Analysis of 300 consecutive cases of pancreatic adenocarcinoma in a single-center in China

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BACKGROUND: Most of the reports on the prognostic indicators of patients with pancreatic adenocarcinoma are from developed countries. The present study focused on the prognostic indicators of Chinese patients with pancreatic adenocarcinoma.

METHODS: A total of 300 patients with pancreatic adenocarcinoma who had undergone curative resection were included. The resection and R0/R1 resection rates for adenocarcinomas from different parts of the pancreas were calculated and clinical characteristics were analyzed.

RESULTS: In 3427 patients diagnosed with pancreatic adenocarcinomas, only 300 (8.8%) were eligible for radical resection. The total median survival of these patients was 19 months, and their 1-, 3-, and 5-year survival rates were 72.5%, 28.0% and 23.4%, respectively. The prognostic factors included socioeconomic status, smoking history, symptoms, high blood glucose, and various tumor characteristics, including perineural and vascular invasion, lymph node metastases, and CA19-9 levels before and after operation. Operation-associated prognostic indicators included operation time, blood loss and transfusions, pancreatic fistula, and complications. Independent predictors of mortality included poor socioeconomic status, smoking history, symptoms, CA19-9, perineural invasion and lymph node metastasis, grade of fistula and complications. Patient survival was not correlated with either resection margin or adjuvant chemotherapy in multivariate analysis.

CONCLUSIONS: The survival rates of patients with curative resection for pancreatic adenocarcinoma in China are close to those in developed countries, but curative resection rate is far below. Socioeconomic status, symptoms, and CA19-9 are the three most prominent prognostic factors, which are helpful in patient selection and perioperative care.

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KEY WORDS: pancreatic adenocarcinoma;
prognostic factor;
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Introduction

Pancreatic adenocarcinoma is a devastating disease because the latent clinical feature and lack of effective treatment, especially in developing countries. In 2014, the incidence and mortality rates of pancreatic adenocarcinoma were identical, and there were 46 420 deaths, making pancreatic cancer the fourth leading cause of cancer death for both men and women in the USA.[1] Based on the nationwide statistics in the USA, less than 6% of patients with pancreatic adenocarcinoma can survive for more than 5 years,[1] and the survival rate is even lower in China.[2] Unfortunately, due to the insidious onset of pancreatic adenocarcinoma, only 10%-20% of these patients are candidates for surgical treatment, which is still the only feasible curative treatment for this highly malignant and lethal disease.[3-9] In addition to the slim probability of a curative resection of pancreatic adenocarcinoma, the long-term survival after surgery is also unlikely. Previous studies[3, 9-12] have indicated that the 5-year survival rate of patients who have received curative resection for pancreatic adenocarcinoma is only 5%-20%. In addition, recent studies[13, 14] demonstrated that the 5-year survival rate after resection is only less than 20%, even in the most advanced and high-volume medical centers.

Currently, there is an improvement in the curative

resection of pancreatic adenocarcinoma. Some scholars have attributed the success to the increased experience, advances in perioperative care, and increased use of adjuvant therapy. The determinants of survival can be sorted into the following categories: (i) patient demographics, such as gender, socioeconomic status (SES),[15, 16] and body mass index (BMI);[17] (ii) tumor factors, such as tumor stage[2, 4, 6, 7] and size;[6, 13, 15, 18] (iii) surgical technique and operative details, such as resection margin;[6, 13, 14, 18] and (iv) perioperative managements including adjuvant therapy[15, 18, 19] and packed red blood cell transfusion.[18]

Most of the studies on pancreatic adenocarcinoma are from developed countries, such as the USA, France, Netherlands, Japan and Korea,[6, 15, 20-23] and a few are from developing countries. Because of the differences in socioeconomic, cultural, and medical environments, the data harvested from developed countries may not be applicable to the developing countries. The present study was to analyze the prognosis of the patients with pancreatic adenocarcinoma who had undergone curative resection at a single, high-volume institution.

Methods

Patients

With the approval from the ethics committee of the hospital, we reviewed our prospectively maintained pancreas database to identify patients with pancreatic adenocarcinoma who had undergone curative resection between 1995 and 2013 in the First Affiliated Hospital of Harbin Medical University. The patients were eligible for study inclusion if they had had a pancreatic adenocarcinoma and had undergone tumor resection with a curative intent.

The curative resection procedure was determined according to the *International Classification of Diseases*, *9th revision*, *Clinical Modification (ICD-9-CM)*. The ICD-9 codes were related to pancreatic resection operations with curative intent, such as the Whipple procedure (52.7), radical pancreaticoduodenectomy (52.7), distal pancreatectomy (52.52), and total pancreatectomy (52.6). The primary tumor origin was mainly determined by pathological diagnosis; however, gross findings and image characteristics were also taken into consideration, especially when the pathological evidence was unclear. After curative resection, patients were followed-up at 6-month intervals until death or loss of follow-up.

Definitions of prognostic factors

Patient demographics and laboratory tests

Most of the patient demographic data were prospectively collected, including age, gender, smoking or drinking history, SES, BMI, symptoms, blood type, glucose, alanine aminotransferase (ALT), asparate aminotransferase (AST), total or direct bilirubin, albumin, lactate dehydrogenase (LDH), triglycerides, total cholesterol, serum or urinary amylase, hepatitis, and Charlson comorbidity score (CCS). The SES was divided as low or high based on the median household income. The census-level of SES is similar to that of the medical record.[24] The BMI was calculated according to patient's height and weight before operation. We identified pre-existing comorbidities from the patients' medical records and graded them by CCS.[25]

Tumor factors

The greatest tumor diameter, encapsulation, lymph node status, peripheral nerve invasion, and vascular invasion were obtained from pathology reports. The tumor location and number in the pancreas were verified by preoperative imaging findings. Additionally, the TNM stage was categorized based on the *TNM Classification of Malignant Tumors*, *7th edition*.[26] Preoperative and postoperative (on the 7th day after resection) CA19-9 or CEA data were collected from the medical records.

Surgical technique and operative details

The operative procedure, technical approach, and operative details such as operation or anesthetic time, blood loss, drain numbers, surgeon experience, and wound protector were collected. Moreover, the resection margin was assessed using the previously validated Leeds Pathology Protocol (LEEPP).[27, 28] And R1 was defined as tumor within one millimeter of the margin.[29] We calculated the rates of resection and R0/R1 resection for adenocarcinomas arising from different parts of the pancreas (when we found that the tumor was unresectable or had metastasis during operation, we closed the abdomen directly without any other medical intervention. This procedure was called O-C, short for open and closure).

Perioperative outcomes

The length of stay or postoperative stay, adjuvant chemotherapy, perioperative blood transfusion and wound infection data were collected. Complications defined as any deviation from the normal postoperative course during the hospital stay were recorded and divided into Grades I-V according to a validated classification.[30]

Grade I: any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections