Systematic review

Systematic review of outcomes after distal pancreatectomy with coeliac axis resection for locally advanced pancreatic cancer

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Background: **Pancreatic cancer involving the coeliac axis is considered unresectable by most guidelines, with a median survival of 6–11 months. A subgroup of these patients can undergo distal pancreatectomy with coeliac axis resection, but consensus on the value of this procedure is lacking. The evidence for this procedure, including the impact of preoperative hepatic artery embolization and (neo)adjuvant therapy, was evaluated.**

Methods: **A systematic review was performed according to the PRISMA guidelines until 27 May 2015. The primary endpoint was overall survival; secondary endpoints included morbidity and radical resection rates.**

Results: **A total of 19 retrospective studies, involving 240 patients, were included. The methodological quality of the studies ranged from poor to moderate. A radical resection was reported in 74·5 per cent (152 of 204), major morbidity in 27 per cent (26 of 96), ischaemic morbidity in 9·0 per cent (21 of 223) and 90-day mortality in 3·5 per cent (4 of 113). Overall, 35·5 per cent of patients (55 of 155) underwent preoperative hepatic artery embolization without an apparent beneficial impact on ischaemic morbidity. Overall, 15·7 per cent (29 of 185) had neoadjuvant and 51·0 per cent (75 of 147) had adjuvant therapy. There was a difference in survival between patient series where less than half of patients had (neo)adjuvant chemotherapy and series where more than half were receiving this treatment: case-weighted median overall survival was 16 (range 9–48) *versus* 18 (10–26) months respectively ($P = 0·002$). Overall median survival for the whole study population was 14·4 (range 9–48) months.**

Conclusion: **Distal pancreatectomy with coeliac axis resection seems a valuable option for selected patients with pancreatic cancer involving the coeliac axis with acceptable morbidity and mortality, and a median survival of 18 months when combined with (neo)adjuvant therapy.**

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Introduction

Current guidelines consider American Joint Committee on Cancer stage III pancreatic cancer either unresectable[1–4] or borderline resectable, provided the tumour is confined to the body of the pancreas and coeliac axis involvement is less than 90–180°[5–8]. In selected patients, resection of the stomach, pancreatic tail and coeliac axis might lead to a radical resection (named the Appleby procedure)[9]. This procedure was modified by Nimura and colleagues[10], who omitted the gastric resection for pancreatic cancer. The procedure is now known as the modified Appleby procedure or distal pancreatectomy with coeliac axis resection.

After coeliac axis resection, the arterial perfusion of the liver and stomach runs by retrograde flow via the superior mesenteric artery, pancreatoduodenal arcades in the pancreatic head and the gastroduodenal artery (*Fig. 1*). Preoperative embolization of the common hepatic artery, as first described by Kondo and co-workers[11] in 2000, has been advocated by some authors to mature this collateral pathway formation, aimed at reducing the rate of ischaemic complications.

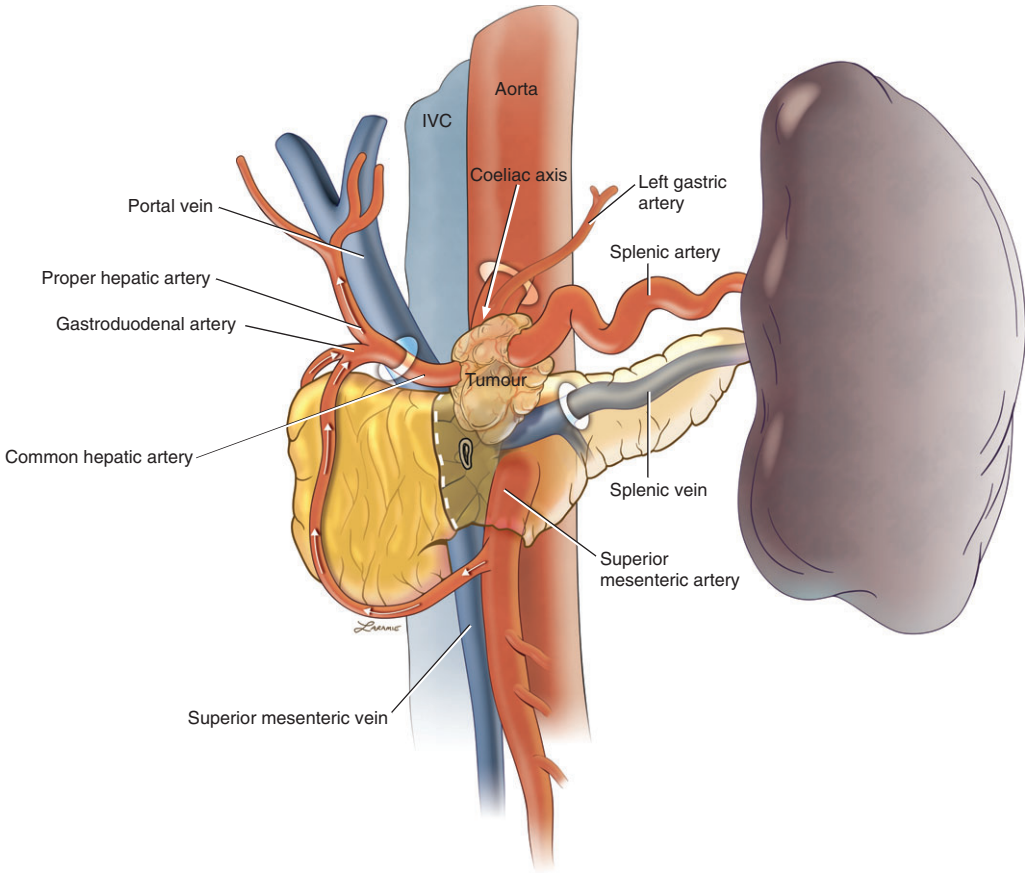

Fig. 1 Locally advanced cancer of the pancreatic body with coeliac axis involvement, eligible for distal pancreatectomy with coeliac axis resection. Resection is feasible only when the gastroduodenal artery, superior mesenteric artery and aorta are not involved. The white arrows represent arterial flow to the liver after resection and the circles around the vessels are the lines of vascular transection. IVC, inferior vena cava

A meta-analysis[12] of the perioperative and long-term outcomes of patients with arterial resection during pancreatectomy for pancreatic cancer concluded that this combination of resections is associated with poor short- and long-term outcomes. In contrast, a Cochrane review[13] of resection *versus* other therapies in locally advanced pancreatic cancer found a 5-year survival benefit in favour of surgery in two randomized trials of surgical intervention *versus* palliative treatment alone (risk ratio 8·7, 95 per cent c.i. 1·1 to 66·9). However, no specific analyses were done on distal pancreatectomy with coeliac axis resection in either review; hence a limited amount of evidence exists on the risks, morbidity and oncological efficacy of this procedure. The aim of this systematic review was to evaluate outcomes, including survival, and the added benefit of preoperative hepatic artery embolization and (neo)adjuvant therapy in distal pancreatectomy with coeliac axis resection for locally advanced pancreatic cancer.

Methods

The study was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[14]. Two authors independently performed the literature search, study selection, data extraction and critical appraisal of the selected studies. Disagreement on article eligibility was resolved by discussion and consensus.

Eligibility criteria

Included articles were those reporting on the perioperative and postoperative outcomes after distal pancreatectomy with coeliac axis resection for locally advanced pancreatic cancer, including non-adenocarcinomas. Excluded were articles in languages other than English or German, and articles reporting on fewer than three patients. In case of overlapping cohorts, either the most recent or the most relevant publication was included.

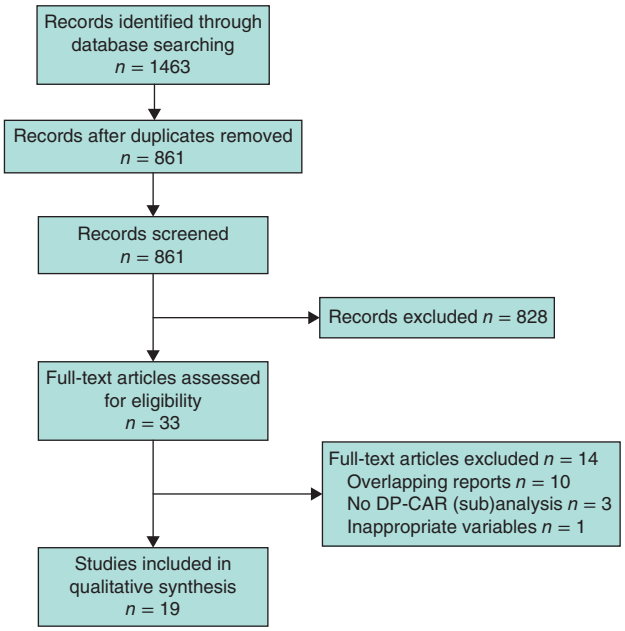

Fig. 2 PRISMA flow diagram of articles included in the systematic review. DP-CAR, distal pancreatectomy with coeliac axis resection

Study selection

A systematic literature search was performed using PubMed, Embase and the Cochrane Library, to identify articles published before 27 May 2015. Search terms were based on organ ('pancreas'), intervention ('surgery'), type of procedure ('pancreatectomy'), additional resection ('celiac', 'vascular' or 'vessel') and possible specific nomenclature ('Appleby'). After removal of duplicates, articles were screened for adherence to the eligibility criteria by title, abstract and subsequently full text. The reference lists of all included studies were screened manually for missed but relevant studies.

Critical appraisal

The methodological quality of the included studies was assessed using the Cochrane Handbook for Systematic Reviews[15] and the Newcastle–Ottawa Scale[16]. Both tools were customized for the purpose of this systematic review, focusing on assessment of observational studies. Retrospective studies were grouped either as cohort studies, if an absolute risk could be calculated from the presented data, or as case series, if patients were selected based on a certain outcome[17]. Quality of follow-up was assessed only when the authors reported on long-term outcomes, such as survival. Each study was classified according to the Oxford Centre for Evidence-Based Medicine levels of evidence[18], ranging from level 1 to level 5.

Data collection

Predefined data extraction forms were used to collect data on variables comprising demographics (sex, age),

Table 1 Study and patient characteristics

Reference	Country	Inclusion period	No. of patients	Sex ratio (M : F)	Median age (years)
Baumgartner *et al.*[20]	USA	2007–2010	11	5 : 6	61
Denecke *et al.*[21]	Germany	2007–2009	6	4 : 2	63
Gagandeep *et al.*[22]	USA	2002–2004	3	3 : 0	60
Hishinuma *et al.*[23]	Japan	1997–2003	7	4 : 3	62
Jing *et al.*[24]	China	2005–2010	24	18 : 6	55*
Kimura *et al.*[25]	Japan	2010–2011	3	1 : 2	66
Konishi *et al.*[26]	Japan	1992–1998	4	0 : 4	57
Mayumi *et al.*[27]	Japan	1975–1994	6	4 : 2	62
Mittal *et al.*[28]	Australia	2007–2014	7	4 : 3	64
Miura *et al.*[29]	Japan	1998–2008	50	26 : 24	64
Okada *et al.*[30]	Japan	2004–2012	37	22 : 15	66*
Shimura *et al.*[31]	Japan	1992–2011	14	10 : 4	69
Sperti *et al.*[32]	Italy	1989–2007	5	3 : 2	70
Takahashi *et al.*[33]	Japan	1993–2010	16	8 : 8	65*
Wang *et al.*[34]	China	2003–2012	15	7 : 8	61
Yamaguchi *et al.*[35]	Japan	n.r.	3	2 : 1	60
Yamamoto *et al.*[36]	Japan	1991–2009	13	10 : 3	64*
Zhou *et al.*[37]	China	2006–2013	12	8 : 4	52
Zureikat *et al.*[38]	USA	2008–2012	4	n.r.	n.r.
Overall		1975–2014	240	139 : 97	63†

*Data originally reported as mean(s.d.); †weighted average of medians. n.r., Not reported.

Table 2 Perioperative variables in 263 patients undergoing distal pancreatectomy with coeliac axis resection

Reference	PHAE (%)	Median duration of surgery (min)	Median blood loss (ml)	PV resection (%)	AR (%)	Radical resection (%)	Major morbidity (%)	Ischaemic morbidity (%)
Baumgartner *et al.*[20]	0	494	700	64	9	91	9	0
Denecke *et al.*[21]	67	267	n.r.	33	n.r.	33	33	33
Gagandeep *et al.*[22]	33	558	1700	0	33	67	33	0
Hishinuma *et al.*[23]	0	n.r.	n.r.	100	0	57§	0	0
Jing *et al.*[24]	n.r.	200*	1779*	n.r.	n.r.	100§	54¶	25
Kimura *et al.*[25]	0	427	185 g#	0	33	100§	100¶	n.r.
Konishi *et al.*[26]	n.r.	357	3669	75	50	75§	33	0
Mayumi *et al.*[27]	n.r.	321*	1777*	17	n.r.	n.r.	33	17
Mittal *et al.*[28]	0	240	340	14	29	86	0	0
Miura *et al.*[29]	100	454	940	64	6	92	54¶	12
Okada *et al.*[30]	> 50	365	1349	22	0	57	n.r.	5
Shimura *et al.*[31]	n.r.	n.r.	n.r.	36	7	n.r.	35	21
Sperti *et al.*[32]	0	233	n.r.	20	20	60	80¶	0
Takahashi *et al.*[33]	0	237*	702 g*#	25	6	56	56	0
Wang *et al.*[34]	0	295	1000	20	27	100	7	0
Yamaguchi *et al.*[35]	0	n.r.	n.r.	0	33	0§	0	0
Yamamoto *et al.*[36]	0	620	1300	23	n.r.	31	92¶	8
Zhou *et al.*[37]	0	330	1200	n.r.	n.r.	n.r.	75¶	0
Zureikat *et al.*[38]	0	371*	200	n.r.	n.r.	n.r.	100	n.r.
Overall	35·5 (55 of 155)‡	365†	1222†	38·5 (77 of 200)‡	10·3 (18 of 175)‡	74·5 (152 of 204)‡	27 (26 of 96)‡	9·0 (21 of 233)‡

*Data originally reported as mean(s.d.); †weighted average of medians; ‡overall proportions in studies reporting on the outcome; §R1/R0 margin definition not reported; ¶overall morbidity; #blood loss reported in grams. PHAE, preoperative hepatic artery embolization; PV, portal vein; AR, additional arterial resection; g, grams; n.r., not reported.

perioperative parameters (preoperative artery embolization, estimated blood loss, duration of surgery, resected arteries, (neo)adjuvant therapy and resection margins), postoperative parameters (major morbidity (defined as Clavien–Dindo[19] grade IIIa), ischaemia-related morbidity, pancreatic ductal adenocarcinoma rate and survival). If the Clavien–Dindo classification was not mentioned in reports, grades were assigned based on the information provided. Ischaemia-related morbidity was defined as ischaemic complications to the liver, gallbladder, omentum, small intestine (if an anastomosis was made) or stomach. Radical resection margin was defined as R0 (microscopically tumour-free). Corresponding authors were contacted and requested to submit additional information on preoperative hepatic artery embolization and (neo)adjuvant treatment, if this was not reported primarily.

