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Patterns of Pancreatic Resection Differ Between Patients with Familial and Sporadic Pancreatic Cancer

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Abstract

Background—Although the increased risk of developing pancreatic cancer (PC) in families with a strong history of the disease is well known, characteristics and outcomes of patients with familial PC is not described well.

Aims—This study aims to evaluate outcomes following resection in patients with familial PC.

Methods—We studied 208 patients who underwent resection of PC from 2000 to 2007 and had prospectively completed family history questionnaires for the Biospecimen Resource for Pancreas

Research at our institution. We compared clinical characteristics and outcomes of familial and sporadic PC patients.

Results—Familial ($N=15$) and sporadic PC patients ($N=193$) did not have significantly different demographics, pre-operative CA19-9, pre-operative weight loss, R0 status, or T-staging (all $p > 0.05$). Familial PC patients had lower pre-operative total serum bilirubin concentrations ($p=0.03$) and lesions outside of the pancreatic head more frequently ($p=0.02$) than sporadic PC patients. There was no difference in survival at 2 years between familial and sporadic PC patients ($p=0.52$).

Conclusions—Familial PC patients appear to develop tumors outside of the pancreatic head more frequently than sporadic PC patients. This difference in tumor distribution may be due to a broader area of cancer susceptibility within the pancreas for familial PC patients.

Keywords

Pancreatic cancer; Familial cancer syndrome; Familial pancreatic cancer

Background

The increased risk of developing pancreatic cancer (PC) in families with a strong history of the disease has been described increasingly since the late 1960s and early 1970s.^{1–5} Since those initial reports, various studies have shown that 4–16% of patients who develop PC have a family history of PC.^{6–8} These figures include patients with a variety of familial cancer syndromes such as hereditary non-polyposis colorectal cancer syndrome (Lynch II variant),⁹ Peutz–Jegher syndrome (PJS),¹⁰ hereditary breast–ovarian cancer syndrome (BRCA2),¹¹ familial atypical multiple mole melanoma syndrome,¹² and hereditary pancreatitis.¹³ Despite the association between these cancer syndromes and PC, most patients with familial PC do not have an identifiable syndrome or known genetic change.¹⁴

Some patients with familial PC have features that could, in theory, affect outcomes. Specifically, familial PC patients with mutations in the Fanconi anemia/BRCA2 pathway are hypersensitive to a variety of chemotherapy agents,¹⁵ patients with PJS may be predisposed to developing PC via intraductal papillary mucinous neoplasia (IPMN) and not pancreatic intraepithelial neoplasia (PanIN),¹⁶ and patients with hereditary nonpolyposis colorectal cancer (HNPCC) have been shown to develop the medullary variant of pancreatic adenocarcinoma^{17,18} which appears to be less lethal than typical PC.¹⁹ Additionally, pancreatic specimens resected in familial PC patients can have multifocal precursor lesions producing a unique pattern of parenchymal atrophy and fibrosis which is not typically seen in sporadic PC.¹⁴ Despite all of these unique associations, differences in clinical features and outcomes between familial PC and sporadic PC patients who undergo pancreatic resection is not described well.

Hypothesis/Study Aim

We hypothesized that familial PC patients and sporadic PC who undergo resection have different clinical features and survival. Our aim was to compare clinical features, pathology, and survival in familial PC patients to sporadic PC patients following pancreatic resection.

Methods

The Biospecimen Resource for Pancreas Research at our institution, supported by the Specialized Program of Research Excellence (SPORE) in Pancreatic Cancer (NCI P50CA102701), prospectively registered 326 patients who underwent resection of various pancreatic lesions from October 2000 to June 2007. Both the SPORE in pancreatic cancer and this study obtained full institutional review board approval at our institution prior to

initiating the investigation. A final study sample was comprised of 234 patients who underwent resection of pancreatic ductal adenocarcinoma and had completed family history questionnaires in conjunction with registration into the Biospecimen Resource for Pancreas Research. Of these 234 patients, 208 had typical ductal adenocarcinoma and 26 had IPMN-invasive carcinoma. The group of 208 patients with typical ductal adenocarcinoma was the primary focus of this study (Fig. 1). We compared demographics, pre-operative clinical variables, surgical variables, staging, and outcomes of patients with familial PC (patients with one or more first-degree relative with PC) to patients with sporadic PC (patients who did not meet familial PC criteria).

