ORIGINAL ARTICLE

Variance in Elective Surgery for Chronic Pancreatitis

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ABSTRACT

Context Evidence to guide selection of optimal surgical treatment for patients with painful chronic pancreatitis is limited. Baseline assessment data are limited and thus patients in different centres may be presenting at different stages of their illness. **Objective** This study undertakes a systematic overview of reports of elective surgical intervention in chronic pancreatitis with particular reference to reporting of quality of life and baseline assessment and relation between disease and type of procedure. **Methods** A computerised search of the PubMed, Embase and Cochrane databases was undertaken for the period January 1997 to March 2007 yielding 46 manuscripts providing data on 4,626 patients undergoing elective surgery for chronic pancreatitis. The median number of patients per study was 71 (range: 4-484). The median period for recruitment of patients was 10 years (range: 2-36 years). **Results** An externally validated quality of life questionnaire is reported in 8 (17.4%) of 46 manuscripts covering 441 (9.5%) of 4,626 patients. Formal comparison of pre-operative and post-operative pain scores was provided in 15 (32.6%) of manuscripts. Only seven (15.2%) reports provide a formal rationale or indication for selection of the type of elective surgical procedure for a stated disease variant and these papers cover 481 (10.4%) patients. **Conclusion** In conclusion, this study demonstrates that there is a lack of standardization between units of the criteria for operative intervention in painful chronic pancreatitis. At a minimum, formal quality of life testing using a validated system should be undertaken in all patients prior to elective surgery for painful chronic pancreatitis.

INTRODUCTION

Chronic pancreatitis is characterised by recurrent abdominal pain and progressive destruction of pancreatic parenchyma leading to exocrine and endocrine deficiency [1, 2, 3]. The spectrum of disease is variable and ranges from mild attacks to severe debilitating disease. The incidence of chronic pancreatitis is not well characterised but a French study reports figures in the order of 5-10 cases per 100,000 population [4]. The pathological changes within the pancreas vary and include dilatation of the main pancreatic duct (either uniformly or in a characteristic segmental form), parenchymal calcification and cystic change. These changes can either be localised or diffusely spread throughout the gland [1].

Surgical treatment for chronic pancreatitis has been reported to provide good relief of symptoms [5, 6]. Types of abdominal surgical intervention for chronic pancreatitis can be broadly categorised into pancreatic resectional procedures or drainage operations. Newer

Received August 13th, 2008 - Accepted October 29th, 2008 **Key words** Pancreatitis, Chronic; Quality of Life; Surgery **Abbreviations** DPPHR: duodenum-preserving pancreatic head resection **Correspondence** Ajith Kumar Siriwardena Hepatobiliary Unit, Manchester Royal Infirmary, Manchester M13 9WL, United Kingdom Phone: +44-161.276.4244; Fax +44-161.276.4530 E-mail: ajith.siriwardena@cmmc.nhs.uk **Document URL** http://www.joplink.net/prev/200901/12.html

operations include minimally invasive division of the splanchnic nerves in the thoracic cavity [7]. However, the evidence to guide the selection of any given intervention is limited. In particular, reporting of baseline clinical assessment data are limited and thus patients in different centres may be presenting and undergoing surgery at different stages of their illness. Also, the information to guide selection between resection and drainage is limited and a number of centres appear to promote an operation or procedure developed within their particular unit. This study undertakes a systematic overview of elective surgery for chronic pancreatitis with particular reference to assessment of indication for surgery, type of surgery employed and relation between indication and type of surgery.

PATIENTS AND METHODS

A computerised search of the PubMed, Embase and Cochrane databases was performed using the search engine ADITUS for the period from June 1997 to June 2007. The Medical Subject Headings (MeSH) "Chronic pancreatitis" and "Surgery" were used. The results were combined using Boolean operators to yield a total of 374 articles. Only articles providing original information were retained. Articles which were reviews, case reports, referred to patients with known pancreatic malignancy or which did not providing original information were excluded. In cases of sequential publication of data, the manuscript providing the most detail was retained. These exclusions produced a final study population of 46 manuscripts providing data on 4,626 patients undergoing elective surgery for chronic pancreatitis. The manuscripts were then reviewed and data extracted on demographic profile including aetiology of chronic pancreatitis, gender, country of publication and study period. Specific information was then sought on whether chronic pancreatitis was defined in the manuscript, whether information was provided on the indication for surgery, whether quality of life assessments were undertaken and on the type of surgery undertaken with particular reference to whether information was provided on the relationship between the indication for surgery and the type of surgery undertaken. Data on outcome of surgery were also sought. All manuscripts were reviewed independently

by two authors and a final agreed dataset utilised for analysis.