Data synthesis and statistical analysis

All statistical analyses were performed using SPSS® for Windows® version 22 (IBM, Armonk, New York, USA). Outcomes were either displayed as reported originally, or calculated from the published raw data if possible. Mean(s.d.) values were converted to median (i.q.r.), in compliance with the Cochrane Handbook[15]. Outcomes were summed and weighted averages of the medians were determined. In cases of proportional data, the overall proportion was determined, censoring studies that did not report on the variable of interest. If survival analysis was not performed, Kaplan–Meier analysis was undertaken based on the published data, provided sufficient reliable raw data were presented. All tests were two-tailed and $P < 0{\cdot}050$ was considered statistically significant.

Results

A systematic search yielded 19 retrospective studies fulfilling the eligibility criteria (*Fig. 2*), comprising 240 patients included between 1975 and 2015, with a case-weighted median age of 63 years (*Table 1*)[20–38]. The majority of patients for whom pathology was reported had pancreatic ductal adenocarcinoma (188 of 194, 96·9 per cent). Other diagnoses were mucinous carcinoma (3 patients), intraductal papillary mucinous neoplasm with high-grade dysplasia (1), anaplastic carcinoma (1) and acinar cell carcinoma (1). Formal meta-analysis was not performed because of obvious clinical heterogeneity between studies and the lack of comparative analyses.

Table 3 Mortality and survival in 240 patients undergoing distal pancreatectomy with coeliac axis resection

Reference	PDAC (%)	Neoadjuvant therapy (%)	Adjuvant therapy (%)	90-day mortality (%)	Median survival (months)
Baumgartner *et al.*[20]	100	100 RT/100 CT	45 CT	18	26
Denecke *et al.*[21]	100	0	83 CT	17	12·4
Gagandeep *et al.*[22]	100	66 UN	100 RT/100 CT	0	n.r.
Hishinuma *et al.*[23]	100	0	86 RT/17 CT	0	19
Jing *et al.*[24]	100	0	0	n.r.	9·3
Kimura *et al.*[25]	100	0	33	0	48
Konishi *et al.*[26]	100	n.r.	n.r.	0	10
Mayumi *et al.*[27]	83	n.r.	n.r.	0	9
Mittal *et al.*[28]	86	14 UN	86 UN	0	n.r.
Miura *et al.*[29]	100	0	72 CT	n.r.	24·7§
Okada *et al.*[30]	92	41 UN	> 50	n.r.	n.r.
Shimura *et al.*[31]	n.r.	n.r.	n.r.	0	10
Sperti *et al.*[32]	100	0	60 UN	0	10
Takahashi *et al.*[33]	n.r.	0	n.r.	6‡	9·7
Wang *et al.*[34]	100	n.r.	30 CT	7	19
Yamaguchi *et al.*[35]	67	0	66 RT	0	10
Yamamoto *et al.*[36]	100	0	31 CT/0 RT	0	20·8
Zhou *et al.*[37]	n.r.	n.r.	n.r.	0	10
Zureikat *et al.*[38]	n.r.	> 50	> 50	0	n.r.
Overall	96·9 (188 of 194)*	15·7 (29 of 185)*	51·0 (75 of 147)*	3·5 (4 of 113)*	14·4†

*Overall proportions in studies reporting on the outcome; †weighted average of medians; ‡30-day mortality; §disease-specific survival. PDAC, pancreatic ductal adenocarcinoma; RT, radiotherapy; CT, chemotherapy; UN, unknown adjuvant therapy; n.r., not reported.

Critical appraisal

Critical appraisal resulted in 18 studies with evidence level 4 and one study with evidence level 2b, with zero to high risk of bias (*Table S1*, supporting information). One study[28] was performed prospectively, but it lacked a control group and the study design was insufficiently solid; it was therefore graded as level 4. Two studies[27,36] had an appropriate control cohort (unresectable locally advanced pancreatic adenocarcinoma), but only one[36] adequately reported on the control group and this article was therefore considered to have the highest level of evidence available for observational studies (2b). Two studies[28,37] were assessed as having a high risk of bias, as they lacked information on follow-up procedures.

Preoperative hepatic artery embolization

Preoperative hepatic artery embolization was reported in 55 (35·5 per cent) of 155 patients, with no reported serious adverse events related to this procedure (*Table 2*). Okada and colleagues[30] referred to earlier publications in which they had described this treatment addition as the standard of operation, as later confirmed by formal correspondence. In three studies (93 patients) more than 50 per cent underwent preoperative hepatic artery embolization. The ischaemic morbidity rate in these patients was 10 (11 per cent) of 93, compared with one (1 per cent) of 99 patients in the 12 studies in which less than 50 per cent of patients had preoperative hepatic artery embolization (*Table 2*).

Surgical outcomes

The overall major morbidity rate was 27 per cent (26 of 96 patients); at least eight had Clavien–Dindo grade IIIb or higher. Reported ischaemia-related complications varied from ischaemic gastropathy (14 patients) to more severe events, such as gastric ulceration or necrosis (4), or liver or gallbladder necrosis (4). The overall radical (R0) resection rate was 74·5 per cent (152 of 204) (*Table 2*). The case-weighted median length of hospital stay was 32 (range 9–76) days. This comprised a case-weighted median of 20 (9–43) days in studies from non-Asian countries (36 patients) *versus* 35 (16–76) days in studies from Asian countries (204 patients) ($P < 0{\cdot}001$). The overall 90-day mortality rate was 3·5 per cent (4 of 113) (*Table 3*).

