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# Surgical Oncology





# Meta-analysis and cost effective analysis of portal-superior mesenteric vein resection during pancreatoduodenectomy: Impact on margin status and survival



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#### ABSTRACT

*Introduction:* The benefit of portal-superior mesenteric vein resection (PSMVR) with pancreatoduodenectomy (PD) remains controversial. This study assesses the impact of PSMVR on resection margin status and survival.

*Method:* An electronic search was performed to identify relevant articles. Pooled odds ratios were calculated for outcomes using the fixed or random-effects models for meta-analysis. A decision analytical model was developed for estimating cost effectiveness.

Results: Sixteen studies with 4145 patients who underwent pancreatoduodenectomy were included: 1207 patients had PSMVR and 2938 patients had no PSMVR. The R1 resection rate and post-operative mortality was significantly higher in PSMVR group (OR1.59[1.35, 1.86] p=<0.0001, and OR1.72 [1.02,2.92] p = 0.04 respectively). The overall survival at 5-years was worse in the PSMVR group (HR0.20 [0.07,0.55] P = 0.020). Tumour size (p = 0.030) and perineural invasion (P = 0.009) were higher in the PSMVR group. Not performing PSMVR yielded cost savings of \$1617 per additional month alive without reduction in overall outcome.

Conclusion: On the basis of retrospective data this study shows that PD with PSMVR is associated with a higher R1 rate, lower 5-year survival and is not cost-effective. It appears that PD with PSMVR can only be justified if R0 resection can be achieved. The continuing challenge is accurate selection of these patients.

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#### 1. Introduction

Invasion of the portal-superior mesenteric vein occurs in almost a quarter of patients undergoing pancreatoduodenectomy (PD). While previously considered a contra-indication to PD, portal-superior mesenteric vein resection (PSMVR) is now being performed more often to decrease the rate of positive resection margins [1–3]. Whether this more aggressive approach translates to clinical benefit is still debated [4]. A systematic review published in 2006 indicated that PSMVR was associated with a high rate of nodal metastases and a worse 5-year survival [5]. Since then published data has been inconsistent with some studies showing improved survival with PSMVR [6] while others have demonstrated no difference [1,7]. The most recent data shows that the increase in PSMVR rate is associated with a decrease in R0 resection rates and survival [8,9]. It would appear that any survival benefit from PSMVR requires a complete resection (R0) [10,11].

Another strategy to improve survival in patients with possible invasion of the portal-superior mesenteric vein is the use of neoadjuvant chemotherapy. Recently an impressive 92% R0 resection rate was achieved after FOLFIRNIOX neoadjuvant chemotherapy in patients considered to be unresectable [13]. Another potential strategy for patients at risk of a positive margin is irreversible electroporation which involves targeted ablation along the SMA margin for what is called 'margin accentuation' [14]. In a cohort study of patients with locally advanced/borderline resectable pancreatic cancer, this technique combined with pancreatoduodenectomy achieved an impressive median overall survival of 22 months [14,15]. These strategies further fuel the debate as to whether PSMVR itself confers any survival benefit for patients with borderline resectable tumours who undergo PD if an RO resection is not achieved. It is not clear whether PSMVR with PD increases the negative SMA margin rate, confers other clinical benefits or is a cost-effective surgical treatment.

Recent meta-analyses have attempted to assess the impact of PSMVR on perioperative outcomes and survival [9,16,17], but there has not been a systematic attempt to determine the impact of PSMVR on the different designated margins of the PD specimen. Unfortunately, the recent meta-analyses included patients undergoing total and distal pancreatectomies in addition to PD, which confounds the analysis of margin status. Furthermore, none of the meta-analyses attempted to undertake a cost-effectiveness analysis. The aim of this review is to conduct both a meta-analysis and cost-effectiveness analysis to determine the impact of PSMVR on margin status and survival after PD (classical and pylorus preserving) for pancreatic ductal adenocarcinoma (PDAC).

## 2. Methods

This meta-analysis was conducted according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [18]. All stages of study selection, data abstraction and quality assessment were carried out independently by two reviewers.

## 2.1. Literature search

A systematic literature search was conducted in the following bibliographic databases: MEDLINE (via PubMed), the Cochrane Library and Embase from the inception of the databases until September 2015. No restrictions were applied with regard to language or publication date. Trial registries, including EU Clinical Trials Register and ClinicalTrials.gov were searched for any ongoing trials in this field. The search strategy for this systematic review was constructed for each database by using a combination of medical subject headings (MeSH) and free-text terms, as shown in the following for MEDLINE::(((('pancreaticoduodenectomy'[MeSHTerms]OR 'pancreaticoduodenectomy'[tiab] OR 'pancreato-duodenectomy'[tiab] OR 'duodenopancreatectomy'[tiab]OR 'Whipple'[tiab] OR 'Kausch-Whipple'[tiab])) AND('Portal vein resection' OR 'vein resection' OR 'Mesenteric vein resection' OR 'vascular resection' AND AND (randomised controlled trial[pt] OR controlled clinical trial[pt] OR randomised[tiab] OR placebo [tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti] NOT (animals[mh] NOT humans[mh])). Filters for comparative studies were applied to limit the number of records. The references from the included studies were searched to identify additional studies. The PRISMA flow diagram is shown in Fig. 1.

# 2.2. Study selection

Portal vein resection is defined as segmental resection or tangential resection of the superior mesenteric vein or main portal vein. Two independent investigators (RB,SP) reviewed all records identified by these search methods. If the abstract (n = 108) suggested relevance, the full article (n = 62) was assessed for eligibility. Only studies meeting the following inclusion criteria were included: at least two study groups comparing outcomes, a comparison of PSMVR versus no PSMVR, and patients undergoing classical or pylorus preserving pancreatoduodenectomy for PDAC. Studies including total and distal pancreatectomies were excluded. In addition, studies including arterial resections along with PSMVR were excluded. There were no restrictions with regard to status of the publication or patients' age.

Data from included studies were extracted by two independent investigators using standardised data extraction forms. If there was disagreement between the reviewers, a third member of the working group was consulted. After discussing the discrepancies, a consensus was reached for each study. The following items were extracted: title of study, year of publication, journal, study duration, study design and sample size. The baseline data extracted were: age, underlying disease type, surgical procedures and perioperative management. Relevant perioperative outcome variables included: pancreatic fistula, morbidity, mortality. The pathological variables analysed included the overall RO and R1 resection rates, other positive margin rates (including SMA margin, pancreatic transection margin/bile duct margin), perineural invasion, lymph node

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