STATISTICS

Two by two tables are analysed by Fisher's exact and the Mann-Whitney U tests using the Statsdirect software package (version 2.6.5., www.statsdirect.com).

RESULTS

Demographic Profile

The study population comprised 4,626 patients reported in 46 studies [8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52]. The median number of patients

First author	Year	ic profiles of patients u Country of origin		Number of patients in	Aetiology of chronic pancreatitis		
i not uutior	i cui		(years)	study	Alcohol Idiopathic Other		
Cahen D [8]	2007	Netherlands	4	20	12	5	3
Yekebas E [9]	2007	Germany	12	37	12	18	0
Pessaux P [10]	2006	France	5	34	32	0	2
Palanivelu C [11]	2006	India	8	12	0	0	12
HSU JT [12]	2005	Taiwan	8	24	14	6	4
Schlosser W [13]	2005	Germany	19	206	158	30	18
Belina F [14]	2005	Czech Republic	5	104	70	25	9
Chaudhry A [15]	2003	India	13	41	22	19	0
Alexakis N [16]	2004	UK	7	112	58	42	12
Anderson DK [17]	2004	USA	2	4	2	2	0
	2004		8	185	140^{2}	0	45
Adam U [18]	2004 2004	Germany	8 5	87	71	0	43 16
Olah A [19]		Hungary					
Schnelldorfer T [20]	2003	USA	6	129	69 60	13	47
Ramesh H [21]	2003	India	5 21	265	60	0	205
Russell RC [22]	2003	UK		175	116	23	36
Witzigmann H [23]	2003	Germany	5	70	59	6	5
Nealon WH [24]	2003	USA	16	103	56	32	15
Farkas G [25]	2003	Hungary	2	30	26	1	3
Keus E [26]	2003	Netherlands	12	36	19	17	0
Howard TJ [27]	2002	USA	5	55	17	11	27
Hutchins RR [28]	2002	UK	21	90	52	29	9
Proca DM [29]	2001	USA	10	44	15	6	23
Rios M [30]	2001	USA	4	29	0	0	29
Massucco P [31]	2001	Italy	12	55	48	7	0
Heise JW [32]	2001	Germany	11	126	93	0	33
Kalady MF [33]	2001	USA	9	60	31	17	12
Sohn TA [34]	2000	USA	16	255	110	97	48
White SA [35]	2000	UK	n/a	30	12	14	4
Falconi M [36]	2000	Italy	28	109	72	17	20
Usatoff V [37]	2000	UK	19	112	80	21	11
Jimenez RE [38]	2000	USA	7	72	20	19	33
Vickers SM [39]	1999	USA	3	32	16	0	16
Beger HG [6]	1999	Germany	26	388	314	74	0
Lucas CE [40]	1999	USA	16	124	118	1	5
Govil S [41]	1999	UK	16	38	23	1	14
Schoenberg MH [42]	1999	Germany	14	74	54	14	6
Sarkofas GH [43]	1999	USA	21	484	246	160	78
Izbicki JR [44]	1998	Germany	4	61	47	14	0
Traverso LW [45]	1997	USA	12	57	43	0	14
Eddes EH [46]	1997	Netherlands	7	19	13	6	0
Evans S [47]	1997	UK	8	63	44	15	4
Byrne RL [48]	1997	UK	12	76	50	19	7
Rumstadt B [49]	1997	Germany	24	134	96	38	Ó
Gonzalez M [50]	1997	Mexico	33	49	23	22	4
Amikura K [51]	1997	Japan	36	206	125	52	29
Fernandez CL [52]	1997	Spain	8	110	n/a	n/a	n/a
Total: 46 reviews	1997	Span	Median: 10	4,626	2,765	893	858

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Pooled data are available on 4,626 patients. Note that in 110 patients there is no information on aetiology. n/a: not available

Table 2. Use of defined terminology, relation between disease and surgery, and assessment of QoL.

