak is higher in pancreatic resection than in palliation therapy. The pancreatic leak could also contribute to the increased length of stay in the pancreatic resection group. Despite advances in preventing postoperative pancreatic leak in pancreatoduodenectomy,\(^47\) the risk of this threatening complication still ranged between 3-45% of pancreaticobiliary resections, even in centres of excellence.\(^46,51\) This complication was associated with higher morbidity, mortality, and length of hospital stay.\(^57\) Conversely, the risk of a pancreatic leak was not added in palliative procedures (biliointestinal bypass or gastroenteroanastomosis).

This present study had several limitations. Only one study was a randomised clinical trial. Consequently, there was a significant risk of selection bias in the included studies when allocating patients to resection or palliation groups. The risk of selection bias contributed to the low certainty of the evidence for most outcomes. Also, there was high inter-study variability, including different surgical techniques, institutional experience across the studies, and neoadjuvant therapies. Currently, the therapy of choice for patients with invasion of the portomesenteric axis was neoadjuvant therapy followed by resection, and most of the included studies did not use neoadjuvant treatment. Future randomised controlled trials with standardised therapeutic protocols and chemotherapy regimens are needed to evaluate the safety and efficacy of pancreatectoduodenectomy with major venous resection. Besides, new palliative treatments are available for treating periampullary cancer and should also be addressed in future studies.

CONCLUSION

In centres with experience in pancreatic surgery, resection may be considered for locally advanced cancer and major venous invasion. Pancreatectoduodenectomy with vascular resection may improve survival for periampullary tumours compared with palliation therapy. However, pancreatectoduodenectomy with major venous resection has a potentially higher morbidity than palliation therapy.

COMPETING INTEREST:
The authors declared no competing interest.

AUTHORS' CONTRIBUTION:
JELPF, SSBM: Search and selection.
ACH: Data extraction.
ARD, JW: Writing and supervision.
FT: Statistical analysis.
All authors approved the final version of the manuscript to be published.

REFERENCES


