Limited resection of pancreatic cancer in high-risk patients can result in a second primary

Dear Editor,

We read with interest the paper by Canto and coworkers recently published in *Gut* that provided guidelines for the management of individuals with a high risk for pancreatic ductal adenocarcinoma (PDAC).[1] Although indications for surgery

Table 1 Perioperative outcomes of total pancreatectomy (TP) versus partial pancreatectomy (PP)

Reference	Cohort		Mortality (%)	Sign. (p value)	Morbidity (%)	Sign. (p value)
Schmidt *et al*[4]	TP n=33		6	n.s.	36	n.s.
	PD n=28		7		54	
Muller *et al*[5]	TP n=87		6	n.s.	31	n.s.
	PD n=87		3		23	
McPhee *et al*[6]	TP n=1399		8.3	0.0002	n/a	n/a
	PD n=27 289		6.6		n/a	
Reddy *et al*[7]	*Period 1970–2007*					
	TP n=100		8		69	
	PD n=1286		1.5	0.0007	38.6	<0.0001
	Subanalysis of period	*TP*	*1.9*			
	2000–2007	*PD*	*1.2*	*0.17*	*No significant change*	
Nathan *et al*[8]	TP n=376		8.6		n/a	
	PP n=3645		6.3	0.09	n/a	n/a
Simons *et al*[9]	TP n=5966		OR 2.90		OR 1.29	
	PD n=56 207		Ref.	<0.0001	Ref.	0.0025
Bhayani *et al*[10]	TP=198		6.1		38	
	PD n=6314		3.1	0.02	30	0.02

n/a, not available; PD, pancreaticoduodenectomy.

are discussed, no recommendations are given regarding the extent of surgery, that is, partial pancreatectomy (PP) or total pancreatectomy (TP), in cases with a small screen-detected PDAC. This is an important issue because it seems very likely that a hereditary background increases the risk for a second primary cancer of the pancreas. Here, we describe two high-risk individuals who developed a second primary tumour after a PP of an early-stage cancer.

Patient 1 is a 62-year-old woman with the common Dutch '*p16-Leiden*' founder mutation in the *CDKN2A* gene and a medical history of melanoma at age 56. This patient was enrolled in the surveillance programme in Leiden in 2008. The first MRI showed a lesion in the head–corpus region of the pancreas, suspicious for an adenocarcinoma. The lesion was confirmed by CT scanning, with no signs of distant metastases. A partial duodenopancreatectomy was performed. Histopathological examination showed a well-differentiated adenocarcinoma of 5 mm, surrounded by PanIN1 lesions and an intraductal papillary mucinous neoplasm lesion. The resection margins were free of tumour and seven lymph nodes were unaffected (T1N0M0). A *KRAS* hotspot mutation in codon 12 was detected in the tumour (c.35G>T). This patient continued pancreatic surveillance. After 54 months, a solitary lesion of 7 mm was found in the corpus–tail region with endoscopic ultrasound (EUS). Cytological examination of an EUS-guided fine-needle aspirate showed atypical cells compatible with adenocarcinoma. Of note, no *KRAS* mutation was detected in these cells. CT scanning confirmed the presence of the lesion without evidence for distant metastases. A completion pancreatectomy with splenectomy was performed and histopathological examination showed one small duct suspicious for adenocarcinoma surrounded by multifocal PanIN1-3 lesions. The resection margins of the specimen were free of tumour and 13 lymph nodes were unaffected (T1N0M0). Fifteen months after pancreatectomy, the patient is alive with no evidence of disease.

Patient 2 is a 46-year-old woman with a germline mutation in the *BRCA2* gene and three relatives with PDAC. In 1984, she developed a painless icterus; CT scanning and endoscopic retrograde cholangiopancreatography revealed a tumour in the pancreatic head. A partial duodenopancreatectomy was performed. Histopathological examination showed a moderately differentiated PDAC of 22 mm. The resection margins were free of tumour and none of 14 lymph nodes were affected. (T2N0M0). In 1987, 33 months later, the tumour marker carbohydrate antigen 19.9 increased to 190 U/mL (normal <39 U/mL) and CT scanning revealed a tumour in the tail of the pancreas. A resection of the remnant pancreas was performed and histopathological examination showed a poorly differentiated adenocarcinoma of 20 mm. The resection margins and eight lymph nodes were free of tumour (T2N0M0). At the last follow-up 28 years after completion pancreatectomy the patient is alive with no evidence of PDAC.

