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Original Article

Oncological outcomes after pancreatoduodenectomy for pancreatic ductal adenocarcinoma in octogenarians: case-control study

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Abstract

Background: By the end of this decade, 70 per cent of all diagnosed pancreatic ductal adenocarcinomas will be in the elderly. Surgical resection is the only curative option. In the elderly perioperative mortality is higher, while controversy still exists as to whether aggressive treatment offers any survival benefit. This study aimed to assess the oncological benefit of pancreatoduodenectomy in octogenarians with pancreatic ductal adenocarcinoma.

Method: Retrospective multicentre case-control study of octogenarians and younger controls who underwent pancreatoduodenectomy for pancreatic ductal adenocarcinoma between 2008 and 2017. The primary endpoint was overall survival and the secondary endpoint was disease-free survival.

Results: Overall, 220 patients were included. Although the Charlson co-morbidity index was higher in octogenerians, Eastern Cooperative Oncology Group performance status, ASA and pathological parameters were comparable. Adjuvant therapy was more frequently delivered in the younger group ($n = 80$, 73 per cent *versus* $n = 58$, 53 per cent, $P = 0.006$). There was no significant difference between octogenarians and controls in overall survival (20 *versus* 29 months, $P = 0.095$) or disease-free survival (19 *versus* 22 months, $P = 0.742$). On multivariable analysis, age was not an independent predictor of either oncological outcome measured.

Conclusion: Octogenarians with pancreatic ductal adenocarcinoma of the head and uncinate process may benefit from comparable oncological outcomes to younger patients with surgical treatment. Due to the age- and disease-related frailty and co-morbidities, careful preoperative assessment and patient selection is of paramount importance.

Introduction

Pancreatic ductal adenocarcinoma (PDAC) will be the second leading cause of cancer-related mortality by the end of this decade[1]. Surgical resection is the only curative option for patients with PDAC, however, only 15–20 per cent are eligible on diagnosis[2]. Oncological outcomes can be substantially improved with completion of the treatment pathway (neoadjuvant and/or adjuvant treatment and surgery)[3,4]. Nonetheless, 5-year survival is only 20–25 per cent due to local or metastatic disease recurrence[5,6]. Historically, the mortality associated with pancreatoduodenectomy (PD) was high and the concern of chronic co-morbidities and frailty amongst the elderly resulted in their exclusion from surgical treatment[7]. Similarly, the perception of elderly patients being poor candidates to receive adjuvant chemotherapy may prevent them being offered a chance of curative treatment pathways[8].

Following the population surge after World War II, the 'baby boomers' have now become octogenarians[9] and a combination of better general health and hence longer life expectancy has seen a rise in the age-specific trend of the incidence of PDAC[10]. By the end of this decade, 70 per cent of all diagnosed PDAC will be in the elderly[11]. The benefit of curative resection in this population is difficult to determine from the literature as it is underrepresented within clinical trials. Most studies on the safety and benefit of the elderly population undergoing PD refer to an age range of 70–75 years, but over the next 50 years the proportion of octogenarians within the population in Europe will double from 6 to 13 per cent[12]. The advances in surgical technique, technology, perioperative management and

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centralization have resulted in a substantial improvement in mortality (from 4.1 to 2.4 per cent) and failure to rescue (from 13 to 7.4 per cent) following PD[13,14]. Although in a previous study of this group, 90-day mortality of octogenarians after PD was double that of younger controls matched on extent of surgery for periampullary malignancies (9 *versus* 3 per cent), age was not an independent predictor of mortality[15]. Careful patient selection and assessment of co-morbidities are of paramount importance in preoperative planning for these patients. Nonetheless, the evidence in the literature is still controversial as to whether aggressive treatment offers any survival benefit for octogenarians with PDAC. The aim of this study was to assess the oncological benefit of PD for octogenarians with PDAC.