Survival

The weighted median postoperative survival was 14·4 months (*Table 3*). The 1-year overall cumulative survival rate varied substantially between 33 and 100 per cent, the 3-year survival rate varied between 0 and 67 per cent, and the 5-year survival rate varied between 0 and 14 per cent.

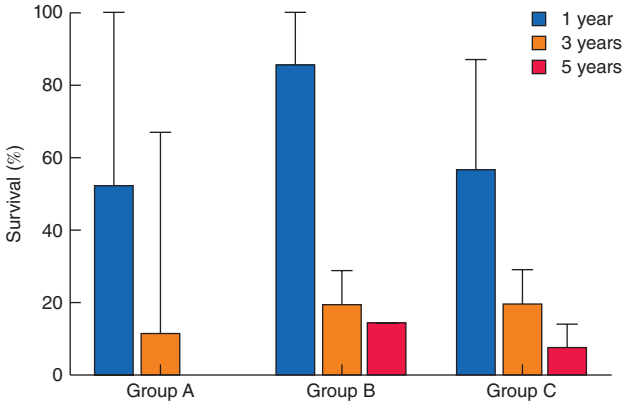

Fig. 3 Overall survival in studies reporting on any form of (neo)adjuvant therapy. In group A (40 patients), comprising three studies[24,25,36], less than 50 per cent of patients received (neo)adjuvant therapy. In group B (133 patients), comprising ten studies[20–23,28–30,32,35,38], more than 50 per cent of patients received (neo)adjuvant therapy. In group C (67 patients), comprising six studies[26,27,31,33,34,37], the (neo)adjuvant regimen was unknown. Proportions were censored for missing data; ranges are denoted by error bars. Weighted median survival times in groups A, B and C were 16, 18 and 12 months respectively

Neoadjuvant and adjuvant therapy

In total, 29 (15·7 per cent) of 185 patients reportedly received neoadjuvant therapy, and 75 (51·0 per cent) of 147 received adjuvant chemotherapy or radiotherapy (*Table 3*). A crude comparative survival analysis was performed, based on the (neo)adjuvant therapy regimen within study populations. There was a difference in survival seen between three studies (40 patients) in which less than 50 per cent of patients received any form of (neo)adjuvant chemoradiotherapy and ten studies (133 patients) in which more than 50 per cent of patients received any form of (neo)adjuvant therapy (median overall survival 16 (range 9–48) *versus* 18 (10–26) months; $P = 0{\cdot}002$) (*Fig. 3*).

Discussion

This systematic review of distal pancreatectomy with coeliac axis resection for pancreatic cancer involving the coeliac axis found a radical (R0) resection rate of 74·5 per cent, a major morbidity rate of 27 per cent, 90-day mortality rate of 3·5 per cent, and a weighted median overall survival of 14·4 months, with a median of 18 months in series where more than 50 per cent of patients received (neo)adjuvant therapy. These findings suggest that this procedure can be a valuable treatment option in selected patients, if combined with neoadjuvant or adjuvant treatment. Available data did not suggest that preoperative hepatic artery embolization reduces the rate of postoperative ischaemic complications.

A recent meta-analysis[39] of case-matched studies of distal pancreatectomy for pancreatic cancer found similar outcomes, with a radical resection rate of 86 per cent (69 of 80), an overall morbidity rate of 35–40 per cent and a 30-day mortality rate of 0–1 per cent. A recent study[40] of distal pancreatectomy with coeliac axis resection in 16 American College of Surgeons National Surgical Quality Improvement Program® centres reported a 10 per cent mortality rate (2 of 20 patients) in centres that performed between one and three procedures over a 14-month period. Additionally, two small studies[41,42] identified after completion of this review had comparable rates of major morbidity, 90-day mortality, radical resection and overall survival.

Only one study[36] compared overall survival in patients who underwent distal pancreatectomy with coeliac axis resection *versus* observation for pancreatic cancer involving the coeliac axis. The authors reported a median survival of 20·8 months in the resection group, compared with 9·8 months in the unresected control group, despite use of less chemotherapy in the resected group (31 *versus* 96 per cent respectively)[36]. The weighted overall median survival in the present analysis was 14·4 (range 9–48) months, somewhat lower than the reported overall median survival rates of 16–19 months for conventional distal pancreatectomy for pancreatic cancer[43–47].

Some authors claim that preoperative hepatic artery embolization is required to reduce the rate of ischaemic complications after distal pancreatectomy with coeliac axis resection, by increasing hepatic arterial inflow via the pancreatic arcade before resection. Preoperative hepatic artery embolization was performed routinely at three centres, covering nearly half of the study population, with no major embolization-related complications reported. However, none of the studies compared outcomes between embolization and immediate resection, hampering an adequate subgroup analysis on its efficacy.