The clinical features of interest included age at resection (years), sex (male, female), body mass index (BMI; per admitting records), the symptoms of jaundice (per initial history), weight loss (per initial history), the use of adjuvant therapy (per oncology records), pre-operative serum total bilirubin concentration (mg/dL; within 30 days prior to operation), pre-operative serum CA 19-9 levels (U/L; within 30 days prior to operation), and lesion location per pre-operative imaging (head or uncinate, body and/or tail, head and body, or other by magnetic resonance imaging or computed tomography). The surgical features of interest included type of resection (pancreatoduodenectomy, distal pancreatectomy, or total pancreatectomy per operative reports), and resection margins (R0 versus R1 or R2 per operative and pathology reports). The pathologic features of interest obtained from the surgical pathologic report included tumor size (mm), tumor grade (1–4), tumor stage (T1, T2, T3, T4), lymph node stage (N0, N1).

Surgical margins were assessed initially by intra-operative frozen section analysis and then by routine permanent section. This approach allowed re-resection to achieve negative margins during the initial operation. Patients with resected PC were staged according to guidelines in the *American Joint Committee on Cancer—Cancer Staging Manual*, 6th edition. The surgical margins evaluated for pancreatoduodenectomy and total pancreatectomy specimens included the proximal common hepatic duct, pancreatic neck, margin at the uncinate process or the superior mesenteric artery, posterior, inferior, and superior (soft tissue) pancreatic margin, portal vein groove, and proximal duodenal margin if the patient was undergoing a pylorus-preserving resection. Margins evaluated for distal pancreatectomy specimens included the site of pancreatic transaction and radial pancreatic soft tissue.

Clinical, pathologic, and surgical features were compared between familial and sporadic PC patients using Wilcoxon rank sum, chi-square, and Fisher's exact tests. Overall survival and recurrence-free survival were estimated using the Kaplan–Meier method and compared between patient groups using log-rank tests. Statistical analyses were performed using the SAS software package (SAS Institute; Cary, NC, USA). All tests were two-sided and p values <0.05 were considered statistically significant.

Results

Clinical Features

Within the group of 208 patients who had typical ductal adenocarcinoma not associated with IPMN, there were 15 patients with familial PC and 193 patients with sporadic PC. These patients did not differ significantly in age, gender, pre-operative BMI or weight loss, pre-operative serum CA 19-9 level, and use of adjuvant therapy (all $p > 0.05$; Table 1). Familial PC patients had significantly lower pre-operative serum total bilirubin concentration and jaundice ($p=0.03$ each).

A total of 13 of 15 familial PC patients had only one first-degree relative with PC; two of these 13 patients had a strong family history of breast cancer (BRCA 2 status unknown), one was a member of an HNPCC kindred, and another was part of the third successive generation with PC. Of the two patients with more than one first-degree relative with PC, one had a parent and a sibling with PC, and one patient had two siblings with PC. The only patient with a documented cancer syndrome or genetic change was the single patient who was part of a known HNPCC kindred as described above.

Pathology

Margin status, nodal status, tumor grade, and tumor diameter did not differ significantly between familial and sporadic PC patients ($p>0.3$; Table 1). Familial and sporadic PC patients had a marginally different T stage distributions ($p=0.05$); T2 lesions were present in 40% of familial PC patients compared to only 26% of sporadic PC patients. When comparing frequencies of lesions that were T3 or higher, however, there was no difference between familial and sporadic PC patients (60% and 72% respectively; $p=0.38$). Familial PC patients had lesions requiring pancreatoduodenectomy in 47%, distal pancreatectomy in 47%, and total pancreatectomy in 7% compared to 82%, 11%, and 2%, respectively, in sporadic PC patients ($p=0.007$). There were no differences in overall or recurrence-free survival between familial PC and sporadic PC patients (all $p>0.5$; Figs. 2 and 3).

Inclusion of IPM-invasive Carcinoma Patients

There were no patients who met criteria for familial PC in the group of 26 patients with IPMN-invasive carcinoma. Inclusion of these 26 patients with the 193 patients who had sporadic and typical ductal adenocarcinoma, revealed no new associations with any of the variables studied (Table 2). Pre-operative total serum bilirubin concentration, jaundice, resection type, and lesion location on imaging remained significantly different between familial PC patients and this larger group of patients with sporadic ($p=0.03$).