First author	CP defined	Indication for surgery	Type of surgery	Relation between type of surgery and indication	Duration of disease prior to intervention (months)	c
Cahen D [8]	Yes	Pain+complications	LPJ=18, PD=1, Frey's=1	No	21	Yes ^a
Yekebas E [9]	Yes	Pain+complications	V-shaped excision of anterior pancreas=37	Yes	55	Yes ^a
Pessaux P [10]	Yes	Intractable pain	Frey's=34	No	37	Yes ^a
Palanivelu C [11]	Yes	Pain+weight loss	Lap LPJ=12	No	n/a	No
HSU JT [12]	No	Pain+complications	PD=13, PPPD=11	No	57	No
Schlosser W [13]	No	Pain+complications	DPPHR=169, CJ=37	No	50	No
Belina F [14]	Yes	Pain+complications	PD=48, Frey's=56	No	66	Yes ^a
Chaudhry A [15]	Yes	Pain+complications	Frey's=41	No	65	No
Alexakis N [16]	Yes	Pain+complications	Beger=47, TP=30, PD=30, DP=5	No	46	No
Anderson DK [17]	No		Ultrasonic pancreatic head excavation with Roux-en-Y PJ=4	No	n/a	No
Adam U [18]	Yes	Pain+complications	PD=23, PPPD=89, Beger=33, Frey's=40	No	36	No
Olah A [19]	No	n/a	CG=39, DPPHR=27, PD=9, DP=4, other drainage=8	No	n/a	Yes
Schnelldorfer T [20]	Yes	Pain+complications	LPJ=129	No	32	No
Ramesh H [21]	Yes	Pain+complications	LPJ=212, Frey's=45, PD=6, DP=2	No	n/a	Yes
Russell RC [22]	Yes	Pain+complications	PD=98, PPPD=67, others=10	No	n/a	No No ab
Witzigmann H [23]	Yes	Pain+complications	PD=32, DPPHR=38	Yes	31	Yes ^{ab}
Nealon WH [24]	Yes	Pain+psuedocyst	LPJ+CJ=56, LPJ=47	Yes	n/a	No
Farkas G [25]	Yes	Pain+complications	WLRPH+drainage=30	No	81	No
Keus E [26]	Yes	Pain	DPPHR=36	No	60	No
Howard TJ [27]	Yes	Pain+complications	Thoracoscopic splanchnotomy=55	No	49	Yes ^a
Hutchins RR [28]	Yes	Pain+complications	DP=90	No	36	No
Proca DM [29]	No	Pain+complications	PD=18, Beger=4, DP=21, TP=1	No	n/a	No
Rios M [30]	Yes	Pain+complications	PD=17, LPJ=9, DP=3	No	54	No
Massucco P [31]	Yes	1	PD=17, PPPD=10, DP=11, STP=2, TP=2, LPJ=3, others=10 (drainage)	Yes	144	Yes
Heise JW [32]	Yes	Pain+complications	PD=10, PPPD=31, PJ=34, Frey's=19, Beger=6, DP=16, Duval=10	Yes	50	No
Kalady MF [33]	No	Pain+complications	LPJ=60	Yes	70.9	Yes
Sohn TA [34]	Yes	Pain+complications	PD=92, DP=67, LPJ=52, sphincteroplasty=37, TP=4, Duval=5	No	n/a	Yes ^a
White SA [35]	Yes	Pain+complications	SPTP=30	Yes	60	No
Falconi M [36]	Yes	Pain+complications	LPJ=61, PD=43, TP=5	No	46	No
Usatoff V [37]	Yes	Pain+complications	CJ=43, CD=2, LPJ=3, DP=33, PPPD=15, PD=1, TP=7, other resection and drainage=8	No	n/a	No
Jimenez RE [38]	Yes	Pain+complications	PD=33, PPPD=39	No	64	No
Vickers SM [39]	Yes	Pain+complications	PPPD=18, PD=14	No	n/a	No
Beger HG [6]	Yes	Pain+complications	DPPHR=342, DPPHR+LPJ=46	No	43	No
Lucas CE [40]	Yes	Pain+complications	LPJ=78, Duval=27, Puestows=15, PD=4	No	0.5	No
Govil S [41]	Yes	Pain+complications	DP=16, SPDP=22	No	n/a	No
Schoenberg MH [42]	No	Pain+complications	DP=61, DP+PJ=9, STP=4	No	18	No
Sarkofas GH [43]	Yes	Pain+complications	PD=105, DP=121,TP=19, Frey's=5, DPPHR=3, LPJ=120, psuedocyst drainage=61, Duval=9, others=41	No	54	No
Izbicki JR [44]	Yes	Pain+complications	LPJ+LPHE=31, PPPD=30	No	60	Yes ^a
Traverso LW [45]	Yes	Pain+complications	PD=4, PPPD=43, TP=10	No	n/a	No
Eddes EH [46]	Yes	Pain+complications	DPPHR=19	No	6.8	No
Evans S [47]	Yes	Pain+complications	PPPD=3, PD=12, DP=13, Beger=18, TP=1, SPTP=2, DPTP=2, D&SPTP=2, CJ=5, LPJ=1, bypass=4	No	24	No
Byrne RL [48]	Yes	Pain+complications	DP=41, PD=24, CJ=6, LPJ=2, bypass=3	No	36	Yes
Rumstadt B [49]	No	Pain+complications	PD=134	No	n/a	No
Gonzalez M [50]	Yes	Pain+complications	LPJ=49	No	n/a	No
Amikura K [51]	No	Pain+complications	LPJ=69, Duval=2, Frey's=11, DP=37, PD=22, PPPD=5,	No	n/a	No
L- J		1	TP=1, DPPHR=3, other drainage=21, others=46			
Fernandez CL [52]	No	Pain+complications		No	n/a	No
Total=46	78%	-	4,639 operations ^c	Yes=15%	-	-
2 Juni - 10	defined CP	_	Resection=2,641 (PD=1,206) Drainage=1,280 (LPJ=989)	No=85%	-	-
			Drainage+resection=513 (Frey's=282)			
			Others=205			

