Surgery ■■ (2017) ■■–■■

Contents lists available at ScienceDirect

Surgery

journal homepage: www.elsevier.com/locate/ymsy

Original Communications

Surveillance of patients with intraductal papillary mucinous neoplasm with and without pancreatectomy with special reference to the incidence of concomitant pancreatic ductal adenocarcinoma

Kenjiro Date [a], Takao Ohtsuka [a,*], So Nakamura [a], Naoki Mochidome [b], Yasuhisa Mori [a], Yoshihiro Miyasaka [a], Yoshinao Oda [b], and Masafumi Nakamura [a,*]

[a] Department of Surgery and Oncology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
[b] Department of Anatomic Pathology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

ARTICLE INFO

Article history:
Accepted 12 September 2017

ABSTRACT

Background. The presence of an intraductal papillary mucinous neoplasm (IPMN) is important in the detection of concomitant pancreatic ductal adenocarcinoma (PDAC). The aim of this study was to elucidate the incidence and timing of development of concomitant PDAC in patients with and without pancreatectomy for IPMN.

Methods. We reviewed retrospectively the surveillance data for 22 patients who underwent pancreatectomy for PDAC concomitant with IPMN (PDAC-resection group), 180 who underwent pancreatectomy for IPMN (IPMN-resection group), and 263 whose IPMNs were left untreated (non-resection group). The incidence and timing of the development of a concomitant PDAC during the surveillance of patients with and without partial pancreatectomy for IPMN were investigated using the Kaplan–Meier method.

Results. During a median surveillance period of 40 months (range 6–262 months), 5 patients in the PDAC-resection group, 6 in the IPMN-resection group, and 8 in the non-resection group developed concomitant PDAC. The estimated 5-year (17%) and 10-year (56%) cumulative incidences of secondary PDAC in the PDAC-resection group were significantly greater than those in the other two groups ($p < 0.01$). Conversely, the difference in the estimated cumulative incidence of concomitant PDAC between the IPMN-resection and non-resection groups was not significant (5-year, 5.0% vs. 2.2%; 10-year, 5.0% vs. 8.7%; $p = 0.87$).

Conclusions. Long-term (≥5-year) surveillance in patients with IPMN is necessary and important because of the potential for development of concomitant PDAC. Those with a history of resection of concomitant PDAC at the time of the initial operation are at quite high risk for the development of secondary PDAC.

Introduction

Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal cancers, and operative resection is considered the only curative treatment, but only an estimated 20% of patients are candidates for resection at the time of initial diagnosis of PDAC.[1] Thus, establishment of an adequate diagnostic strategy with which to detect resectable PDAC is needed. Intraductal papillary mucinous neoplasm (IPMN) of the pancreas is a cystic precursor of pancreatic cancer. IPMNs have unique features, and multiple sites of occurrence in the same pancreas are often observed. In addition, several studies have revealed that patients with an IPMN often develop concomitant PDAC that is distinct from the IPMN both synchronously and/or metachronously. According to these reports, the incidence of development of a concomitant PDAC during surveillance of unresected IPMNs ranges from 2.0% to 8.0%.[2-6] Thus, patients

Conflicts of interest and source of funding: The authors declare no conflicts of interest. This study was supported by Grant-in-Aid for Scientific Research (B) (Grant Number 16H05417).

Authors' contributions: Date K and Nakamura S contributed to establishment of the study population database and performed the data extraction and analysis. Ohtsuka T, Mori Y, Miyasaka Y, and Nakamura M contributed to the study conception and design and performed the pancreatectomy and follow-up of the study population. Mochidome N and Oda Y made the pathological diagnoses. Date K wrote the manuscript. Ohtsuka T contributed to the interpretation of the results and manuscript revision. All authors discussed the results and commented on the manuscript. Nakamura M gave the final approval for this article.

* Corresponding authors. Takao Ohtsuka and Masafumi Nakamura, Department of Surgery and Oncology, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan.

E-mail address: takao-o@surg1.med.kyushu-u.ac.jp (T. Ohtsuka), mnaka@surg1.med.kyushu-u.ac.jp (M. Nakamura).