Comparison of Resection Type and Tumor Location

The type of resection performed was compared to tumor location within the pancreas as depicted on preoperative imaging studies for all 234 patients assessed in this study. Pancreatic head and uncinate tumors were resected by pancreatoduodenectomy (PD) in 96% of patients. Body and/or tail lesions were resected by distal pancreatectomy in 92%. The location of the lesion on imaging was significantly associated with resection type ($p<0.0001$).

Analysis of Patients who did not Complete Family History Questionnaires

Family history questionnaires were not completed by 73 (24%) patients who had been consented for participation into the Biospecimen Resource for Pancreas Research but, otherwise, would have met inclusion criteria for our study. Comparison of these 73 patients to the 234 patients who met final inclusion criteria revealed that patients who did not complete family history questionnaires had shorter overall survival ($p=0.003$) and a different distribution of resection types ($p=0.01$). Patients who completed family history questionnaires underwent PD in 80%, distal pancreatectomy in 18%, and total pancreatectomy in 3%; patients who did not complete family history questionnaires underwent PD in 85%, distal pancreatectomy in 7%, and total pancreatectomy in 8%. Lesion location on pre-operative imaging, however, was not different between patients with and without completed family history questionnaires ($p=0.09$). There was no significant difference between these groups for any of the remaining variables studied in Tables 1 and 2 ($p>0.06$).

Discussion

Our findings indicate that patients with familial PC required resections outside of the pancreatic head more frequently than sporadic PC patients. This difference correlates to a broader distribution of lesions within the pancreas on pre-operative imaging for patients with familial PC. Serum total bilirubin was significantly lower in familial PC patients likely reflecting the differences in lesion distribution. Serum CA 19-9 trended towards higher concentrations in familial PC patients, albeit not significantly ($p=0.05$), which may reflect a difference in tumor characteristics and not just lesion distribution. Interestingly, despite these differences, overall and recurrence-free survival was similar between familial PC and sporadic PC patients.

There has been a wide variety of inclusion criteria in studies assessing the impact a family history has on the risk of developing PC.²⁰ We chose to study patients with one or more first-degree relative with PC which is in keeping with what the National Familial Pancreas Tumor Registry (NFPTR) at The Johns Hopkins Hospital considers familial PC: a parent-offspring pair or pair of siblings with pancreatic cancer in the kindred.¹⁴ The risk of developing PC in first-degree relatives of patients with PC is about 6.5-fold greater than the background rate of 1:10,000 cases. When there are two relatives with PC, the risk of developing PC in first-degree relatives increases to 18-fold the background rate; with three affected relatives, the risk is increased to 57-fold.²¹ These figures highlight not only the markedly increased risk of developing PC in first-degree relatives of patients with PC but the rationale behind the NFPTR definition of familial PC.

As discussed previously, patients with PJS appear to develop PC via IPMN as opposed to PanIN.¹⁶ In order to isolate these two proposed pathways for PC development, we chose to analyze our cohort with and without IPMN patients. There were no familial PC patients in the IPMN group. Conversely, of the 15 patients with familial PC, there were no patients diagnosed with PJS. In fact, only one patient was diagnosed with an inherited cancer syndrome out of the 15 patients with familial PC; this reflects the finding that a majority of familial PC patients do not have a documented cancer syndrome or genetic change.¹⁴

Despite differences in lesions distribution, we were unable to show a difference in survival between familial PC and sporadic PC patients. Since October 2000, 69% of patients who were seen at our institution for pancreatic lesions were consented for inclusion in our institution's Biospecimen Resource for Pancreas Research. Additionally, familial PC patients represented 7% of the study sample. Although our percentage of familial PC mirrors rates found in other studies,^{6–8,20} both the overall recruitment rate (69%) and the percentage of familial PC patients in this study are potential limitations which may introduce selection bias and, by decreasing overall sample size, could affect our ability to detect a significant difference in survival and, perhaps, other variables studied. In order to detect a difference in survival of 50% versus 35% at 2 years between familial PC and sporadic PC patients (assuming 80% power and two-sided alpha of 0.05), we would need a sample size three times larger than in our current study. Given the use of prospectively collected family history questionnaires and our inclusion criteria, accruing a sample of this size would be difficult in a single institution.