Methods

Study design

A multicentre retrospective case-control analysis of prospectively maintained databases was performed, including PD undertaken over a 10-year interval between January 2008 and December 2017. Octogenarians who underwent PD were matched with consecutively operated younger patients (control group) with a 1:1 ratio, based on extent of surgery (venous, arterial or additional organ resection). An invitation to participate in this study was sent out to all specialist pancreatic centres across the UK. Six centres agreed to participate, resulting in data from a total of seven centres included. Institutional board approval was sought and obtained by each centre separately. Data collection was carried out by each centre using a standardized proforma. The primary outcome set for this study was overall survival (OS; defined as time from diagnosis to death) and the secondary outcome disease-free survival (DFS; defined as time from surgery to diagnosis of recurrence). Reporting of results was performed in line with the STROBE statement[16].

Data collection

The preoperative data collected included: demographics, ASA score, Eastern Cooperative Oncology Group (ECOG) performance status, Charlson co-morbidity index (CCI), co-morbidities, preoperative echocardiogram, pulmonary function test and or cardiopulmonary exercise testing (CPEX), preoperative biliary stenting, steroid use, preoperative haemoglobin, serum albumin, bilirubin and use of neoadjuvant chemotherapy and/or radiotherapy.

Intraoperative data included: type of PD (classic Whipple or pylorus preserving), additional organ resection or venous resection.

Postoperative data included: histological type of tumour, lymph node ratio, resection margin status (defined as R0: no tumour cells for at least 1 mm from margin, R1: tumour cells within 1 mm)[17], presence of perineural and intravascular invasion, 30- and 90-day mortality, complications categorized using the Clavien–Dindo classification, 30-day re-admission, OS and DFS.

Statistical methods

Chi squared with exact statistics and ANOVA were used as appropriate to compare variables and outcomes between the two groups, with statistical significance set at $P < 0.050$. Survival analysis (OS and DFS) was performed using the Kaplan–Meier method and the log-rank test for comparing differences between survival curves. Univariable and multivariable time to event analyses were performed using the Cox proportional hazard model for OS and DFS. Variables were subjected to a univariable analysis first and those with $P < 0.20$ were introduced into a multivariable model. Hazard ratios (HR) and associated 95 per cent confidence intervals were calculated. A two-tailed P value <0.050 was considered statistically significant. All statistical analyses were performed using the software package SPSS Statistics for Windows® (version 23.0; SPSS Inc., Chicago, IL, USA).

Results

Cohort characteristics

A total of 220 patients comprising 110 octogenerian and 110 non-octogenerian patients underwent PD (*Table 1*). The octogenarian cohort was matched on complexity of resection with consecutive patients from a younger cohort where 54 (24.5 per cent) of patients underwent vein resections. Although CCI was higher in octogenerians, ECOG performance status and ASA were comparable. Neoadjuvant therapy was not commonly performed in either cohort, but adjuvant therapy was delivered more commonly in the younger cohort ($n = 80$ (72.7 per cent) *versus* $n = 58$ (52.7 per cent), $P = 0.006$). There was no difference in the tumour stage, lymph node ratio or resection margin status between the groups. There was no significant difference in the recurrence pattern between the groups.

Survival analysis

There was no significant difference in OS (octogenarians median: 20 months, range: 14–26 months *versus* controls median: 29 months, range: 24–34 months; $P = 0.095$) or DFS (octogenarians median: 19 months, range: 13–24 months *versus* controls median: 22 months, range: 15–29 months; $P = 0.742$) between octogenarians and controls (*Fig. 1*).

Risk analysis

Overall survival

Table 2 shows the results of the univariable Cox regression analysis for OS. Multivariable analysis identified history of angina/percutaneous coronary intervention/coronary surgery (OR = 3.149; c.i. = 1.351–7.341; $P = 0.008$), preoperative albumin levels (OR = 0.592; c.i. = 0.383–0.914; $P = 0.018$) and lymph node ratio (OR = 10.048; c.i. = 3.388–29.801; $P < 0.001$) as independent predictors of OS. Of note, age was not significant.