Various patient characteristics have been associated with survival in the included studies, in favour of patients under the age of 60 years[34] and those who had a microscopically radical tumour resection[33]. Miura and colleagues[29] even proposed a risk model to predict which patients would benefit most from a distal pancreatectomy with coeliac axis resection. Three significant preoperative predictors for worse survival were found, comprising low platelet count (less than 150×10^9/l), raised C-reactive protein level (0·4 mg/dl or higher) and increased carbohydrate antigen 19–9 level (300 units/ml or above), as median survival was

significantly lower in patients with all three predictors present (7·7 months *versus* 50·6 months in patients with none of the 3 predictors)[29]. Despite these internally validated risk models and survival predictors, adequate reporting on patient selection for distal pancreatectomy with coeliac axis resection remains an important issue affecting the quality of assessment of this procedure.

The major limitation of this review is the lack of high-quality studies. All studies reported on highly selected patients, and only one[36] reported survival outcomes of an adequate control group, posing a substantial risk of bias. Owing to these limitations, meta-analysis was considered inappropriate. This also made it impossible to assess the effect of preoperative staging and margin status on survival. The majority of patients were reported from Asian countries (85·0 per cent), but, except for differences in length of hospital stay, a sensitivity analysis revealed largely similar surgical outcomes after excluding Asian studies.

Although distal pancreatectomy with coeliac axis resection appears to provide a meaningful treatment option in patients with pancreatic cancer involving the coeliac axis, prospective studies are needed to assess the added benefits of preoperative hepatic artery embolization and to optimize (neo)adjuvant treatment. Given the low incidence of both procedures, such studies would probably involve multicentre (international) registries[48].

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S.K. and T.d.R. contributed equally to this work.

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References

1 Callery MP, Chang KJ, Fishman EK, Talamonti MS, William Traverso L, Linehan DC. Pretreatment assessment of resectable and borderline resectable pancreatic cancer: expert consensus statement. *Ann Surg Oncol* 2009; **16**: 1727–1733.

2 Varadhachary GR, Tamm EP, Abbruzzese JL, Xiong HQ, Crane CH, Wang H *et al*. Borderline resectable pancreatic cancer: definitions, management, and role of preoperative therapy. *Ann Surg Oncol* 2006; **13**: 1035–1046.

3 Landelijke Werkgroep Gastrointestinale Tumoren. [*Pancreatic Cancer: Dutch Guidelines, version 2·0*.] Integraal Kankercentrum Nederland; 2011. http://www.oncoline.nl/pancreascarcinoom [accessed 5 January 2015].

4 Seufferlein T, Bachet JB, Van cutsem E, Rougier P. Pancreatic adenocarcinoma: ESMO–ESDO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2012; **23**: vii33–vii40.

5 Katz MH, Marsh R, Herman JM, Shi Q, Collison E, Venook AP *et al*. Borderline resectable pancreatic cancer: need for standardization and methods for optimal clinical trial design. *Ann Surg Oncol* 2013; **20**: 2787–2795.

6 Tempero MA, Malafa MP, Behrman SW, Benson AB, Casper ES, Chiorean EG *et al*. Pancreatic adenocarcinoma, version 2·2014. *J Natl Compr Cancer Netw* 2014; **12**: 1083–1093.

7 Bockhorn M, Uzunoglu FG, Adham M, Imrie C, Milicevic M, Sandberg AA *et al*. Borderline resectable pancreatic cancer: a consensus statement by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery* 2014; **155**: 977–988.

8 Fishman EK, Al-Hawary M, Francis IR, Merchant NB, Sahani D, Tamm E. *NCCN Clinical Practice Guidelines in Oncology: Pancreatic Adenocarcinoma. Version 2.2015*. National Comprehensive Cancer Network; 2015. http://www.nccn.org/professionals/physician_gls [accessed 2 January 2015].

9 Appleby LH. The coeliac axis in the expansion of the operation for gastric carcinoma. *Cancer* 1953; **6**: 704–707.

10 Nimura Y, Hattory T, Miura K, Nakajima N, Hibi M. Our experience of resection of carcinoma of the body and tail of the pancreas by Appleby's procedure. *Operation* 1976; **15**: 885–889.

11 Kondo S, Katoh H, Shimizu T, Omi M, Hirano S, Ambo Y *et al*. Preoperative embolization of the common hepatic artery in preparation for radical pancreatectomy for pancreas body cancer. *Hepatogastroenterology* 2000; **47**: 1447–1449.

12 Mollberg N, Rahbari NN, Koch M, Hartwig W, Hoeger Y, Büchler MW *et al*. Arterial resection during pancreatectomy for pancreatic cancer: a systemic review and meta-analysis. *Ann Surg* 2011; **254**: 882–893.

13 Gurusamy KS, Kumar S, Davidson BR, Fusai G. Resection *versus* other treatments for locally advanced pancreatic cancer. *Cochrane Database Syst Rev* 2014; (2)CD010244.

14 Liberati A, Altman D, Tetzlaff J, Mulrow C, Gøtzsche P, Ioannidis J *et al*. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009; **339**: b2700.

15 Higgins J, Green S. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0*. The Cochrane Collaboration; 2011. http://www.cochrane-handbook.org [accessed 5 January 2015].

