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Resection or cryosurgery relates with pancreatic tumor type: Primary pancreatic cancer with previous non-pancreatic cancer or secondary metastatic cancer within the pancreas

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ABSTRACT

Objectives: We investigated the incidence of primary pancreatic cancer with previous non-pancreatic cancer (PPC) and secondary metastatic cancer within the pancreas (SMC) to elucidate the differential diagnosis and treatment of these lesions.
Methods: The clinical data of 2539 patients with pancreatic mass in Tianjin Cancer Hospital from January 2000 to December 2012 were retrospectively analyzed. All of the 66 patients who showed double or multiple primary cancers or metastatic pancreatic malignancies were included into the PPC group or SMC group, respectively. In addition, PPC patients were compared with 570 patients suffering from pancreatic cancer (PC) alone.
Results: For the PPC group ($n = 34$), the most common previous non-pancreatic cancers were gastric cancer, breast cancer, and thyroid cancer. For the SMC group ($n = 32$), the most common metastatic tumors were lung cancer, renal cell carcinoma (RCC), and gastric cancer. Multivariate analysis identified age (OR = 1.099; 95% CI, 1.007–1.199), previous tumor type (OR = 1.164; 95% CI, 1.046–1.296), and time interval between two tumors (OR = 1.021; 95% CI, 1.003–1.039) as significant indicators. Significantly better survival times were observed after resection than after cryosurgery in the PPC group ($p < 0.001$) but not in the SMC group ($p = 0.670$).
Conclusions: Overall, primary pancreatic cancers are as common as metastasis to the pancreas in patients with a previous cancer. A longer time interval between two tumors indicates a higher possibility that a new pancreatic cancer will occur. Some cancers (particularly RCC) are more likely to metastasize to the pancreas than other cancers. For metastatic cancers, cryosurgery is as effective as resection as a treatment option.

1. Introduction

Treating patients with a lesion in the pancreas and a history of a previous cancer is a clinical conundrum, something that every experienced clinician would inevitably encounter in clinical work. The extremely poor survival associated with pancreatic cancer (PC) implies that accurate diagnosis must be made at an earlier stage to facilitate the application of relative measures and improve survival. Recently, with improved clinical awareness, screening methods, and possibly some other potential influencing factors, it has been our impression that PC incidence in patients with a history of extrapancreatic malignant neoplasms seems to have increased in frequency. The overall reported incidence of PC associated with extrapancreatic malignancies is 1.2%–20.0% [1]. Metastatic carcinoma to the pancreas from another site accounts for approximately 2%–4% of pancreatic malignancies, but this percentage increases to 40% in patients with pancreatic mass and another malignancy in their history [2,3]. In a large autopsy series, the prevalence of pancreatic metastases is as high as 6%–11% [4]. However, because of the low occurrence rate, studies that simultaneously report the

Abbreviations: PPC, primary pancreatic cancer with previous non-pancreatic cancer; SMC, secondary metastatic cancer within the pancreas; PC, pancreatic cancer; isPMs, isolated pancreatic metastasis; RCC, renal clear cell carcinoma.

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difference between primary PC with previous non-PC (PPC) and secondary metastatic cancer within the pancreas (SMC) are lacking. Reported cases and series suggest that the resection for pancreatic metastases or primary PC with a malignancy history can be performed safely, especially in patients with isolated pancreatic tumor, and that long-term survival can be expected with pancreatic resection in a highly selected subset of patients [5–12]. However, no guidelines exist on the appropriate management of such lesions.

Over the recent decades, cryosurgery has been used to treat malignancies of the skin, lung, liver, prostate, breast, pancreas, and other organs. Compared with surgical resection, cryosurgery has several potential advantages, particularly the minimally invasive nature of the treatment, less damage to surrounding tissues, and improved results [13]. In addition, the potential cryo-immunologic response advantages in the treatment of especially advanced solid tumors have been intensively studied in recent years [14–16]. Therefore, more studies on the incidence, characteristics, differential diagnosis, and treatment of PPC and SMC are needed.

