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Invasive Intraductal Papillary Mucinous Carcinomas of the Pancreas:

Predictors of Survival and the Role of Lymph Node Ratio

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Abstract

Introduction—Intraductal papillary mucinous neoplasms (IPMNs) are being increasingly recognized, and often harbor cancer. Lymph node metastases are an important prognostic factor for patients with invasive intraductal papillary carcinoma (I-IPMC), but the role of lymph node ratio (LNR) in predicting survival after surgery for I-IPMC is unknown.

Methods—The combined databases from the Surgical Department of Massachusetts General Hospital of Boston and the University of Verona were queried. We retrospectively reviewed clinical and pathologic data of all patients with resected, pathologically confirmed, I-IPMC between 1990 and 2007. Univariate and multivariate analysis were performed.

Results—I-IPMCs were diagnosed in 104 patients (55 males and 49 females), median age was 69 years. Recurrent disease was identified in 49 patients (47.1%) and the median 5-year disease specific survival (DSS) was 60.1%. The median number of resected/evaluated nodes was 15 (range, 5–60). There were 60 (57.7%) patients who had negative lymph nodes (N0), whereas 44 (42.3%) had lymph node metastases (N1). Patients with lymph node metastases had a shorter 5-year DSS (28.9%) compared with patients with negative lymph nodes (80.3%; $P < 0.05$). As the LNR increased, 5-year DSS decreased (LNR = 0, 86.5%; LNR > 0 to 0.2, 34.4%; LNR > 0.2, 11.1%; $P < 0.05$). On multivariate analysis, LNR, the presence of a family history of pancreatic cancer and a preoperative value of Ca 19.9 > 37 U/L were significant predictors of survival ($P < 0.05$).

Conclusions—Lymph node ratio is a strong predictor of survival after resection for invasive intraductal papillary mucinous carcinoma.

Intraductal papillary mucinous neoplasms (IPMNs) were defined by the World Health Organization (WHO) in 2000 as intraductal mucin-producing neoplasms that can involve the main pancreatic duct but may also affect the side branches or a combination of the two.¹

Currently, IPMNs are the most common of the cystic neoplasms of the pancreas² and an increasingly well-recognized clinical and pathologic entity accounting for 8% to 20% of all resected pancreatic neoplasms.³

According to the International Consensus Guidelines,⁴ surgical resection for branch duct IPMN (BD-IPMNs) is advocated in selected patients, whereas it is recommended for main duct papillary mucinous neoplasms (MD-IPMNs) because of the high risk of malignancy.

Long-term survival for completely resected IPMN is markedly better than that of ductal adenocarcinoma,^{5,6} although a recent report from the Mayo Clinic group showed invasive IPMN behaves as aggressively as ductal carcinoma.⁷ The presence of invasive carcinoma is known to be a strong adverse predictor of survival.^{8–16} After resection of invasive intraductal papillary mucinous carcinoma (I-IPMC), recurrence occurs in 40% to 65% of patients and lymph node involvement, vascular invasion, surgical margin involvement, and the presence of jaundice are poor prognostic factors.^{17,18}

Several studies have demonstrated that rather than simple lymph node status, the total number of lymph nodes resected/evaluated and the ratio between metastatic and examined lymph nodes (LNR) are better predictors of survival in patients with gastrointestinal malignancies, including pancreatic and ampullary carcinoma.^{19–21} LNR, however, has not been examined in carcinoma arising in IPMNs.

The aim of our study was to identify clinical and pathologic prognostic features in a large cohort of invasive IPMN and in particular to evaluate the role of LNR.

PATIENTS AND METHODS

The prospective databases of the Surgical Departments of Massachusetts General Hospital (MGH) of Boston and University of Verona (UV) were analyzed to identify patients with IPMN with invasive carcinoma (I-IPMC) who underwent surgical resection between January 1990 and December 2006. Demographic data (including the presence of first and/or second-degree relatives with a history of pancreatic cancer), presenting symptoms, operative and pathologic data were analyzed.

The neoplasms in the head, neck or uncinate process of the pancreas were treated with pancreaticoduodenectomy; neoplasms localized in the pancreatic body or tail were treated with distal pancreatectomy with splenectomy or with middle pancreatectomy as appropriate; a total pancreatectomy was performed for tumors involving the entire gland. The extension of the lymphadenectomy was determined by the operating surgeon. All the resections were performed with an open approach.