16 Wells G, Shea B, O'Connell D, Petersos J, Welch V, Losos M *et al*. *The Newcastle–Ottawa Scale (NOS) for Assessing the*

Quality of Nonrandomized Studies in Meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp [accessed 1 May 2015].
17 Dekkers OM, Egger M, Altman DG, Vandenbroucke JP. Distinguishing case series from cohort studies. *Ann Intern Med* 2012; **156**: 37–40.
18 Phillips R, Ball C, Sackett D, Badenoch D, Straus S, Haynes B *et al. Oxford Centre for Evidence-Based Medicine – Levels of Evidence (March 2009)*. http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009 [accessed 1 May 2015].
19 Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; **240**: 205–213.
20 Baumgartner JM, Krasinskas A, Daouadi M, Zureikat A, Marsh W, Lee K *et al*. Distal pancreatectomy with *en bloc* celiac axis resection for locally advanced pancreatic adenocarcinoma following neoadjuvant therapy. *J Gastrointest Surg* 2012; **16**: 1152–1159.
21 Denecke T, Andreou A, Podrabsky P, Grieser C, Warnick P, Bahra M *et al*. Distal pancreatectomy with *en bloc* resection of the celiac trunk for extended pancreatic tumor disease: an interdisciplinary approach. *Cardiovasc Intervent Radiol* 2011; **34**: 1058–1064.
22 Gagandeep S, Artinyan A, Jabbour N, Mateo R, Matsuoka L, Sher L *et al*. Extended pancreatectomy with resection of the celiac axis: the modified Appleby operation. *Am J Surg* 2006; **192**: 330–335.
23 Hishinuma S, Ogata Y, Tomikawa M, Ozawa I. Stomach-preserving distal pancreatectomy with combined resection of the celiac artery: radical procedure for locally advanced cancer of the pancreatic body. *J Gastrointest Surg* 2007; **11**: 743–749.
24 Jing W, Zhu G, Hu X, Jing G, Shao C, Zhou Y *et al*. Distal pancreatectomy with *en bloc* celiac axis resection for the treatment of locally advanced pancreatic body and tail cancer. *Hepatogastroenterology* 2013; **60**: 187–190.
25 Kimura A, Yamamoto J, Aosasa S, Hatsuse K, Nishikawa M, Nishiyama K *et al*. Importance of maintaining left gastric arterial flow at Appleby operation preserving whole stomach for central pancreatic cancer. *Hepatogastroenterology* 2012; **59**: 2650–2652.
26 Konishi M, Kinoshita T, Nakagori T, Inoue K, Oda T, Kimata T *et al*. Distal pancreatectomy with resection of the celiac axis and reconstruction of the hepatic artery for carcinoma of the body and tail of the pancreas. *J Hepatobiliary Pancreatic Surg* 2000; **7**: 183–187.
27 Mayumi T, Nimura Y, Kamiya J, Kondo S, Nagino M, Kanai M *et al*. Distal pancreatectomy with *en bloc* resection of the celiac artery for carcinoma of the body and tail of the pancreas. *Int J Pancreatol* 1997; **22**: 15–21.
28 Mittal A, De Reuver PR, Shanbhag S, Staerkle RF, Neale M, Thoo C *et al*. Distal pancreatectomy, splenectomy, and celiac axis resection (DPS-CAR): common hepatic arterial stump pressure should determine the need for arterial reconstruction. *Surgery* 2015; **157**: 811–817.
29 Miura T, Hirano S, Nakamura T, Tanaka E, Shichinohe T, Tsuchikawa T *et al*. A new preoperative prognostic scoring system to predict prognosis in patients with locally advanced pancreatic body cancer who undergo distal pancreatectomy with *en bloc* celiac axis resection: a retrospective cohort study. *Surgery* 2014; **155**: 457–467.
30 Okada K, Kawai M, Tani M, Hirono S, Miyazawa M, Shimizu A *et al*. Preservation of the left gastric artery on the basis of anatomical features in patients undergoing distal pancreatectomy with celiac axis *en-bloc* resection (DP-CAR). *World J Surg* 2014; **38**: 2980–2985.
31 Shimura M, Ito M, Horiguchi A, Miyakawa S. Distal pancreatectomy with *en bloc* celiac axis resection performed while monitoring hepatic arterial flow by using a transonic flowmeter during operation. *Hepatogastroenterology* 2012; **59**: 1498–1500.
32 Sperti C, Berselli M, Pedrazzoli S. Distal pancreatectomy for body–tail pancreatic cancer: is there a role for celiac axis resection? *Pancreatology* 2010; **10**: 491–498.
33 Takahashi Y, Kaneoka Y, Maeda A, Isogai M. Distal pancreatectomy with celiac axis resection for carcinoma of the body and tail of the pancreas. *World J Surg* 2011; **35**: 2535–2542.
34 Wang X, Dong Y, Jin J, Liu Q, Zhan Q, Chen H *et al*. Efficacy of modified Appleby surgery: a benefit for elderly patients? *J Surg Res* 2015; **194**: 83–90.
35 Yamaguchi K, Nakano K, Kobayashi K, Ogura Y, Konomi H, Sugitani A *et al*. Appleby operation for pancreatic body–tail carcinoma: report of three cases. *Surg Today* 2003; **33**: 873–878.
36 Yamamoto Y, Sakamoto Y, Ban D, Shimada K, Esaki M, Nara S *et al*. Is celiac axis resection justified for T4 pancreatic body cancer? *Surgery* 2012; **151**: 61–69.
37 Zhou YM, Zhang XF, Li XD, Liu XB, Wu LP, Li B. Distal pancreatectomy with *en bloc* celiac axis resection for pancreatic body–tail cancer: is it justified? *Med Sci Monit* 2014; **20**: 1–5.
38 Zureikat AH, Moser AJ, Boone BA, Bartlett DL, Zenati M, Zeh III HJ. 250 Robotic pancreatic resections: safety and feasibility. *Ann Surg* 2013; **258**: 554–559.
39 Ricci C, Casadei R, Taffurelli G, Toscano F, Pacilio CA, Bogoni S *et al*. Laparoscopic *versus* open distal pancreatectomy for ductal adenocarcinoma: a systematic review and meta-analysis. *J Gastrointest Surg* 2015; **19**: 770–781.
40 Beane JD, House MG, Pitt SC, Kilbane EM, Hall BL, Parmar AD *et al*. Distal pancreatectomy with celiac axis resection: what are the added risks? *HPB* 2015; **17**: 777–784.
41 Cesaretti M, Abdel-Rehim M, Barbier L, Dokmak S, Hammel P, Sauvanet A. Modified Appleby procedure for borderline resectable/locally advanced distal pancreatic adenocarcinoma: a major procedure for selected patients. *J Visc Surg* 2016; [Epub ahead of print].

