

Original article

Surgical and oncological impact of main pancreatic duct spread in invasive ductal adenocarcinoma: A clinicopathological study of 184 resected cases



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ABSTRACT

Background/Objectives: This study examined main pancreatic ductal spread in invasive ductal adenocarcinoma (IDC) of the pancreas.

Methods: Data from IDC patients who underwent radical surgery from 1990 to 2013 in our hospital were examined retrospectively. Incidence of intraductal spread of pancreatic cancer (IS), distance from the tumor edge, direction of IS and clinicopathological factors associated with the presence of IS were retrospectively examined with data from IDC patients who underwent radical surgery.

Results: Among 260 IDC patients who underwent surgery, 184 eligible cases, IS was identified in 42 patients (22.8%) and mean length of IS was 18.7 ± 21.6 mm. Mean distances on the ampullary and distal sides of IS were 11.1 mm and 11.6 mm. IS was significantly more frequent in localized tumors (UICC T1–2 vs. 3–4, $p = 0.007$), with tumor diameter ≤ 2 cm ($p = 0.034$) and in cases with scarce microscopic perineural invasion ($p = 0.047$). Among patients who underwent pancreaticoduodenectomy and distal pancreatectomy, IS presence (11.6 vs. 21.8%), mean distance to the contralateral side (11.4 vs. 11.6 mm), and IS ≥ 2 cm (3.3 vs. 4.7%) showed no significant differences. Overall survival did not differ significantly between IS-positive and -negative patients in the full analysis set or propensity score-matched patients (42 matched pairs).

Conclusions: In setting resectional margins at 2 cm, a small proportion of cases (3.8%) showed positive surgical margins. Localized tumor (UICC: T1–2, or < 2 cm in diameter) requires more care with surgical margins, warranting intraoperative frozen sections.

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Introduction

Invasive ductal adenocarcinoma of the pancreas (IDC) reportedly possesses the poorest prognosis among the gastrointestinal malignancies and has been ranked as the fourth leading cause of cancer mortality in Western countries [1] and Japan [2]. More than 80% of cases are diagnosed as unresectable because pancreatic

cancer often shows high tumor grade [3]. Despite marked improvements in diagnostic modalities [4,5], the absence of distinctive symptoms and the systemic nature impair early detection of pancreatic cancer [6]. For resectable disease, although various treatments have been described [7–10], the most effective and potentially curative treatment for pancreatic cancer remains radical surgery [11]. During radical surgery, R0 resection without remnant cancer cells on histological examination is essential to guarantee a long disease-free interval. To secure negative surgical margins, setting appropriate distances is quite important. Most pancreatic cancer is thought to develop from pancreatic ducts, and the manner of local progression is divided into interstitial infiltration or intraductal spread [12,13]. However, little evidence is available

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regarding the setting of surgical margins during pancreatectomy. Many surgeons have striven to secure resectional margins of 2 cm based on experience performing radical surgery for IDC. Intraoperatively, negative margins are usually confirmed on the examination of frozen sections. However, primary pancreatic cancer sometimes spreads intraductally along the main pancreatic ductal system (Fig. 1) and cancer-positive margins at the main pancreatic duct may be incidentally encountered during the operation. Although the large branch ducts, small branch ducts and main pancreatic duct represent routes of pancreatic cancer spread, a positive pancreatic cut margin pattern has been encountered only at the main pancreatic duct with intraductal spread (IS) or at the pancreatic stump with invasive carcinoma [14]. In those cases with IS, additional resection is generally required until cancer-negative margins are secured. Such ductal spread has a decisive influence on setting the resection line, but is quite difficult to detect preoperatively, despite the evolution of various diagnostic modalities. To clarify the surgical and oncological implications of pancreatic ductal spread in patients with resection of pancreatic cancer, we retrospectively examined surgical cases in our hospital and clarified the appropriate setting of surgical margins.

Methods

A total of 260 consecutive patients with IDC underwent surgery at our hospital between January 1990 and December 2013. Fifty-six cases were excluded from the present investigation because non-radical surgery comprising bypass surgery, exploratory laparotomy, colostomy or metastasectomy had been performed. Radical surgery with curative intent was performed in the remaining 204 cases. Pathological diagnosis of IS was unconfirmed in 20 of the 204 cases, which were excluded because they could not be evaluated retrospectively. In total, 184 cases were analyzed in this study (Fig. 2).