The observed overall survival of familial PC patients may be affected by issues other than selection bias and sample size. It is plausible that familial PC patients seek medical care sooner than sporadic PC patients due to prior exposure and knowledge of the disease. Seeking earlier medical care could improve the overall survival of familial PC patients despite different tumor distribution.

Family history questionnaires were not completed by 73 (24%) patients who had been consented for participation into the Biospecimen Resource for Pancreas Research but, otherwise, would have met inclusion criteria for our study. In order to assess this possible selection bias, we compared these 73 patients to the 234 patients who met final inclusion criteria. Interestingly, these patient groups had different overall survival which limits the conclusions that can be inferred from our study particularly for survival. It is not clear why patients who did not complete family history questionnaires have lesser overall survival. It is plausible but unsubstantiated that the burden of their disease may have affected their ability to complete all of the questionnaires associated with participation in the Biospecimen Resource for Pancreas Research. More importantly, it is unclear if this selection bias may have affected our ability to detect a difference between familial and sporadic PC patients for survival and even other variables investigated. A study assessing risk factors and outcomes in familial PC patients registered at the NFPTR, however, found no difference in survival as well between familial PC and sporadic PC patients.²²

Although resection types performed were different between patients who did and did not complete family history questionnaires, lesion location on pre-operative imaging was similar. The difference found for resection types is driven largely by a slightly higher percentage of patients who underwent total pancreatectomy in the group of patients who did not complete family history questionnaires compared to those who did complete the family history questionnaires (8% vs. 3%). Interestingly, these groups had an equal absolute number of patients who underwent total pancreatectomy ($N=6$). Therefore, the difference in resection type between patients who did and did not complete family history questionnaires does not indicate that the differences found for lesion location between sporadic and familial PC patients is biased.

The role of family history in the occurrence of pancreatic cancer highlights the importance of further investigation of this role and the need for delineating screening programs for familial PC kindreds. Although a few patients in this study were recruited into multi-institutional studies investigating screening programs for patients with familial PC, the patients in our study were not part of any broad clinical screening program. Despite current screening programs under investigation at other institutions, there are no evidence-based standard of care recommendations for screening and interventions (other than genetic testing) in familial pancreatic cancer. Furthermore, there is no screening modality of choice since interpretation of findings, particularly with endoscopic ultrasound (EUS), is not clear. Therefore, EUS is not routinely offered at Mayo as a matter of course; however, it is made available to family members who request it.

In conclusion, familial PC patients who undergo resection appear to develop tumors outside of the pancreatic head more frequently than sporadic PC patients, as reflected by differences in the types of resections performed. As a result of these findings, we hypothesize that patients with familial PC may have a broader or at least different area of cancer *susceptibility* within the pancreas than patients with sporadic PC. These findings highlight the need for further pathological, genetic, and molecular studies of familial PC.

References

1. Reimer RR, Fraumeni JF Jr, Ozols RF, Bender R. Pancreatic cancer in father and son. *Lancet*. Apr 23; 1977 1(8017):911. [PubMed: 67325]
2. Friedman JM, Fialkow PJ. Familial carcinoma of the pancreas. *Clin Genet*. May; 1976 9(5):463–469. [PubMed: 1269168]
3. Appel MF. Hereditary pancreatitis. Review and presentation of an additional kindred. *Arch Surg*. Jan; 1974 108(1):63–65. [PubMed: 4808576]