2. Materials and methods

2.1. Patients

From January 2000 to December 2012, a total of 2539 patients with pancreatic mass were identified from the hospital record database of Tianjin Cancer Hospital, China, and the records were retrospectively analyzed. The following criteria were used for diagnosing PPC or SMC. 1) The patients should have a history of extrapancreatic malignant neoplasms or at least another extrapancreatic tumor simultaneously with the pancreatic tumor. 2) The tumor should have been confined without obvious symptoms, which would indicate recurrence. 3) Histological diagnosis must have been assessed using core needle biopsy or surgery sample. 4) The patients should have received radical removal, cryosurgery, or other aggressive therapies for the newly developed pancreatic tumor. 5) The patients should have been subsequently classified into the PPC or SMC group. In addition, 570 patients presenting PC alone without extrapancreatic malignancy, who received adjuvant chemotherapy regularly after surgery or not, were included for comparison with PPC patients. Based on these criteria, 1903 patients were excluded from this study. Among the excluded 1869 cases were patients with PC alone, and 1085 cases comprised patients who did not return for follow up, those who died within a month after surgery, or those with positive resection margins. A total of 784 of the excluded cases did not receive adjuvant chemotherapy or radiotherapy regularly. Thirty-four cases among those excluded showed ambiguous pathology results of diagnoses for primary or metastatic PC (Fig. 1). A written informed consent was obtained from each patient for the treatment received, and the study was approved by the research committees of Tianjin Cancer Hospital.

2.2. Surgical treatments

Resections performed with curative intent were characterized as R0 when no evidence of malignant glands was identified in any of the resection margins [17]. R1 resection status was defined as microscopic evidence of tumor within 1 mm from a resection margin [18]. Some discrepancy in literature exists regarding whether or not R1 margins significantly change patient outcomes in pancreatic ductal adenocarcinoma [19,20]. Therefore, radical surgery was performed, and only the patients with pathologically negative resection margins (R0) were included. Cryosurgery was performed with Cryocare Operative System (Endocare CA, USA). The number and size of the cryoprobes used to freeze a lesion depended on the size of the lesion. The cryoprobe was inserted after the abdomen was opened and the pancreas tumor was exposed under color ultrasound guidance. Two freeze–thaw cycles were performed. The duration of freezing depended on the formation of an ice ball that extended 1 cm beyond the boundaries of the tumor. Generally, the maximal freezing time for one session was 15 min, followed by thawing for 5 min, and this cycle was subsequently repeated. The blood pressure and heart rates of all of the patients were monitored throughout the procedure.

2.3. Evaluated variables

Data on sex, age at diagnosis of pancreatic tumor, extrapancreatic tumor type, pancreatic tumor location, tumor size, time interval between extrapancreatic malignancies and pancreatic tumor, follow up time after diagnosis of PC, 7th UICC stage, and grading degree of PC were obtained.

2.4. Statistical analysis

Categorical variables were statistically compared using the chi-square test or Fisher's exact test. Continuous data were statistically compared using the Mann–Whitney *U* test for each or both groups. Logistic regression was applied in the multivariable analysis. Overall survival calculated from the date of pancreatic tumor

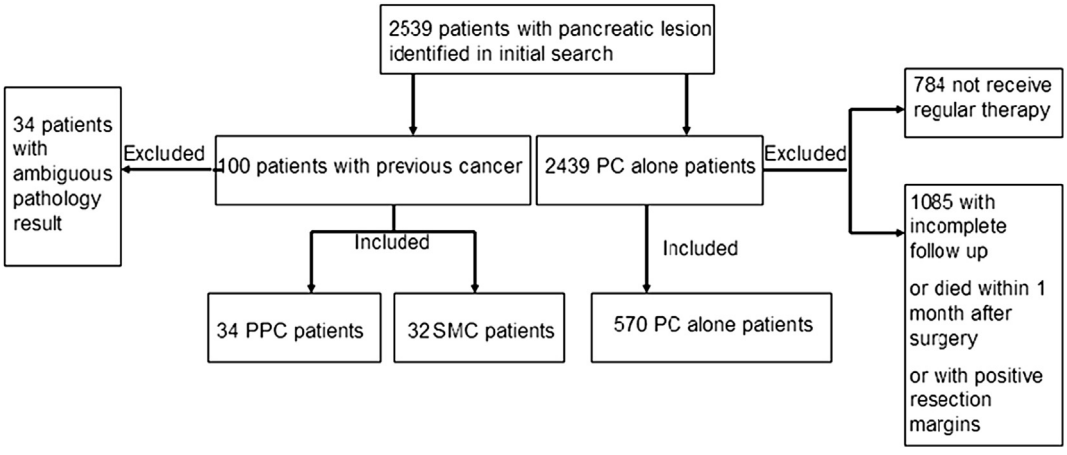

Fig. 1. Flow diagram of patients included and excluded in the study.