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Original Research

Prognostic impact of splenic artery invasion for pancreatic cancer of the body and tail

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HIGHLIGHTS

- Only two studies have focused on histological splenic artery (SA) invasion.
- Histologic SA invasion was significantly worse than non-SA invasion **by using the log-rank test**.
- Histologic SA invasion was not a crucial independent prognostic factor compared to lymph node metastases or R1 resection.

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ABSTRACT

Background: The prognostic impact of splenic artery (SA) invasion after resection for pancreatic cancer of the body and tail has not been investigated. The aim of this study was to assess the clinical value of SA invasion for pancreatic cancer of the body and tail.

Methods: Between 1993 and 2015, 64 patients who underwent distal pancreatectomy (DP) for histologically confirmed pancreatic ductal adenocarcinoma of the body and tail were included in this study. Clinicopathological prognostic factors for survival were analyzed using a prospectively collected database.

Results: Of the 64 study patients, histologic invasion of the SA was confirmed in 23 (35.9%) cases. The prognosis of patients with SA invasion was significantly worse than that of patients with non-SA invasion (median survival: 16.0 versus 34.7 months, $p = 0.014$). Multivariate analysis indicated that lymph node metastases (risk ratio: 2.817, $p = 0.005$) and R1 resection (risk ratio: 2.715, $p = 0.006$) were independently associated with overall survival after DP for pancreatic cancer of the body and tail. In contrast, SA invasion was not extracted as an independent prognostic factor.

Conclusions: SA invasion after resection for pancreatic cancer of the body and tail does not have the prognostic impact that surpasses lymph node metastases.

1. Introduction

Pancreatic cancer is one of the most aggressive and lethal malignant diseases. Surgery accompanied with adjuvant chemotherapy leads to the best chance of survival. Distal pancreatectomy (DP) with splenectomy is the standard curative intent treatment for pancreatic cancer of the body and tail. However, less than 20% of patients are candidates for surgical resection due to the high incidence of distant metastases or local advanced disease at the time of diagnosis. The 5-year survival rate after resection is approximately 20% [1–4]. Various authors have performed studies to identify clinicopathological prognostic markers in pancreatic cancer. Lymph node metastases have consistently been characterized as one of the strongest predictors of survival after resection of pancreatic cancer of the body and tail [1,5,6]. Recently, Kanda et al. reported that splenic artery (SA) invasion was a crucial independent prognostic factor and a stronger factor than lymph node metastases in a multivariate analysis of 51 patients who underwent DP for pancreatic cancer of the body and tail [7]. However, evidence about the prognostic impact of SA invasion has not been established due to the limited number of cases. The aim of this study was to assess the clinical value of SA invasion for pancreatic cancer of the body and tail.

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2. Patients and methods

Between July 1993 and July 2015, 73 consecutive patients with histologically confirmed pancreatic ductal adenocarcinoma of the body and tail underwent DP, which was defined as the complete removal of tumors detected by preoperative imaging or intraoperative inspection, at the Ogaki Municipal Hospital. Nine patients were diagnosed with distant metastases (M1) disease, including microscopically para-aortic lymph node metastases. As a result, the final study cohort included 64 patients. Surgical outcome and histologic data were compared between patients with SA invasion and those without SA invasion. Long-term survival in patients with DP for pancreatic cancer of the body and tail was also analyzed. **In addition, the prognosis of patients with histologic SV invasion was also analyzed.**

2.1. Preoperative tumor staging and surgical approach

The extent of the tumor was examined preoperatively using conventional ultrasonography, contrast-enhanced computed tomography (CT), and endoscopic retrograde pancreatography. Other imaging approaches, including magnetic resonance imaging (MRI) and positron emission tomography (PET), were utilized in selected patients when necessary. **Since 1999,** DP combined with celiac axis resection (DP-CAR) was indicated in patients who had a cancerous invasion around the celiac axis and the origin of the common hepatic artery (CHA) and/or the SA [8,9].

In this study period, surgical technique of the DP has not changed along with one senior hepato-pancreato-biliary surgeon (Y.K). DP was performed using an antegrade approach [10], which consisted of en bloc resection for DP and splenectomy. The regional and peripancreatic lymph nodes, including those along the CHA, around the celiac axis, and on the left side of the aorta, were routinely dissected. The left side of the superior mesenteric artery (SMA) was also dissected with the surrounding lymph node and nerve plexus. If necessary, a combined resection of the surrounding organs, such as the stomach, small intestine, colon, and portal/superior mesenteric vein, was performed to obtain a negative surgical margin. The procedure for DP-CAR has been previously described [8].