Perioperative mortality, defined as in-hospital or 30-day death, as well as postoperative complications were recorded; the pancreatic fistula definition was retrospectively assessed according to the International Study Group on Pancreatic Fistula (ISGPF) recommendations.²² Routine postoperative chemotherapy and/or radiation therapy was not part of the treatment strategy.

The neoplasms were classified into noninvasive IPMNs (adenoma, borderline, and in situ intraductal papillary mucinous carcinoma) and I-IPMC on the basis of the WHO classification.¹ For the purpose of this study only patients with a pathologically confirmed I-IPMC were included. Part of this series was previously published.^{14,16}

Main duct I-IPMCs (MD-I-IPMCs) were defined as I-IPMCs grossly or microscopically involving the main pancreatic duct, whereas branch duct I-IPMCs (BD-I-IPMCs) were

defined as I-IPMCs that did not grossly or microscopically involve the main pancreatic duct. I-IPMCs that involved both the main and the branch ducts (mixed type) were classified as MD-I-IPMCs.

The following pathologic factors were reviewed to identify prognostic factors: size of tumor (considering the entire neoplasm), perineural invasion, microvascular invasion, resection margin status, and lymph node metastasis.

Lymph node ratio (LNR) was calculated by dividing the total number of lymph nodes harboring metastases by the total number of examined nodes.

Patients were followed up at regular intervals after discharge either by clinical examination or by contacting their General Practitioner. Recurrence was defined as presence of recurrent I-IPMC in the pancreatic remnant or as local or distant metastatic disease by radiologic imaging techniques, and was confirmed histologically when possible.

Statistical Analysis

Distribution of continuous variables are reported as median and interquartile range (IQR) (25th; 75th percentiles). Categorical variables are presented as numbers and percentages.

The comparison between subgroups, identified by status at end of follow-up (alive or disease related deaths) or by node status, was carried out using Student *t* test, or Mann-Whitney *U* test, for continuous variables. Qualitative data were compared by the χ^2 test or Fisher exact test when necessary. Radiologic and histologic size of neoplasms was compared using Wilcoxon signed rank test.

Survival was defined as the time from diagnosis to disease-related-death and was censored at the last follow-up date if no events had occurred. Follow-up was updated on May 2009, giving a potential minimum follow-up of 28 months to each survivor. Survival probability was estimated according to the Kaplan-Meier method, whereas the log-rank test was used for comparison of survival in different subgroups. Univariate and Multivariate analysis was performed by the Cox regression model to evaluate significant mortality predictors and their relative role.

P values were considered significant when less or equal than 0.05.

RESULTS

Demographic and Clinical Data

Between January 1990 and December 2006, 363 patients with an IPMN were operated. Of those, 104 (28.7%) pancreatic resections were performed for patients with a histologically confirmed I-IPMC; there were 55 males (52.9%) and 49 females (47.1%) with a median age of 69 years (IQR: 61; 74 years); 53 (51%) patients were from MGH and 51 (49%) were from UV.

In all, 10 patients (9.6%) had a familial history of pancreatic cancer and 25 (24%) had a previous malignant or benign extrapancreatic tumor; 90 (78.5%) patients had symptoms whereas in 14 (13.5%) the diagnosis was incidental.

The most common presenting symptoms were weight loss in 55 patients (52.9%), followed by abdominal pain in 53 (51%), jaundice in 34 (32.7%), and steatorrhea in 13 (12.5%).

The demographic characteristics and presenting symptoms are summarized in Table 1. The median value of Ca 19.9 was 31.5 U/mL (IQR: 12.7; 111.3 U/mL). Preoperative radiologic

assessment revealed a main pancreatic duct dilatation in 23 (22.1%) patients, a cystic lesion in 36 (34.6%), and a solid one in 45 (43.3%). In this latter 2 groups, the median radiologic diameter of the lesion was 40 mm (IQR: 25; 60 mm).

Intraoperative Course

Sixty-nine patients (66.3%) underwent pancreaticoduodenectomy (PD), while a distal pancreatectomy (DP) was performed in 14 patients, a total pancreatectomy (TP) in 19 cases (18.3%) and a middle pancreatectomy (MP) in 2 (1.9%).