4. MacDermott RP, Kramer P. Adenocarcinoma of the pancreas in four siblings. *Gastroenterology*. Jul; 1973 65(1):137–139. [PubMed: 4720820]
5. Lynch HT. Cancer families: Adenocarcinomas (endometrial and colon carcinomas) and multiple primary malignant neoplasms. *Recent Results Cancer Res*. 1967; 12:125–142.
6. Price TF, Payne RL, Oberleitner MG. Familial pancreatic cancer in south Louisiana. *Cancer Nurs*. Aug; 1996 19(4):275–282. [PubMed: 8768685]
7. Fernandez E, La Vecchia C, D'Avanzo B, Negri E, Franceschi S. Family history and the risk of liver, gallbladder, and pancreatic cancer. *Cancer Epidemiol Biomarkers Prev*. Apr-May;1994 3(3): 209–212. [PubMed: 8019368]
8. Ghadirian P, Boyle P, Simard A, Baillargeon J, Maisonneuve P, Perret C. Reported family aggregation of pancreatic cancer within a population-based case–control study in the Francophone community in Montreal, Canada. *Int J Pancreatol*. Nov-Dec;1991 10(3–4):183–196. [PubMed: 1787333]
9. Lynch HT, Voorhees GJ, Lanspa SJ, McGreevy PS, Lynch JF. Pancreatic carcinoma and hereditary nonpolyposis colorectal cancer: a family study. *Br J Cancer*. Aug; 1985 52(2):271–273. [PubMed: 4027169]
10. Giardiello FM, Brensinger JD, Tersmette AC, et al. Very high risk of cancer in familial Peutz–Jeghers syndrome. *Gastroenterology*. Dec; 2000 119(6):1447–1453. [PubMed: 11113065]
11. Goggins M, Schutte M, Lu J, et al. Germline BRCA2 gene mutations in patients with apparently sporadic pancreatic carcinomas. *Cancer Res*. Dec 1; 1996 56(23):5360–5364. [PubMed: 8968085]
12. Lynch HT, Fusaro RM, Lynch JF, Brand R. Pancreatic cancer and the FAMMM syndrome. *Fam Cancer*. 2008; 7(1):103–112. [PubMed: 17992582]
13. Lowenfels AB, Maisonneuve P, DiMagno EP, et al. Hereditary pancreatitis and the risk of pancreatic cancer. International Hereditary Pancreatitis Study Group. *J Natl Cancer Inst*. Mar 19; 1997 89(6):442–446. [PubMed: 9091646]
14. Shi C, Hruban RH, Klein AP. Familial pancreatic cancer. *Arch Pathol Lab Med*. Mar; 2009 133(3): 365–374. [PubMed: 19260742]
15. van der Heijden MS, Brody JR, Dezentje DA, et al. In vivo therapeutic responses contingent on Fanconi anemia/BRCA2 status of the tumor. *Clin Cancer Res*. Oct 15; 2005 11(20):7508–7515. [PubMed: 16243825]
16. Sato N, Rosty C, Jansen M, et al. STK11/LKB1 Peutz–Jeghers gene inactivation in intraductal papillary-mucinous neoplasms of the pancreas. *Am J Pathol*. Dec; 2001 159(6):2017–2022. [PubMed: 11733352]
17. Banville N, Geraghty R, Fox E, et al. Medullary carcinoma of the pancreas in a man with hereditary nonpolyposis colorectal cancer due to a mutation of the MSH2 mismatch repair gene. *Hum Pathol*. Nov; 2006 37(11):1498–1502. [PubMed: 16996571]
18. Wilentz RE, Goggins M, Redston M, et al. Genetic, immunohistochemical, and clinical features of medullary carcinoma of the pancreas: A newly described and characterized entity. *Am J Pathol*. May; 2000 156(5):1641–1651. [PubMed: 10793075]
19. Nakata B, Wang YQ, Yashiro M, et al. Prognostic value of microsatellite instability in resectable pancreatic cancer. *Clin Cancer Res*. Aug; 2002 8(8):2536–2540. [PubMed: 12171881]
20. Permuth-Wey J, Egan KM. Family history is a significant risk factor for pancreatic cancer: results from a systematic review and meta-analysis. *Fam Cancer*. Sep 2.2008
21. Tersmette AC, Petersen GM, Offerhaus GJ, et al. Increased risk of incident pancreatic cancer among first-degree relatives of patients with familial pancreatic cancer. *Clin Cancer Res*. Mar; 2001 7(3):738–744. [PubMed: 11297271]
22. Yeo TP, Hruban RH, Brody J, Brune K, Fitzgerald S, Yeo CJ. Assessment of “gene-environment” interaction in cases of familial and sporadic pancreatic cancer. *J Gastrointest Surg*. Aug; 2009 13(8):1487–1494. [PubMed: 19459017]

326
Patients prospectively
registered in Mayo Clinic
Biospecimen Resource for
Pancreas Research who
underwent pancreatic
resection from October 2000
to June 2007