https://doi.org/10.1016/j.surg.2017.09.040
0039-6060/

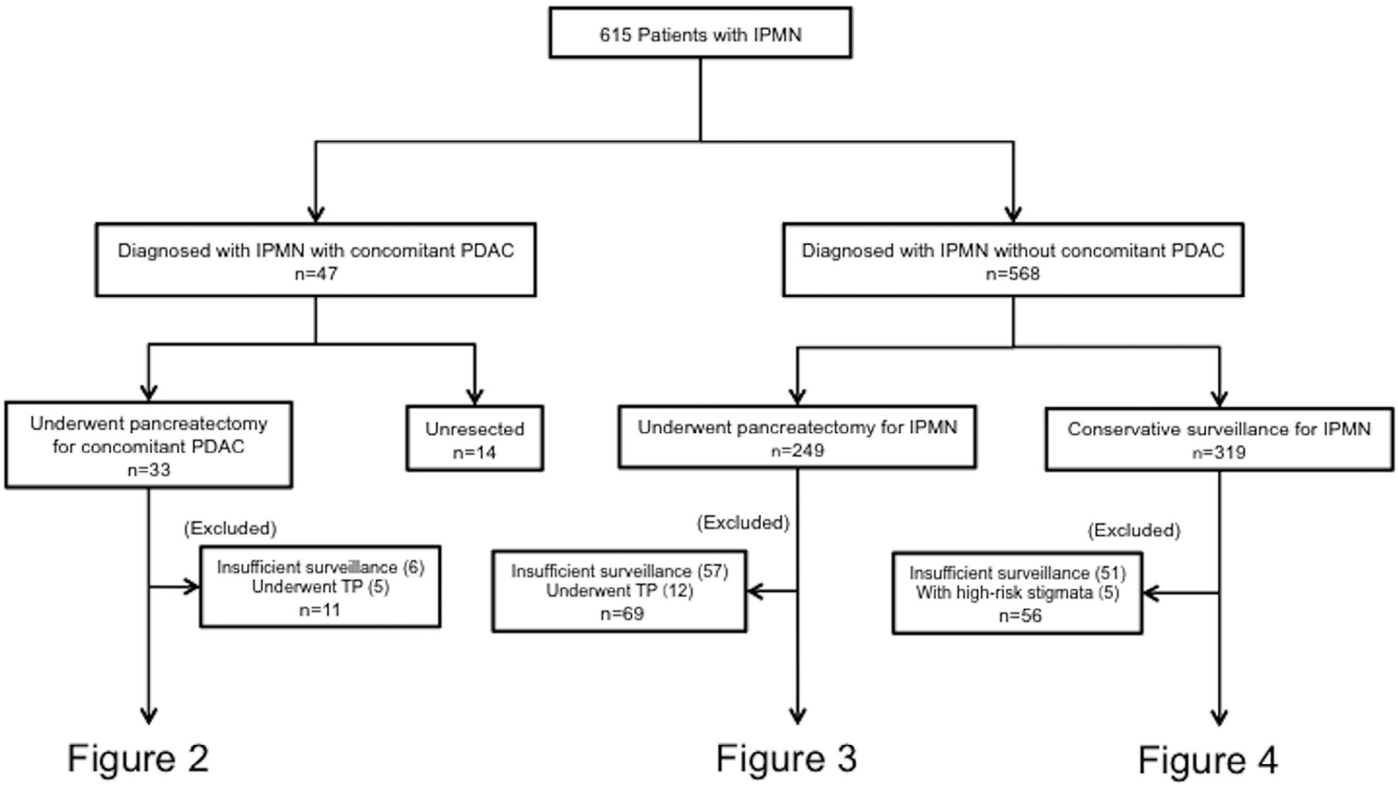

Fig. 1. Flow diagram of 615 patients with intraductal papillary mucinous neoplasm.
IPMN, intraductal papillary mucinous neoplasm; PDAC, pancreatic ductal adenocarcinoma; TP, total pancreatectomy.

with IPMNs should be recognized as having a high risk for the development of concomitant PDAC, and close attention should be paid to both progression of the IPMN and the possibility of development of concomitant PDAC during surveillance.

Several articles have reported that patients surveyed after partial pancreatectomy for IPMNs were also at risk for the development of secondary/recurrent IPMNs or metachronous/recurrent concomitant PDAC in the remnant pancreas.[7-9] These findings indicate that close attention should also be paid to the remnant pancreas for the possible development of concomitant PDAC. Few studies, however, have compared the risk of development of concomitant PDAC between the untreated pancreas and the remnant pancreas after partial pancreatectomy in patients with IPMN. Thus, the aim of this study was to elucidate the incidence and timing of the development of concomitant PDAC in these two IPMN groups.

Methods

Study population

This study was approved by the Ethics Committee of Kyushu University and conducted following the guidelines for research ethics of the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare of Japan (http://www.lifescience.mext.go.jp/bioethics/ekigaku.html). The medical records of 615 patients diagnosed with IPMN at the Department of Surgery and Oncology, Kyushu University Hospital from July 1987 to December 2015 were reviewed retrospectively. IPMNs were classified into main duct (MD)-IPMN and branch duct (BD)-IPMN based on the radiologic findings described in our previous reports.[7,10,11] The definition of IPMN was based on imaging findings described in the 2012 International Consensus Guidelines,[12] and the diagnosis was confirmed when the IPMN was resected. Analysis of yst fluid using endoscopic ultrasound-guided fine needle aspiration are not performed at our institution because of concern for peritoneal dissemination and gastric wall seeding in cases of malignancy.

The patients were divided into three groups (Fig 1): those who were surveyed after partial pancreatectomy for concomitant PDAC (PDAC-resection group), those who were surveyed after partial pancreatectomy for IPMN (IPMN-resection group), and those who were surveyed without pancreatectomy (non-resection group). In the PDAC-resection and IPMN-resection groups, patients with a postoperative surveillance period of <6 months and who had undergone a one-step total pancreatectomy were excluded. In the non-resection group, patients with a surveillance period of <6 months and high-risk stigmata as determined by the 2012 International Consensus Guidelines at the time of initial examination were also excluded.[12] In the PDAC-resection and IPMN-resection groups, patients with residual IPMN in the remnant pancreas at the first imaging study after the initial pancreatectomy were considered to have a residual IPMN. The data of patients who underwent partial pancreatectomy for IPMNs were used in our recent study to identify predictive factors for the development of high-risk lesions in the remnant pancreas.[8]

Histologic examination and adjuvant therapy

All resected specimens in the operative cases were classified according to the World Health Organization criteria of 2010[13] and divided into three pathologic grades according to the recommendations from the recent consensus meeting[14]: low-grade (LG), high-grade (HG), and IPMN with an associated invasive adenocarcinoma (INV). They were also classified into four histologic subtypes: gastric, intestinal, pancreatobiliary, and oncocytic. The pancreatic cut margins were examined intraoperatively in all patients who underwent partial

Please cite this article in press as: Kenjiro Date, Takao Ohtsuka, So Nakamura, Naoki Mochidome, Yasuhisa Mori, Yoshihiro Miyasaka, Yoshinao Oda, and Masafumi Nakamura, Surveillance of patients with intraductal papillary mucinous neoplasm with and without pancreatectomy with special reference to the incidence of concomitant pancreatic ductal adenocarcinoma, Surgery (2017), doi: 10.1016/j.surg.2017.09.040