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Original article

Prognostic Implications of the Standardized Study of Resection Margins in Pancreatic Cancers[☆]



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ABSTRACT

Introduction: Involvement of surgical resection margins is a fundamental prognostic factor in pancreatic oncological surgery. However, there is a lack of standardized histopathology definition. The aims of this study are to investigate the real rate of R1 resections when surgical specimens are evaluated according to a standardized protocol and to study its survival implications.

Patients and methods: One hundred consecutive surgically resected patients with pancreatic ductal adenocarcinoma were included in the study. They were further divided into 2 groups: pre-protocol, evaluated before the introduction of the standardized protocol and post-protocol, analyzed with the standardized protocol.

Results: R0 resection rate in the pre-protocol group was 78%, falling to 47% after the introduction of the standardized protocol ($P=.003$). The posterior retroperitoneal margin was the most frequently involved margin. In cases with tumors located at the pancreatic head and analyzed according to the standardized protocol R1 involvement negatively affected survival. Median survival in the R0 group was 22 months versus 16 in those with the margin involved (HR: 2.044; IC 95% 1.00–4.16; $P=.043$).

Conclusions: Standardized evaluation of the retroperitoneal margins in pancreatic cancer increases the rate of R1 patients. In cases with pancreatic cancer located at the pancreatic head involvement of posterior retroperitoneal margin significantly decreases survival.

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Implicaciones pronósticas del estudio estandarizado de los márgenes de resección en el cáncer de páncreas

RESUMEN

Palabras clave:

Cáncer de páncreas
Duodenopancreatectomía
Resección oncológica
Resección R1

Introducción: La afectación microscópica de los márgenes de resección es un factor pronóstico fundamental en la cirugía del cáncer de páncreas. Sin embargo, su definición anatómopatológica no está estandarizada. Este estudio pretende identificar el porcentaje real de pacientes con resecciones R1 al analizar las piezas quirúrgicas con un protocolo estandarizado y evaluar sus implicaciones sobre la supervivencia.

Pacientes y métodos: Serie de 100 pacientes consecutivos intervenidos por adenocarcinoma ductal de páncreas y resecciones macroscópicamente completas, divididos en 2 grupos: pre- y posprotocolo, según se intervinieran antes o después de la aplicación de un protocolo estandarizado de las piezas de resección.

Resultados: En el grupo preprotocolo la tasa de resecciones R0 fue del 78%, mientras que tras la aplicación del mismo, se redujo al 47% ($p = 0,003$). El margen posterior retroperitoneal es el que se encuentra afectado con mayor frecuencia. En los casos con tumores localizados en cabeza de páncreas y analizados con el protocolo estandarizado, la detección del margen retroperitoneal afecto (R1) influye de forma negativa en la supervivencia. La mediana de supervivencia del grupo R0 fue de 22 meses frente a 16 meses en los que presentaban margen afecto (HR: 2,044; IC 95% 1,00-4,16; $p = 0,043$).

Conclusiones: La aplicación de un protocolo estandarizado para el estudio del margen retroperitoneal en el cáncer de páncreas incrementa la proporción de pacientes R1. En los pacientes con cáncer de cabeza de páncreas, la afectación del margen posterior retroperitoneal reduce significativamente la supervivencia.

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Introduction

Pancreatic ductal adenocarcinoma is a biologically very aggressive tumor. Less than 25% of the patients are eligible for surgical treatment with curative intent, the only option used to achieve long-term survival.

One factor that could have a greater impact on surgical oncology outcomes is the involvement of resection margins, both in microscopic (R1) and macroscopic (R2) forms. Therefore, it is surprising that, unlike other types of tumors, many pancreatic cancer patients with oncologic resections also have high local recurrence and poor survival rates, regardless of whether surgical resections are R0 or R1. The lack of clear and direct relationship between microscopic involvement of resection margins and survival that has been demonstrated in different case series and a meta-analysis¹⁻⁷ could be a reflection of the great variability in the case series rate of margin involvement, ranging between 16% and 85%.^{6,8} This variability leads to the consideration that there is a lack of standardized protocols for the histopathological analysis of resected specimens, making it likely that the true rate of R1 resections is being underestimated.

This study aims to identify the actual percentage of patients with R1 resections when analyzing surgical specimens with a standardized protocol, and also to evaluate the prognostic effect of microscopic margin involvement on survival.

Patients and Method

Selection of Patients

All patients were operated on consecutively at the Hepato-Biliary-Pancreatic Surgery Unit of the Hospital Clínico Universitario de Valencia [Valencia Clinical University Hospital] for a period of 14 years (January 1, 1999–December 31, 2012) and included prospectively in a database. Of the 213 pancreatic resections performed with curative intent, in 100 cases it was performed for ductal adenocarcinoma of the pancreas; these patients formed the study group. In late 2003, after we found a high rate of R0 resections in the pathological reports of patients operated until then, but the same low survival rate described in the literature, and in the context of a multidisciplinary team for the treatment of tumors in the hepatobiliopancreatic area, the procedure used until then for treating and preparing the specimens was updated, and a standardized protocol developed for resection specimens.⁹ After its development and implementation by the Department of Pathology, its application started in early 2004. Consequently, in our study, the patients included were divided into 2 groups: those operated before 2004, the “pre-protocol” group in which the specimens were analyzed without a standardized protocol, and those operated since 2004, the “post-protocol” group. The cohort observational flow chart of patients included in this study is shown in Fig. 1.

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