42 Latona JA, Lamb KM, Pucci MJ, Maley WR, Yeo CJ. Modified Appleby procedure with arterial reconstruction for locally advanced pancreatic adenocarcinoma: a literature review and report of three unusual cases. *J Gastrointest Surg* 2016; **20**: 300–306.
43 Kooby DA, Hawkins WG, Schmidt CM, Weber SM, Bentrem DJ, Gillespie TW *et al*. A multicenter analysis of distal pancreatectomy for adenocarcinoma: is laparoscopic resection appropriate? *J Am Coll Surg* 2010; **210**: 779–785.
44 Mitchem JB, Hamilton N, Gao F, Hawkins WG, Linehan DC, Strasberg SM. Long-term results of resection of adenocarcinoma of the body and tail of the pancreas using radical antegrade modular pancreatosplenectomy procedure. *J Am Coll Surg* 2012; **214**: 46–52.
45 Marangos IP, Buanes T, Røsok BI, Kazaryan AM, Rosseland AR, Grzyb K *et al*. Laparoscopic resection of exocrine carcinoma in central and distal pancreas results in a high rate of radical resections and long postoperative survival. *Surgery* 2012; **151**: 717–723.
46 Magge D, Gooding W, Choudry H, Steve J, Steel J, Zureikat A *et al*. Comparative effectiveness of minimally invasive and open distal pancreatectomy for ductal adenocarcinoma. *JAMA Surg* 2013; **148**: 525–531.
47 de Rooij T, Tol JA, van Eijck CH, Boerma D, Bonsing BA, Bosscha K *et al*. Outcomes of distal pancreatectomy for pancreatic ductal adenocarcinoma in the Netherlands: a nationwide retrospective analysis. *Ann Surg Oncol* 2016; **23**: 585–591.
48 Fusai GK, Pereira S, Valente R, Ravikumar R, Lykoudis P. *The Arterial Study Network*; 2015. https://www.thearterialstudy.net [accessed 10 September 2015].

Supporting information

Additional supporting information may be found in the online version of this article:

Table S1 Risk-of-bias assessment (Word document)

Editor's comments

This collective series highlights a procedure that is rarely performed even in high-volume centres. As the authors point out, the accumulated data are heterogeneous and influenced by a few centres performing a majority of the procedures. The collective median overall survival of 14·4 months reported in this series, with an occasional long-term survivor, was improved only slightly (median 18 months) in patients who had either neoadjuvant or adjuvant therapy. Notably, the GEST study[1] and the SCALOP study[2] achieved a median overall survival of 15·9 and 15·2 months respectively in patients with locally advanced pancreatic cancer. It is thus timely to recall a two-decades-old analogy on the kingdom of cancer made by Blake Cady[3]: 'Biology is King; selection of cases is Queen, and the technical details of surgical procedures are princes and princesses of the realm who frequently try to overthrow the powerful forces of the King and Queen, usually to no long-term avail, although with some temporary apparent victories.' Both surgical and medical strategies require a highly selective approach to achieve reasonable outcomes in patients with pancreas cancer. Thus, to battle this disease, we need to overthrow the King.

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Editor, BJS

References

1 Ueno H, Ioka T, Ikeda M, Ohkawa S, Yanagimoto H, Boku N *et al*. Randomized phase III study of gemcitabine plus S-1, S-1 alone, or gemcitabine alone in patients with locally advanced and metastatic pancreatic cancer in Japan and Taiwan: GEST study. *J Clin Oncol* 2013; **31**: 1640–1648.
2 Mukherjee S, Hurt CN, Bridgewater J, Falk S, Cummins S, Wasan H *et al*. Gemcitabine-based or capecitabine-based chemoradiotherapy for locally advanced pancreatic cancer (SCALOP): a multicentre, randomised, phase 2 trial. *Lancet Oncol* 2013; **14**: 317–326.
3 Cady B. Basic principles in surgical oncology. *Arch Surg* 1997; **132**: 338–346.