Postoperative mortality was nil, whereas the overall complication rate was 44.2%; the most common abdominal complication was pancreatic fistula that occurred in 16 patients (18.9%) who underwent partial pancreatectomy. Nine patients (8.7%) required a reoperation; in 2 cases the reoperation was for intra-abdominal abscess and the remaining 7 patients were reexplored because of hemorrhage. The postoperative length of stay was 11.5 days (IQR: 7; 18.8 days).

Pathology

Eighty-eight I-IPMCs (84.6%) were main-duct type while 16 (15.4%) were branch duct type. The final pathologic analysis revealed a median tumor size of 35 mm (IQR: 26; 60 mm) which was similar to radiologic median tumor size ($P = 0.33$); the surgical margin for adenoma/borderline was positive in 13 patients (12.5%); a positive margin for denudation in the pancreatic cut was observed in 12 patients (11.5%). No patients had a positive margin for carcinoma. Microvascular and perineural invasion were found in 25 (24%) and 42 (40.4%) patients, respectively. Histologic findings are summarized in Table 2.

The median number of nodes evaluated was 15 (IQR: 9, 23); the median number of nodes evaluated at UV was 18 (IQR: 12, 29) while was 12 (IQR: 6, 19) at MGH ($P < 0.001$). Between 1990 and 1998, the median number of resected/harvested lymph nodes was 10 (IQR: 7.5; 16); between 1999 and 2000, it was 12 (IQR: 8.5, 19), between 2001 and 2004 19.5 (IQR: 11.7; 37) and after 2005 it was 21 (IQR: 13.3, 28.8) ($P < 0.001$). Of the 104 patients, 60 (57.7%) had negative nodes (N0) while 44 (42.3%) had lymph node metastases.

On the final pathologic analysis, in I-IPMCs without lymph node involvement, the median number of nodes evaluated was 12 (IQR: 8, 21) and it was 17 (IQR: 11, 24.5) for I-IPMCs with lymph node metastases ($P = 0.001$). Of the 44 patients with lymph node involvement, 26 (59.1%) had a ratio less than 0.2 and 18 (40.9%) had a LNR > 0.2 .

Follow-up and Survival

At a median follow up of 44 months (IQR: 17.7, 96.9), 41 patients (39.4%) remained alive, 44 (42.3%) died with recurrence and 19 (18.3%) died of other causes. The 5-year overall survival was 54.5% (Fig. 1A) with a median survival of 65.8 months and the 5-year disease specific survival 60.1% with a median survival of 109.5 months (Fig. 1B). Thirty-nine (37.5%) patients underwent postoperative chemo and/or radiation, 25 (64.1%) of them at MGH and 14 (35.9%) at UV ($P = 0.04$). Patients who received adjuvant therapy had more advanced tumors and their 5-year survival was 39.4% compared with 74.5% of those patients who were not treated with chemo and/or radiation ($P = 0.001$).

During follow up, 49 patients (47.1%) developed tumor recurrence. This was local (pancreatic remnant) in 10 patients (20.4%). In the remaining it was primarily liver ($n = 30$), lung ($n = 4$), peritoneum ($n = 3$), lymph nodes ($n = 3$) and brain ($n = 1$); 3 (6.1%) patients had multiple metastases in 2 or more distant sites. The 5-year disease specific survival for patients without lymph node involvement was 80.3% compared with 28.9% for N1 patients.

Of the 49 patients who experienced tumor recurrence, 43 (87.8%) died of the disease whereas the remaining 6 (12.2%) were still alive at the time of last follow-up. Of the 60 patients with LNR = 0, 12 (20%) died of disease, whereas 16 (61.5%) and 16 (88.9%) of patients with a $0 < \text{LNR} \leq 0.2$ and $\text{LNR} > 0.2$, respectively, died of recurrence.

By univariate analysis (Table 3), factors associated with worse survival included: the presence of a family history of pancreatic cancer (hazard ratio [HR] = 4.58; 95% confidence interval [95% CI]: 1.91–10.99), presence of jaundice (HR: 2.37; 95% CI: 1.30 – 4.23), a preoperative value of Ca 19.9 > 37 U/mL (HR = 3.02; 95% CI: 1.62–5.63), lymph node involvement (HR = 4.62; 95% CI: 2.48 – 8.61), microvascular invasion (HR = 2.62; 95% CI: 1.54 – 4.47), perineural invasion (HR = 3.25; 95% CI: 1.77–5.97), positive margin for denudation (HR = 2.37; 95% CI: 1.30 – 4.31), $0 < \text{LNR} \leq 0.2$ (HR = 5.05; 95% CI: 2.38–10.73) and $\text{LNR} > 0.2$ (HR: 11.57; 95% CI: 5.31–25.31). Univariate analysis failed to demonstrate any significant difference in terms of survival between MD-I-IPMC and BD-I-IPMC.