Others=205

^a Eight studies which used validated questionnaires (SF-36, EORTC QLQ C-30 plus PAN-26). These 8 studies accounted for a total of 636 patients but 441 patients only would have completed the QoL questionnaire.

^b Pre- and post-operative values were not available.

^c There were a few patients who underwent more than one operation. This reported in two manuscripts (Sohn TA, *et al.* [34], total number of patients 255 and total number of operations 257; Amikua K, *et al.* [51], total number of patients 206 and total number of elective operations 217).

CP: chronic pancreatitis; n/a: not available

<u>Type of surgery.</u> CD: cystoduodenostomy; CG: cystogastrostomy; CJ: cystojejunostomy; D&SPTP: duodenum and spleen preserving total pancreatectomy; DP: distal pancreatectomy; DPPHR: duodenum-preserving pancreatic head resection; DPTP: duodenum preserving total pancreatectomy; Duval: Duval procedure; Frey's: Frey lateral pancreaticojejunostomy; JI-PJA: jejunal interposition pancreaticojejunal anastomosis; Lap LPJ: laparoscopic lateral pancreaticojejunostomy; LPHE: local pancreatic head excision; LPJ: lateral pancreaticojejunostomy; PD: pancreaticoduodenectomy; SPDP: spleen preserving distal pancreatectomy; SPTP: spleen preserving total pancreatectomy; STP: subtotal pancreatectomy; TP: total pancreatectomy; WLRPH: wide local resection pancreatic head

per study was 71 (range 4-484) (Table 1). Twenty six (56.5%) reports originated from Europe, 14 (30.4%) from the United States of America, 5 (10.9%) from Asia/Far-East and 1 (2.2%) from Mexico. The median study period for recruitment (including follow-up) of patients was 10 years (range: 2-36 years). There were 3,337 (72.1%) males. The most common aetiology was alcohol in 2,765 (61.2%) patients (note that aetiology was not available for 110 patients). Other aetiologies included idiopathic chronic pancreatitis in 893 (19.8%), tropical chronic pancreatitis in 209 (4.6%) and "others" in 649 (14.4%).

Description of Indications for Surgery

We found one only study without indications (Olah A, *et al.* [19]); therefore, the indication for surgery was described in 45 of 46 articles (97.8%) for a total of 4,539 patients. Of the listed indications, abdominal pain was the principal factor in 3,833 (84.4%) patients (Table 2). Formal comparison of pre-operative and post-operative pain scores was provided in 15 manuscripts (32.6%) (Table 3). Similarly, pre and post-operative analgesic usage was reported in 18 (39.1%).