2.2. Postoperative management

Postoperative complications were assessed according to the Clavien–Dindo classification system [11]. Postoperative pancreatic fistula was defined according to the definitions of an international study group (i.e., ISGPF) [12]. The specimens were serially sectioned perpendicular to the long axis of the pancreas at 5-mm intervals. The surgical margins of the pancreatic stump and retroperitoneal soft tissue, including the celiac ganglion and nerve plexus around the SMA, were evaluated in all sections. Pathologic findings were described using the TNM Classification of Malignant Tumors of the International Union Against Cancer (7th Edition, 2009) [13]. After surgery, all patients were evaluated every 3 months, and follow-up examinations consisted of measurements of serum CEA and cancer antigen 19-9 levels, as well as enhanced computed tomography and/or ultrasonography. Other imaging approaches, including MRI and PET, were utilized in selected patients when necessary.

No neoadjuvant chemotherapy was utilized in this study. Postoperative adjuvant chemotherapy using gemcitabine hydrochloride or tegafur-gimeracil-oteracil potassium was administered in 25 patients beginning in 2006.

2.3. Statistics

The continuous data are expressed as the mean ± the standard deviation. The statistical analyses were performed using Student's *t*-tests, χ^2 tests, and Fisher's exact probability tests as appropriate. A *p*-value <0.05 was considered statistically significant. The overall survival curves were generated by the Kaplan-Meier method, and differences in survival rates were compared using the log-rank test. The variables identified as potentially significant by univariate analysis were selected for multivariate analysis with the Cox proportional hazards model to identify independent predictors of survival. All statistical calculations were performed using the IBM SPSS Statistics 21 software package (IBM Japan Inc., Tokyo, Japan).

3. Results

3.1. Patient characteristics

Of the 64 study patients, histologic invasion of the SA was confirmed in 23 (35.9%) cases. Mean age, gender, and tumor location did not differ between the SA invasion group and the non-SA invasion group. However, tumor size was larger in the SA invasion group than in the non-SA invasion group (4.8 cm versus 3.5 cm, $p = 0.011$) (Table 1).

3.2. Surgical outcome

Operation time, blood loss, and combined with portal vein resection rate did not differ between the SA invasion group and the non-SA invasion group. However, the combined with celiac axis resection rate was higher in the SA invasion group than in the non-SA invasion group (65.2% versus 31.7%, $p = 0.008$). The morbidity, mortality, and postoperative adjuvant chemotherapy rate was also similar in the two groups (Table 1).

3.3. Histologic data

Table 2 displays the results of the comparison of the histologic data of the patients in the SA invasion and non-SA invasion groups. The differentiation, retroperitoneal invasion, and surgical margin status did not differ between the two groups. On the other hand, the rate of anterior serosal infiltration, perineural invasion, lymph vessel invasion, lymph node metastasis, and splenic vein invasion

Table 1
Patient characteristics and surgical outcome.

	SA invasion (n = 23)	Non-SA invasion (n = 41)	*P*
Age (year)	66 ± 8	69 ± 8	0.177
Gender (male/female)	13/10	25/16	0.794
Tumor location			1.000
Body	16 (69.6%)	29 (70.7%)	
Tail	7 (30.4%)	12 (29.3%)	
Tumor size (cm)	4.8 ± 1.6	3.5 ± 1.9	0.011
Operative time (min)	222 ± 70	198 ± 79	0.240
Blood loss (mL)	612 ± 443	588 ± 453	0.839
With portal vein resection	6 (26.1%)	7 (17.1%)	0.519
With celiac axis resection	15 (65.2%)	12 (31.7%)	0.008
Mobidity (≥Clavien grade III)	7 (30.4%)	10 (24.4%)	0.769
Pancreatic fistula (≥grade B)	6 (26.1%)	7 (17.1%)	0.519
Intraabdominal abscess	3 (13.0%)	1 (2.4%)	0.128
Intraabdominal bleeding	0	2 (18.2%)	0.532
Aspiration pneumonia	2 (8.7%)	0	0.125
Motality*	1 (4.3%)	0	0.359
Adjuvant chemotherapy	12 (52.2%)	13 (31.7%)	0.120

SA, splenic artery; *, due to aspiration pneumonia.