Fig. 1.
Patient selection flowsheet

Fig. 2. Kaplan-Meier curve comparing overall survival following resection for familial PC patients compared sporadic PC patients

Fig. 3. Kaplan-Meier curve comparing recurrence-free survival following resection for familial PC patients compared to sporadic PC patients

Table 1

Clinical, surgical, and pathologic features between familial PC and sporadic PC patients with typical ductal adenocarcinoma only

	Sporadic PC (N=193)	Familial PC (N=15)	
Feature	Median (range)		P value
Age at resection (years)	64 (38–85)	69 (54–84)	0.11
BMI (N=206)	26.8 (16.5–41.3)	27.3 (22.8–35.0)	0.38
Bilirubin (mg/dL; N=183)	1.5 (0.2–32.4)	0.6 (0.3–12.4)	0.03
CA19-9 (U/L; N=158)	140 (0–335,300)	601 (17–2,860)	0.05
Tumor diameter (mm)	34 (6–95)	32 (20–55)	0.34
	N(%)		
Male sex	106 (55)	11 (73)	0.17
Jaundice (N=201)	114 (61)	4 (30)	0.03
Weight loss (N=203)	104 (55)	9 (64)	0.50
Lesion location on imaging (N=207)			
Head or uncinate	151 (79)	7 (47)	0.02
Body and/or tail	27 (14)	6 (40)	
Head and body	4 (2)	0	
No mass/NOS	10 (5)	2 (13)	
Type of resection			
Pancreatoduodenectomy	159 (82)	7 (47)	0.006
Distal pancreatectomy	29 (15)	7 (47)	
Total pancreatectomy	5 (3)	1 (7)	
Margins at Resection			
R0	156 (81)	11 (73)	0.59
R1	34 (18)	4 (27)	
R2	3 (2)	0	
Tumor grade (N=207)			
1	0	0	0.36
2	29 (15)	3 (20)	
3	132 (69)	8 (53)	
4	31 (16)	4 (27)	
Tumor stage			
T1	7 (4)	0	0.05
T2	48 (25)	6 (40)	
T3	158 (72)	8 (53)	
T4	0	1 (7)	
Nodal metastases (N=207)	112 (58)	7 (50)	0.56
Adjuvant treatment (N=217)	150 (84)	15 (87)	1.00

Table 2

Clinical, surgical, and pathologic features between familial PC and sporadic PC patients with typical ductal adenocarcinoma OR IPMN adenocarcinoma

	Sporadic PC (N=219)	Familial PC (N=15)	
Feature	Median (range)		P value
Age at resection (years)	66 (37–89)	71 (54–84)	0.15
BMI (N=231)	26.7 (16.5–44.5)	27.1 (22.8–35.0)	0.36
Bilirubin (mg/dL; N=205)	1.5 (0.2–32.4)	0.7 (0.3–12.4)	0.03
CA19-9 (U/L; N=175)	131 (0–335,300)	456 (17–2,860)	0.05
Tumor diameter (mm; N=232)	34 (6–95)	32 (20–55)	0.31
	N(%)		
Male sex	120 (55)	11 (73)	0.16
Jaundice (N=223)	126 (60)	4 (30)	0.04
Weight Loss (N=228)	114 (53)	9 (64)	0.41
Lesion location on imaging (N=233)			
Head or uncinate	172 (79)	7 (47)	0.02
Body and/or tail	31 (14)	6 (40)	
Head and body	4 (2)	0	
No mass/NOS	11 (5)	2 (13)	
Type of resection			
Pancreatoduodenectomy	182 (82)	7 (47)	0.007
Distal pancreatectomy	34 (16)	7 (47)	
Total pancreatectomy	5 (2)	1 (7)	
Margins at resection			
R0	179 (82)	11 (73)	0.43
R1	37 (17)	4 (27)	
R2	3 (1)	0	
Tumor grade (N=233)			
1	0	0	0.37
2	39 (18)	3 (20)	
3	147 (67)	8 (53)	
4	32 (15)	4 (27)	
Tumor stage			
T1	9 (4)	0	0.05
T2	56 (26)	6 (40)	
T3	154 (70)	8 (53)	
T4	0	1 (7)	
Nodal metastases (N=233)	124 (57)	7 (50)	0.63
Adjuvant treatment (N=217)	161 (80)	13 (87)	0.74