No statistical significant difference in terms of survival was observed between patients with more than 15 nodes evaluated and patients with less than 15 nodes (HR 0.90; 95% CI: 0.49 – 1.85). Multivariate analysis (Table 4) confirmed that a family history of pancreatic cancer, a value of Ca 19.9 > 37 U/mL and LNR were significant and independent indicators of poor prognosis after pancreatic resection for I-IPMC. Specifically, the 5-year disease specific survival rate for patients with a family history of pancreatic cancer was 16.7% (Fig. 2A), whereas in patients without this history it was 62.9% ($P = 0.02$). The 5-year survival rate for patients with a preoperative value of Ca 19.9 ≤ 37 U/mL was 72.5% compared with 44.2% of those patients with Ca 19.9 > 37 U/L ($P = 0.02$) (Fig. 2B). The 5-year disease specific survival rates for patients with LNR = 0, LNR > 0 and ≤ 0.2 and for those who had a LNR > 0.2 were 86.5%, 34.4%, and 11.1%, respectively (Fig. 3).

The clinical and histologic variables of patients with and without lymph node metastases are summarized in Table 5.

DISCUSSION

Although IPMNs of the pancreas are an increasingly well-recognized entity, long-term outcomes of surgical resection of I-IPMC have not been fully clarified.

We have previously shown that malignancy, either in situ or invasive carcinoma, is present in 60% of main duct and combined IPMNs,¹⁶ and 22% of branch duct tumors,¹⁴ and that I-IPMCs have a poorer prognosis compared with noninvasive tumors. This data is consistent with that of several other studies.^{8–11}

In the present study, we analyze the outcomes and survival of patients with invasive IPMN. The cohort of 104 patients represents one of the largest experiences with this entity. The demographic and clinical characteristics of our patients were comparable to those found in most series.^{9,10,12,16,17} In the current study, the 5-year overall survival rate of resected invasive adenocarcinoma arising with IPMN was 54.5%, which was worse than that of noninvasive IPMNs, but is higher than the usual 5-year survival rates described for resected ductal pancreatic adenocarcinoma. Our results are consistent with those reported by Maire et al⁵ who found a 5-year overall survival of 48% analyzing a large cohort of 73 malignant IPMNs, but different than those of Sohn et al¹⁰ and Schnelldorfer et al,⁷ who reported 5-year overall survivals of 43% and 31%, respectively. A possible reason for these differences may be due to different pathologic interpretation, with inclusion of some cases of mucinous adenocarcinoma in the survival analysis.

On univariate analysis, microvascular invasion, perineural invasion and the presence of denudation at the pancreatic margin were associated with a worse prognosis, corroborating similar findings from other experiences.^{11,17,18} In particular, in 12 patients the presence of denudation of the pancreatic cut margin at final pathologic examination was associated with a HR of 2.37 and 5 of 12 had a recurrence in the pancreatic stump, 4 in the liver and only 3 are free of disease (data not shown). We believe that the detection of denudation in the frozen sections has to be considered as “positive margin” and should lead the surgeon to extend the resection. Another predictor of survival was the preoperative value of Ca 19.9. Patients with a value of Ca 19.9 more than 37 U/mL had a 5-year survival rate of 44.2%, compared with 72.5% in patients with a normal Ca 19.9. The powerful of Ca 19.9 as an adverse prognostic factor was confirmed on multivariate analysis adjusted by jaundice, which was also found to be a significant predictor on univariate analysis. Similar findings regarding Ca 19.9 and jaundice were found by Maire et al and Schnellendorfer et al.^{5,7}

We also found the presence of a family history of pancreatic cancer was a strong predictor of survival in patients with I-IPMC, both on univariate and multivariate analysis. Patients who had a family history of pancreatic cancer had a nearly 4-fold worse 5-year survival (16.7% vs. 62.9%) than those without this history. To our knowledge, this is the first study that investigated and demonstrated the influence of a family history of pancreatic cancer on the survival of patients affected by malignant IPMN.

