

REVIEW ARTICLE

A systematic review of the role of periadventitial dissection of the superior mesenteric artery in affecting margin status after pancreatoduodenectomy for pancreatic adenocarcinoma

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Abstract

Background: Resectable pancreatic ductal adenocarcinoma continues to carry a poor prognosis. Of the controllable clinical variables known to affect outcome, margin status is paramount. Though the importance of a R0 resection is generally accepted, not all margins are easily managed. The superior mesenteric artery [SMA] in particular is the most challenging to clear. The aim of this study was to systematically review the literature with specific focus on the role of a SMA periadventitial dissection during PD and its effect on margin status in pancreatic adenocarcinoma.

Study design: The MEDLINE, EMBASE and Cochrane databases were searched for abstracts that addressed the effect of margin status on survival and recurrence following pancreatoduodenectomy [PD]. Quantitative analysis was performed.

Results: The overall incidence of a R1 resection ranged from 16% to 79%. The margin that was most often positive following PD was the SMA margin, which was positive in 15–45% of resected specimens. Most studies suggested that a positive margin was associated with decreased survival. No consistent definition of R0 resection was observed.

Conclusions: Margin positivity in resectable pancreatic adenocarcinoma is associated with poor survival. Inability to clear the SMA margin is the most common cause of incomplete resection. More complete and consistently reported data are needed to evaluate the potential effect of periadventitial SMA dissection on margin status, local recurrence, or survival.

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Introduction

Among patients who undergo pancreatoduodenectomy (PD) for pancreatic adenocarcinoma (PDA), multiple clinical variables have been determined to be associated with postoperative prognosis.^{1,2} Of these, margin status appears to be one of the most important.³ The American Joint Committee on Cancer staging guidelines have attempted to standardize the pathologic evaluation of PD specimens to facilitate margin assessment.⁴ According to these guidelines, PD specimen margins that should be evaluated by the pathologist include the pancreatic

neck, bile duct, duodenum, stomach, as well as the superior mesenteric artery margin. The last of these margins, referred to as the SMA- or uncinete-margin, is specifically emphasized. Recent work by Verbeke *et al.*, has illustrated that standardization of the histopathological examination of PD specimens can allow for a tighter correlation between histological staging and outcomes.^{5,6}

The SMA margin comprises the tissue that connects the uncinete process to the right lateral border of the proximal 3–4 cm of the SMA (Fig. 1). PDA has a propensity to spread through this tissue along the perineural autonomic plexus that surrounds the

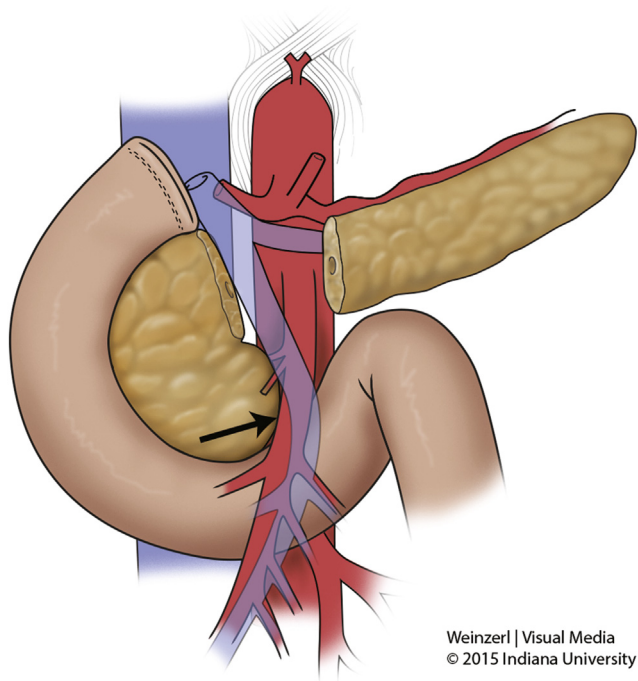


Figure 1 Superior mesenteric artery margin. Negative resection margin in the uncinate process is complicated by its proximity to the superior mesenteric artery

artery. The SMA margin is similar to the mesorectal margin emphasized during rectal surgery. However, the SMA cannot be removed and reconstructed at surgery in the absence of considerable morbidity. Many surgeons therefore strongly recommend that a periadventitial dissection of the SMA be performed at PD to skeletonize the right lateral aspect of the vessel from the uncinate process and adjacent tissues, to maximize the likelihood of obtaining a negative margin in the retroperitoneum.

Although this recommendation is commonly made, the association between the status of the SMA margin and oncologic outcomes is unclear. Indeed, the incidence of a positive SMA margin and any association between margin status and outcome may also reflect “tumor biology” rather than surgical approach or technical skill.^{1,7} The contribution of this specific surgical technique to postoperative outcome is therefore incompletely understood. The aim of this systematic review of the literature was to determine current reporting practices and the effect on outcomes of performing a periadventitial dissection of the SMA during PD.

Methods

The MEDLINE, EMBASE and Cochrane databases were searched for English-language articles published from January 1990 through January 2014 that addressed the effect of margin status

on survival and recurrence following PD. Search terms for “pancreas,” “retroperitoneal margin,” “pancreaticoduodenectomy,” “Whipple,” “margin,” “SMA dissection,” “mesopancreas,” “retroperitoneal dissection,” “morbidity,” and “uncinate dissection” were queried both in isolation and combination; duplicate references were removed prior to analysis.

The two investigators who performed the primary search (SAA and NJZ) independently reviewed the titles and abstracts of all returned references regardless of publication status to identify studies for inclusion in the analysis. Inclusion criteria dictated that articles selected for analysis focused on margin status following PD, and reported outcomes related to margin status. Review articles, and studies failing to document follow-up interval were excluded. All identified articles were examined using a predesigned proforma and the data collected were entered into a database for subsequent analysis. Articles selected for the analysis were specifically scrutinized for standardization of the surgical technique for SMA dissection, pathologic evaluation of the retroperitoneal margin, and margin status-related outcomes including local recurrence and overall survival. The methodological quality of studies was assessed for a minimum Oxford Center for Evidence-Based Medicine (CEBM) level of 2C.⁸

Results

The initial search yielded 520 unique articles; from these, 43 were selected for quantitative analysis. Fig. 2 documents flow of references through the systematic review. The articles selected for analysis focused specifically on pancreas cancer, commented on margin status following PD, and reported outcomes related to margin status. Of the 43 articles selected, 5 were prospective trials; the others were retrospective reviews of institutional databases (37 articles) or national registry data (1 article). The overall reported incidence of a R1 resection ranged from 16% to 79%. The margin that was most often positive following PD was the SMA margin. It was positive in 15–45% of resected specimens, and was implicated in 46–88% of R1 resections.

Retrospective studies of margin status, survival, and local recurrence

Thirty-eight retrospective studies meeting the eligibility criteria were evaluated with a minimum evidence level of 2C (Table 1). Only 16 studies reported the status of different margins individually; among these 16 studies, the SMA margin was the most frequently positive margin. None specifically evaluated the potential effect of periadventitial SMA dissection on margin status, local recurrence, or survival.

Among the 38 retrospective studies, 33 concluded that a positive resection margin (any margin) correlated with poorer overall survival, whereas 5 reported that margin positivity did not influence survival. Only 5 studies commented on the

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