



## Review

## Systematic review and meta-analysis of prognostic role of splenic vessels infiltration in resectable pancreatic cancer

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### Abstract

**Background:** Identification of factors associated with dismal survival after surgery in resectable pancreatic ductal adenocarcinoma is important to select patients for neoadjuvant treatment. The present meta-analysis aimed to compare the results of distal pancreatectomy for resectable adenocarcinoma of the pancreatic body-tail with and without splenic vessels infiltration.

**Methods:** A systematic search was performed of PubMed, Embase and the Cochrane Library in accordance with PRISMA guidelines. The inclusion criteria were studies including patients who underwent distal pancreatectomy for pancreatic cancer with or without splenic vessels infiltration. 5-year overall survival (OS) was the primary outcomes. Meta-analysis was carried out applying time-to-event method.

**Results:** Six articles with 423 patients were analysed. Patients with pathological splenic artery invasion had a worse survival compared with those without infiltration (Hazard ratio 1.76, 95% CI 1.36–2.28;  $P < 0.0001$ ). A similar results was found when considering pathological splenic vessels infiltration, showing that survival was significantly poorer when splenic vein infiltration was present (Hazard ratio 1.51, 95% CI 1.19–1.93;  $P = 0.0009$ ).

**Conclusions:** This meta-analysis showed worse survival for patients with splenic vessels infiltration undergoing distal pancreatectomy for pancreatic cancer. Splenic vessels infiltration represents the stigmata of a more aggressive disease, although resectable.

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**Keywords:** Pancreatic cancer; Splenic artery; Splenic vein; Surgery; Survival; Recurrence

### Introduction

The standard of care for potentially resectable pancreatic ductal adenocarcinoma is surgical resection followed by adjuvant chemotherapy [1,2]. However, only 15–20% of patients are candidates for surgery, being the remaining patients diagnosed with metastatic or locally-advanced disease [2].

The presence of infiltration of the coeliac or superior mesenteric arteries is usually considered as an unresectable, locally advanced-tumor. In fact resections of these arteries are associated with poor postoperative and oncological outcomes and surgery is usually not indicated in these cases [3,4]. Tumors involving portal or superior mesenteric vein (PV-SMV) are considered as borderline resectable or locally-advanced depending on the type of vascular involvement [5,6]. These tumors can be treated with upfront surgery or neoadjuvant chemotherapy, and there is no definitive consensus regarding their management [6–8]. In this setting, a recent

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meta-analysis showed an increased postoperative mortality, higher rates of non-radical surgery and worse survival after pancreatectomy with PV-SMV resection, supporting the use of neoadjuvant therapy in these patients [9]. On the other hand, although adenocarcinoma of the distal pancreas involving splenic vessels alone is “technically” a resectable disease, recent data indicate that pathological infiltration of splenic artery and splenic vein [10–12] is associated with worse survival, suggesting that splenic vessels infiltration may be the expression of a more aggressive disease. In this context, the aim of this systematic review and meta-analysis was to evaluate survival and postoperative outcomes of splenic artery and splenic vein infiltration in patients undergoing distal pancreatectomy for adenocarcinoma of the body-tail of the pancreas. (See Table 1)

## Patients and methods

### Study selection

A systematic review was performed examining available data on controlled randomized and non-randomized trials assessing distal pancreatectomy for resectable carcinoma of the body and tail of the pancreas with invasion of the splenic vessels (artery or vein) in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) standards [13]. A systematic literature search was conducted using the PubMed, Embase and Cochrane Library databases engine up until April 30th, 2017 employing the terms: “distal pancreatectomy” combined with “splenic artery” and/or “splenic vein”.

Full-text papers were independently screened by 2 authors (SC and RC) for eligibility. When multiple articles were published from a single study group and where overlapping study periods were reported, only the most recent article was considered so as to avoid duplication of data [14]. The Pubmed function “related articles” was used to broaden each search, and the reference list of all potentially eligible studies was analysed. To minimize retrieval, bias a manual search method including the Science Citation Index

Expanded, Scopus and Google Scholar databases was performed. The final decision on eligibility was reached by consensus between the 2 screening authors.

### Inclusion and exclusion criteria

To be included in the present meta-analysis, a study had to satisfy the following criteria: histological diagnosis of pancreatic ductal adenocarcinoma (articles on pancreatic neuroendocrine neoplasia or other histology were excluded); tumors located in the body-tail of the gland; presence of resectable pancreatic cancer (no evidence of distant disease, no evidence of tumor abutment/encasement of the superior mesenteric artery, coeliac axis, common hepatic artery, portal vein and superior mesenteric vein); radiological and/or pathological details of presence versus absence of splenic artery (SA) and eventually of splenic vein (SV) infiltration; comparison of the results of distal pancreatectomy with versus without SA/SV infiltration in patients undergoing surgery for pancreatic cancer. Only studies which reported data on the primary outcome of interest were considered, including comparative studies of both randomized controlled trials (RCTs) and non-randomized controlled trials (non-RCTs).

### Data extraction

Data were extracted by 2 authors based on an intention to treat principle. Any disagreement was resolved through discussion with a reassessment of the data and/or by involving a senior author. For each study, the following information (where available) was extracted and summarized: 1) Author's surname and year of publication; 2) Country of the hospital in which the procedures were performed; 3) Study design; 4) Number of patients and 5) Underlying diseases.

### Outcomes

The primary outcome of interest was the 5-years overall survival (OS). The following were considered as secondary

Table 1  
5-year overall survival and disease free survival.

Authors	5-year overall survival SA neoplastic invasion			5-year overall survival SV neoplastic invasion			5-years disease free survival SA invasion		
	SA Positive	SA Negative	P value	SV Positive	SV Negative	P value	SA Positive	SA Negative	P value
Fukami et al. 2016 [29]	0 of 23 pts <sup>b</sup>	12.2% of 41 pts <sup>b</sup>	0.014	3.2% of 31 pts <sup>b</sup>	12.1% of 33 pts <sup>b</sup>	0.033	NR	NR	
Takahashi 2015 [12]	20% of 32 pts <sup>a</sup>	76% of 51 pts <sup>a</sup>	<0.001	NR	NR		NR	NR	
Partelli 2011 [11]	0 of 19 pts <sup>b</sup>	31.5% of 68 pts <sup>b</sup>	0.014	9.4% of 47 pts <sup>b</sup>	41.4% of 40 pts <sup>b</sup>	0.027	0 of 19 pts <sup>b</sup>	24% of 68 pts <sup>b</sup>	0.009
Kanda 2010 [10]	0 of 17 pts <sup>b</sup>	7.8% of 34 pts <sup>b</sup>	NR	0 of 24 pts <sup>b</sup>	9.8% of 27 pts <sup>b</sup>	NR	NR	NR	
Fujita 2010 [27]	0 of 13 pts <sup>b</sup>	20.7 of 37 pts <sup>b</sup>	NS	12% of 24 pts <sup>b</sup>	36.1% of 26 pts <sup>b</sup>	NS	NR	NR	
Shimada 2006 [29]	9% of 25 pts <sup>b</sup>	23% of 63 pts <sup>b</sup>	0.8083	6% of 48 pts <sup>b</sup>	31% of 40 pts <sup>b</sup>	0.0489	NR	NR	

SA: splenic artery.

SV: splenic vein.

<sup>a</sup> Radiological evaluation performed before preoperative chemoradiation therapy.

<sup>b</sup> Histopathologic evaluation of the operative specimen.

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