Type of Surgery

Pancreatic head resectional surgery (either conventional Whipple or pylorus-preserving variant) was the most frequently undertaken procedure in this series being undertaken in 1,206 (26.1%) (Table 2). Duodenum-preserving pancreatic head resection (DPPHR) was undertaken in 745 (16.1%). Distal pancreatectomy (with or without splenic preservation) was undertaken in 563 (12.2%). Total pancreatectomy (with or without spleen and duodenum preservation) was undertaken in 122 (2.6%). Of drainage procedures, pancreatico-jejunostomy lateral was the most frequently reported being described in 989 (21.4%).

In terms of the distribution of procedures across centres, the number of services reporting the use of DPPHR was13, of which 4 services reported a combined total of 16 patients undergoing DPPHR. The number of centres reporting the use of the V-shaped excision of pancreatic head was 1 (in 37 patients). Only seven (15%) reports provide a formal rationale or indication for selection of the type of elective surgical procedure for a stated disease variant and these papers cover 481 (10.4%) patients.

Operative Outcome

There were 179 (3.9%) in-hospital deaths after surgery. One thousand and seventy five (23.2%) patients had one or more surgical complications. Thirty eight (82.6%) reports gave information on a total of 1,609 (39.7%) patients with post-operative diabetes from a total population of 4,056 patients in these reports. Prior to surgery, 908 (22.0%) of 4,129 patients were reported to have diabetes mellitus. After surgery (interval not consistently reported), 1,609 (39.7%) of 4,056 were diabetic and this difference was significant (P<0.001; Fisher's exact test).

Pain Assessment

Fifteen studies provided data on pain scores before and after surgery (Table 3). Comparison of pooled preoperative pain scores to those after surgery (accepting the variable median follow-up) shows a significant reduction in pain (P<0.002; Mann-Whitney U test).

Use of Quality of Life Assessments

An externally validated quality of life questionnaire such as either the short form 36 (SF-36) or the European Organisation for Research and Treatment of Cancer's quality of life questionnaire with pancreasspecific module (EORTC QLQ C-30 plus PAN-26) [53] is reported in 8 (17.3%) of 46 manuscripts covering 441 (9.5%) of 4,626 patients (Table 2). Seven of these studies reported quality of life assessment comparing pre and post operative values. In addition, 5 studies have described the outcome/quality of life using non-validated questionnaire.

DISCUSSION

This article has undertaken a systematic overview of reports on elective surgery for chronic pancreatitis.

Author	No. of patients	Pre-operative pain score	Post-operative pain score	Duration of follow-up	
		(0-100)	(0-100)	(months)	
Cahen D [8]	20	69	25	24	
Yekebas E [9]	37	64	3	83	
Pessaux P [10]	34	46 ^a	41 ^a	15	
Belina F [14]	104	70	28	39	
Alexakis N [16]	112	70 ^a	20 ^a	18-24	
Ramesh H [21]	265	75 ^b	50 ^b	41	
Nealon WH [24]	103	96	0	75	
Howard TJ [27]	55	74 ^a	50 ^a	36	
Rios M [30]	29	90 ^a	30 ^a	30	
Heise JW [32]	126	88 ^a	21 ^a	63	
Sohn TA [34]	255	40 ^a	71 ^a	55	
Vickers SM [39]	32	90 ^a	30 ^a	40	
Izbicki JR [44]	61	81	12	24	
Evans S [47]	63	100 ^b	0 ^b	60	
Byrne RL [48]	76	n/a	24	82	

^a The pain scores were reported with a visual analogue score (VAS) from 0 to 10. We have multiplied these by a factor of 10 to bring them in line with scores reporting out of 100.

^b The pain scores were reported with a VAS from 0 to 4. These were multiplied by 25 to produce a value out of 100.