The 5-year survival of patients with positive lymph nodes was 28.9%, compared with 80.3% in N0 patients. These results are consistent with several other studies. Nakagohri et al²³ reported that lymph node metastases are an independent prognostic factor after pancreatic resection for IPMN, and D’Angelica et al⁸ reported 5-year survival of 30% in patients with lymph node positivity, compared with 83% in patients without lymph node metastases. In a previous experience from UV, Falconi et al¹¹ described that for patients with IPMN, the survival rate is very poor when the disease has reached the stage of lymph node involvement, and that this biases the surgeon towards extended lymphadenectomy.

In our study, we found that LNR is the strongest prognostic indicator, with a LNR > 0.2 being associated with a 5-year survival of only 11.1%. Many recent studies in gastrointestinal malignancies, have established that rather than simple lymph node status, the number of lymph nodes evaluated and the ratio of metastatic to examined lymph nodes may be more powerful predictors of survival.^{24–29} In pancreatic cancer, both Pawlik et al¹⁹ and Slidell et al²⁰ have found that LNR is more accurate to stratify patients after pancreatic resection. A recent experience published by one of our institutions²¹ concluded that lymph node ratio is a powerful prognostic factor to predict survival after resection for carcinoma of the ampulla of Vater.

Undoubtedly, a variation in the number of lymph nodes resected can be present from institution to institution. In our study, we recorded a significant different number of nodes evaluated/resected between the MGH and the University of Verona (12 vs. 18), and also found a significant difference in the number of lymph nodes harvested/resected during 4 different periods. It is unclear if the latter is related to a more extensive lymphadenectomy or to more attention to the lymph node involvement by the pathologist.

Intuitively, LNR is advantageous for stratifying I-IPMC because it provides a more relevant point of comparison for a heterogeneous grade of patients with lymph node involvement. LNR has been showed to reduce the stage migration effect in ductal carcinoma.^{19–20} In the current study, no differences in terms of survival were observed between patients with less than 15 lymph nodes evaluated compared with patients with more than 15 lymph nodes examined. Remarkably, N1 patients had a higher median number of lymph nodes harvested,

thereby demonstrating a slight stage migration effect that, however, had no influence on prognosis. One could speculate that this small influence may be due to the higher incidence of N0 tumors as compared with ductal carcinoma.

The potential impact of the findings of this study on the care of patients with IPMN are unclear. Until imaging methods that can accurately identify metastatic lymph nodes are found, LNR will remain a postoperative predictor. Perhaps these patients should be offered adjuvant treatment in the hopes of improving outcomes. The potential benefit of a more extensive lymphadenectomy (be it for treatment or prognosis) remains speculative and cannot be addressed by this study. On the other hand, a family history of pancreatic cancer and Ca 19.9 value >37 U/mL are predictors that can be identified preoperatively. One could argue that a prophylactic total pancreatectomy could improve the survival of patients with one or both these factors, nevertheless in our cohort, all the patients with a familial history of pancreatic cancer and the 83% of patients with a Ca 19.9 > 37 U/mL, had recurrent disease in the form of distant metastases (data not shown).

The presence of a family history of pancreatic cancer could potentially play a role in the decision making of branch duct IPMNs management. A greater proportion of BD variants are noninvasive¹⁴ and surgery is recommended only in selected patients.⁴ Perhaps patients with BD-IPMN and a family history of pancreatic cancer should be offered surgery regardless of the absence of other signs of malignancy (ie, size, nodules, symptoms). The number of invasive BD-IPMN in this study, however, is too small to conclude this.

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FIGURE 1.

A, Overall survival after resection for I-IPMC (Kaplan-Meier). B, Disease specific survival after resection for I-IPMC (Kaplan-Meier).

FIGURE 2.

A, Survival curves after resection for I-IPMC in relation to the presence (n = 10) or not (n = 94) of family history of pancreatic cancer ($P = 0.02$) (Kaplan-Meier). B, Survival curves after resection for I-IPMC comparing patients with a preoperative value of $\text{Ca } 19.9 \leq 37 \text{ U/mL}$ and $\text{Ca } 19.9 > 37 \text{ U/mL}$ ($P = 0.02$). (Kaplan-Meier).

FIGURE 3.

Survival curves after resection for I-IPMC comparing patients with a LNR = 0 (n = 60), $0 < \text{LNR} \leq 0.2$ (n = 26) and $\text{LNR} > 0.2$ (n = 18) ($P < 0.0001$) (Kaplan-Meier).