Patients comprised 100 men and 84 women, with a mean age of 66.4 years at the time of surgery (range, 41–86 years). To avoid confusion, IS was handled separately from low grade-pancreatic intraepithelial neoplasia (PanIN) in peripheral branches of the pancreatic duct and from branch-duct intraductal papillary

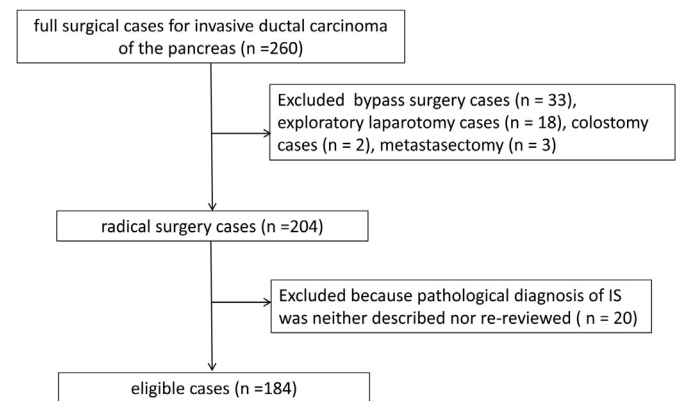


Fig. 2. Case-selection flowchart for IDC patients with histological examination of IS. A total of 260 cases with IDC of the pancreas underwent surgery. Fifty-six cases were excluded from analysis because of non-radical surgery, including bypass surgery, exploratory laparotomy, creation of colostomy and metastasectomy. In the remaining 204 cases, 20 cases were excluded because a pathological diagnosis of IS was not described and retrospective evaluation could not be performed.

mucinous neoplasm (IPMN). IS was defined as the spread of cancer cells in the main pancreatic duct in a continuous manner beyond the part of IDC. If spread of PanIN III in the main pancreatic duct in a continuous manner from the IDC was hard to differentiate from IS, that was diagnosed as IS, if necessary. The main outcomes included the presence or absence of IS, direction (ampullary or distal side) and distance from tumor edge (in millimeters). These findings were re-evaluated and confirmed retrospectively by two pathologists (S.S. and T.H.). Surgical procedures were pancreaticoduodenectomy (PD) in 120 cases and distal pancreatectomy (DP) in 64 cases. In the operating theater, the attending surgeons usually set the resection line for the pancreas under intraoperative ultrasonography with a distal contralateral-sided surgical margin of 2 cm from the pancreatic tumor edge.

Tumor stage was classified according to Union for International Cancer Control (UICC) criteria. More detailed information about pathological findings for the local tumor were characterized

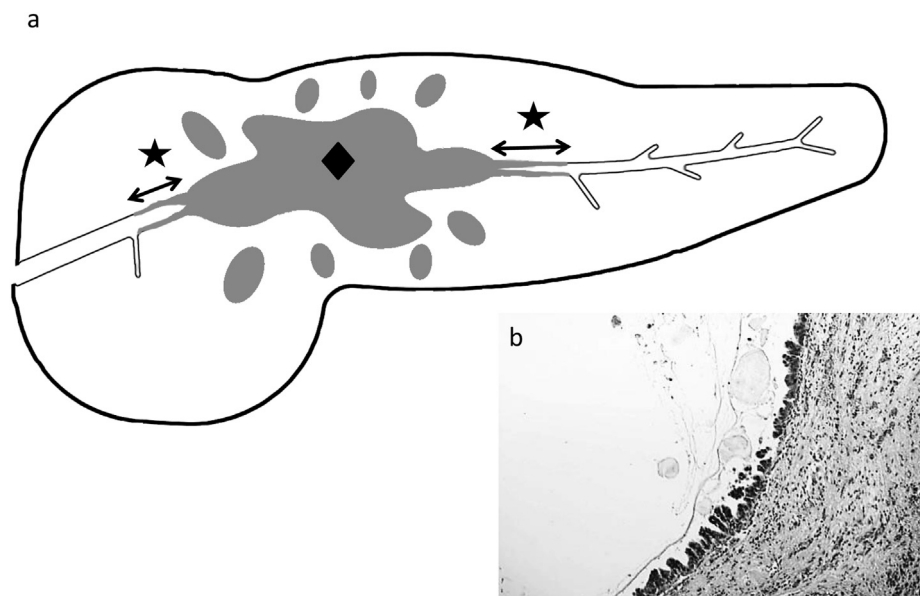


Fig. 1. Schematic representation of intraductal spread in pancreatic ductal adenocarcinoma (IS). IS was determined as the spread of cancer cells in the main pancreatic duct in a continuous manner beyond the part of IDC. **a** ★, intraductal spread of pancreatic cancer (IS); ◆, invasive pancreatic cancer. **b** Microscope photograph of intraductal spread in IDC.

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