With 4,626 patients undergoing elective surgery included in the study population of 46 reports, this is one of the largest patient cohorts reported. It is accepted that despite stringent computerised database searches and the precaution of cross-checking databases it is likely that not all relevant articles will have been captured and that there will be a bias toward publication of manuscripts with "positive" results. Nevertheless, the study population is thought to be representative of surgical practice in chronic pancreatitis. Other important methodological limitations are likely to include variation in definition of chronic pancreatitis, differences in case selection and probably differences in interpretation of the exact nature of a specific surgical procedure (such as the DPPHR) between reports. However, interpretation of the data presented here while keeping these limitations in mind has highlighted several interesting and consistent trends across reports.

First, our study shows that almost twice as many reports originate from Europe as compared to the United States of America (Table 1). The reason for this difference is not apparent from these studies and may be multifactorial but could also reflect differences in clinical practice rather than true differences in disease incidence.

Second, it can be seen that median recruitment time to these studies is lengthy (Table 1), suggesting that even in specialist units, relatively few patients are submitted to surgery. In turn, this may mean that individual units are less able to sustain randomized comparative trials and also that collective experience of the surgical management of chronic pancreatitis may be relatively limited.

The findings that alcohol was the most frequent etiologic agent and pain the most often quoted indication for surgery are not new.

Although "pain and complications" were the most frequently cited indications for surgery (Table 2), the relative dearth of use of pre-operative pain scores or quality of life assessments could be regarded as a critical limitation of the published literature. It is difficult to compare between reports (in particular reports recommending different procedures for chronic pancreatitis) when it is not certain whether all reports are referring to the same baseline disease burden or pain levels. Similarly, it is not possible from the wide variety of operative interventions undertaken in patients with "pain and complications" to match type of surgical intervention to disease presentation. It could be further argued that the wide variation in duration of disease interval prior to surgery (Table 2) is indirect evidence that centres are reporting operative interventions on patients at different disease stages.

Although all reports refer to elective surgery in patients with chronic pancreatitis, some operative procedures are carried out for the complications of chronic pancreatitis rather than undertaking resection or drainage of the diseased gland and hence the range of reported interventions include pseudocyst drainages (Table 2).

In a chronic and essentially stable although disabling condition, it was a surprising finding to report that so few studies undertook formal quality of life assessment. One explanation could be that questionnaires validated for use in chronic pancreatitis have only recently become widely available. However, over a decade ago, Izbicki's group were using quality of life assessment questionnaires to assess the outcome of surgery [44].

In terms of the type of surgery undertaken, although the Whipple-type pancreatic head resection was the most frequently undertaken, it appears that a contemporary trend is more towards duodenumpreserving pancreatic head resection. Of particular interest is the limited information provided in terms of matching of operative procedure to disease variant. Further, it appears that particular units undertake procedures developed within those units.

Currently available pointers for selection of treatment option include head resection by pancreaticoduodenectomy where there may be concerns about underlying malignancy and drainage in patients with duct dilatation in the absence of a pancreatic head mass. However, the treatment of patients with small duct disease remains unclear and in our study, patients with this type of disease were treated by the Izbicki operation by one group [9] but by other procedures by others [21, 43]. Similarly, criteria for case selection for duodenum preserving head resection compared to pancreaticoduodenectomy are unclear. A rational allocation of role in this management algorithm for thoracoscopic splanchnic nerve division is also required.

It is encouraging to note that there is more recent published evidence providing long-term outcome data on a randomized trial comparing Whipple pancreaticoduodenectomy to duodenum-preserving pancreatic head resection [54].

In conclusion, this study demonstrates that there remains a pressing lack of standardization between units in relation to the criteria for operative intervention in painful chronic pancreatitis. In a vulnerable patient group and in the setting of an essentially stable disease, this lack of concordance is clearly highlighted in this overview and is difficult to justify in contemporary surgical practice. From our findings, it would seem logical to suggest that if clinicians are to undertake surgery for chronic pancreatitis that at a minimum, formal quality of life testing using a validated system is undertaken in all patients prior to elective surgery for painful chronic pancreatitis. In addition, longer-term follow-up is required before reporting of data.

Acknowledgements Papers based on this manuscript were read at the 8th World Congress of the International Hepato-Pancreato-Biliary Association, Mumbai, India, 29th February 2008 and appeared in abstract form (HPB 2008; 10: Suppl 1) and also as a poster at the American Hepato-Pancreato-Biliary Association, Fort Lauderdale, USA, March 2008 (HPB 2008; 10: Suppl 2).

Conflicts of interest None

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