TABLE 1

Demographic and Presenting Symptoms of Patients Undergoing Resection for I-IPMC

Variable	
Age (yr), median (IQR)	69.1 (60.7; 74.5)
Gender	
Male	55 (52.9%)
Female	49 (47.1%)
Family history of pancreatic cancer	10 (9.6%)
Weight loss	55 (52.9%)
Pain	53 (51%)
Jaundice	34 (32.7%)
Pancreatitis	3 (2.9%)
CA 19.9 (U/mL), median (IQR)	31.5 (12.8; 111.3)

TABLE 2

Histological Findings of the 104 Patients After Curative Resection for I-IPMC

Variable	
Type	
Main duct	88 (84.6%)
Branch duct	16 (15.4%)
Tumor size (mm), median (IQR)	35 (20; 50)
Pancreatic margin	
Adenoma/borderline	13 (12.5%)
Denudation	12 (11.5%)
Microvascular invasion	25 (24%)
Perineural invasion	42 (40.4%)
Nodes evaluated, median (IQR)	15 (9; 23)
Lymph node involvement (N1)	44 (42.3%)
Lymph node ratio (LNR)	
LNR = 0	60 (57.7%)
$0 < \text{LNR} \leq 0.2$	26 (25%)
LNR >0.2	18 (17.3%)

TABLE 3

Univariate Analysis of Prognostic Factors for Patients Following Resection for I-IPMC

Variable	HR	CI	95%	P
Age				
≤60 yr	1			
>60 yr	0.91	0.52	1.60	0.91
Gender				
Female	1			
Male	1.00	0.56	1.83	0.98
Family history of pancreatic cancer	4.58	1.91	10.99	0.002
History of diabetes	0.63	0.43	1.67	0.63
History of chronic pancreatitis	0.65	0.16	2.67	0.55
History of previous non pancreatic neoplasm	1.64	0.87	3.09	0.13
Jaundice	2.37	1.30	4.23	0.01
Ca 19.9 > 37 U/mL vs. Ca 19.9 ≤ 37 U/mL	3.27	1.78	6.03	0.001
Site of tumor				
Proximal	1			
Distal	0.62	0.28	1.38	0.25
Diffuse	1.35	0.61	3.01	0.46
Postoperative complications	0.96	0.59	1.58	
MD-I-IPMC vs. BD-I-IPMC	1.47	0.70	3.09	0.31
Histological tumor size (increasing of 1 cm)	0.99	0.98	1.01	0.40
Pancreatic margin				
Adenoma or borderline	1			
Denudation	2.37	1.30	4.31	0.01
Microvascular infiltration	2.62	1.54	4.47	0.001
Perineural infiltration	3.25	1.77	5.97	0.001
Nodal status	4.62	2.48	8.61	<0.0001
Nodes evaluated >15	0.90	0.49	1.63	0.72
LNR				
LNR = 0	1			
0 < LNR ≤ 0.2	5.05	2.38	10.73	<0.0001
LNR >0.2	11.57	5.31	25.31	<0.0001

TABLE 4

Multivariate Analysis of Prognostic Factors for Patients Following Resection for I-IPMC

Variable	HR	CI	95%	P
Family history of pancreatic cancer	3.11	1.34	8.54	0.02
Ca 19.9 > 37 U/mL	2.31	1.15	3.28	0.02
LNR				
0 < LNR ≤ 0.2	3.30	1.45	7.48	0.01
LNR > 0.2	6.15	2.44	15.46	<0.0001

TABLE 5

Comparison Between Patients With (N1) and Without (N0) Lymph Nodes Metastases

Variable	N1 Patients	N0 Patients	P
Men (n)	36 (57.1%)	27 (42.9%)	0.28
Age (median)	68 yr	69 yr	0.87
Preoperative Ca 19.9 (median)	75 U/mL	21 U/mL	0.002
Weight loss (n)	25 (61%)	30 (47.6%)	0.18
Pain (n)	22 (53.7%)	31 (49.2%)	0.66
Jaundice (n)	22 (53.7%)	12 (19%)	<0.0001
Pancreatitis (n)	0	3 (4.8%)	0.28
Nodes harvested (median)	17	12	0.03
MD-I-IPMC	38 (92.7%)	50 (79.4%)	0.07
Microvascular invasion	20 (48.8%)	5 (8.1%)	<0.0001
Perineural invasion	27 (65.9%)	15 (23.8%)	<0.0001