What are the implications of our findings? Should we offer TP to all patients with a genetic predisposition and an early-stage cancer? A well-known disadvantage of TP is the development of 'brittle' diabetes which is associated with substantial morbidity. However, recent studies all concluded that TP is safe, with acceptable mortality and morbidity.[2 3] Studies that compared the perioperative mortality and morbidity of TP with PP produced more conflicting results[4–10] (see table 1). Two recent reports demonstrated that the quality of life following TP is acceptable and similar to that reported for PP.[3 5]

In light of these recent studies, the best approach is to discuss the various advantages and disadvantages of TP with high-risk patients with early-stage PDAC and come to a decision together.

T P Potjer,[1] D K Bartsch,[2] E P Slater,[2] E Matthäi,[2] B A Bonsing,[3] H F A Vasen[4]

[1]Department of Clinical Genetics, Leiden University Medical Center, Leiden, The Netherlands
[2]Department of Visceral, Thoracic and Vascular Surgery, Philipps University Marburg, Marburg, Germany
[3]Department of Surgery, Leiden University Medical Center, Leiden, The Netherlands
[4]Department of Gastroenterology & Hepatology, Leiden University Medical Center, Leiden, The Netherlands

Correspondence to Dr H F A Vasen, Department of Gastroenterology & Hepatology, Leiden University Medical Center, Albinusdreef 2, Leiden 2333 ZA, The Netherlands; hfavasen@stoet.nl

Acknowledgements We thank the following colleagues who were involved in the management of the patients: Dr Lars Perk, Professor Dr Hans Morreau and Christoph Schick.

Contributors Design of manuscript: TPP, HFAV. Writing of first draft of manuscript: TPP, HFAV, DKB. Editing the first draft and approving the final draft of the manuscript: DKB, EPS, EM, BAB, HFAV.

Funding This work was supported by the ZOLEON foundation (no. 12.09 to HFAV).

Competing interests None.

Provenance and peer review Not commissioned; internally peer reviewed.

To cite Potjer TP, Bartsch DK, Slater EP, *et al*. *Gut* 2015;**64**:1342–1344.

Received 11 March 2015
Accepted 17 March 2015
Published Online First 2 April 2015

Gut 2015;**64**:1342–1344.
doi:10.1136/gutjnl-2015-309568

REFERENCES

1 Canto MI, Harinck F, Hruban RH, *et al*. International Cancer of the Pancreas Screening (CAPS) Consortium summit on the management of patients with increased risk for familial pancreatic cancer. *Gut* 2013;62:339–47.
2 Billings BJ, Christein JD, Harmsen WS, *et al*. Quality-of-life after total pancreatectomy: is it really that bad on long-term follow-up? *J Gastrointest Surg* 2005;9:1059–66.
3 Epelboym I, Winner M, DiNorcia J, *et al*. Quality of life in patients after total pancreatectomy is comparable with quality of life in patients who

undergo a partial pancreatic resection. *J Surg Res* 2014;187:189–96.
4 Schmidt CM, Glant J, Winter JM, *et al*. Total pancreatectomy (R0 resection) improves survival over subtotal pancreatectomy in isolated neck margin positive pancreatic adenocarcinoma. *Surgery* 2007;142:572–8.
5 Muller MW, Friess H, Kleeff J, *et al*. Is there still a role for total pancreatectomy? *Ann Surg* 2007;246:966–74.
6 McPhee JT, Hill JS, Whalen GF, *et al*. Perioperative mortality for pancreatectomy: a national perspective. *Ann Surg* 2007;246:246–53.
7 Reddy S, Wolfgang CL, Cameron JL, *et al*. Total pancreatectomy for pancreatic adenocarcinoma: evaluation of morbidity and long-term survival. *Ann Surg* 2009;250:282–7.
8 Nathan H, Wolfgang CL, Edil BH, *et al*. Peri-operative mortality and long-term survival after total pancreatectomy for pancreatic adenocarcinoma: a population-based perspective. *J Surg Oncol* 2009;99:87–92.
9 Simons JP, Shah SA, Ng SC, *et al*. National complication rates after pancreatectomy: beyond mere mortality. *J Gastrointest Surg* 2009;13:1798–805.
10 Bhayani NH, Miller JL, Ortenzi G, *et al*. Perioperative outcomes of pancreaticoduodenectomy compared to total pancreatectomy for neoplasia. *J Gastrointest Surg* 2014;18:549–54.

Limited resection of pancreatic cancer in high-risk patients can result in a second primary

T P Potjer, D K Bartsch, E P Slater, E Matthäi, B A Bonsing and H F A Vasen

Gut 2015 64: 1342-1344 originally published online April 2, 2015
doi: 10.1136/gutjnl-2015-309568