In an effort to identify predictors of mortality that can be used to council octogenarian patients, separate multivariable analyses were performed within that subgroup for all parameters and for preoperative parameters only as shown in *Table S1*. Amongst preoperative parameters history of peptic ulcer disease (OR = 18.502; c.i. = 2.205–155.284; $P = 0.007$), preoperative use of steroids (OR = 2.440; c.i. = 1.105–5.389; $P = 0.027$) and preoperative albumin levels (OR = 0.528; c.i. = 0.330–0.844; $P = 0.008$) were independent predictors of OS. When the postoperative parameters were also included in the model, preoperative haemoglobin levels (OR = 0.653; c.i. = 0.475–0.898; $P = 0.009$), lymph node ratio (OR = 16.300; c.i. = 3.039–87.419; $P = 0.001$), type of resection (OR = 0.234; c.i. = 0.100–0.546; $P = 0.001$) and adjuvant chemotherapy (OR = 2.227; c.i. = 1.004–4.939; $P = 0.049$) were also significant predictors.

Disease-free survival

Table 3 shows the results of the univariable Cox regression analysis for DFS. Multivariable analysis identified history of angina/percutaneous coronary intervention (PCI)/coronary surgery (OR = 2.394; c.i. = 1.173–4.884; $P = 0.016$), preoperative albumin levels

Table 1 Comparison of demographic, treatment and pathology characteristics between octogenarians and controls

Demographics	Total $n = 220$	Controls $n = 110$	Octogenarians $n = 110$	*P*
Age (years), median (range)	79 (36–88)	69 (36–79)	81 (80–86)	<0.001*
Sex				0.135
Male	123 (55.9)	67 (60.9)	56 (50.9)	
Female	97 (44.1)	43 (39.1)	54 (49.1)	
Charlson co-morbidity index				<0.001*
1–2	6 (2.7)	6 (5.5)	0	
3–4	34 (15.5)	34 (30.9)	0	
>5	167 (75.9)	62 (56.4)	105 (95.5)	
ECOG performance status				0.756
0–1	197 (89.5)	98 (89.1)	99 (90)	
2–4	9 (4.1)	4 (3.6)	5 (4.5)	
ASA				0.635
I–II	149 (67.7)	77 (70)	72 (65.5)	
III–IV	38 (17.3)	18 (16.4)	20 (18.2)	
Treatment				
Neoadjuvant therapy				
Chemotherapy	5 (2.3)	3 (2.7)	2 (1.8)	0.651
Radiotherapy	3 (1.4)	2 (1.8)	1 (0.9)	0.561
Operation				0.786
Whipples	122 (55.5)	60 (54.5)	62 (56.4)	
PPPD	98 (44.5)	50 (45.5)	48 (43.6)	
Vein resection	54 (24.5)	28 (25.5)	26 (23.6)	0.754
Adjuvant chemotherapy	138 (62.7)	80 (72.7)	58 (52.7)	0.006*
Pathology				
T stage				0.271
pT1	8 (3.6)	3 (2.7)	5 (4.6)	
pT2	10 (4.5)	7 (6.4)	3 (2.7)	
pT3	197 (89.6)	99 (90)	98 (89.1)	
pT4	5 (2.3)	1 (0.9)	4 (3.6)	
Resection margin				0.499
R0	101 (45.9)	48 (43.6)	53 (48.2)	
R1	119 (54.1)	62 (56.4)	57 (51.8)	
Lymph node ratio, median (range)	0.15 (0–1)	0.19 (0–1)	0.14 (0–0.75)	0.132
Perineural invasion	187 (85)	93 (84.5)	94 (85.5)	0.278
Perivascular invasion	171 (77.7)	84 (76.4)	87 (79.1)	0.183
Outcomes				
30-day mortality	5 (2.3)	2 (1.8)	3 (2.7)	0.636
90-day mortality	13 (5.9)	4 (3.6)	9 (8.2)	0.143

Values are *n* (%) unless otherwise stated. *P values are significant. ECOG, Eastern Cooperative Oncology Group; PPPD, pylorus-preserving pancreatoduodenectomy.

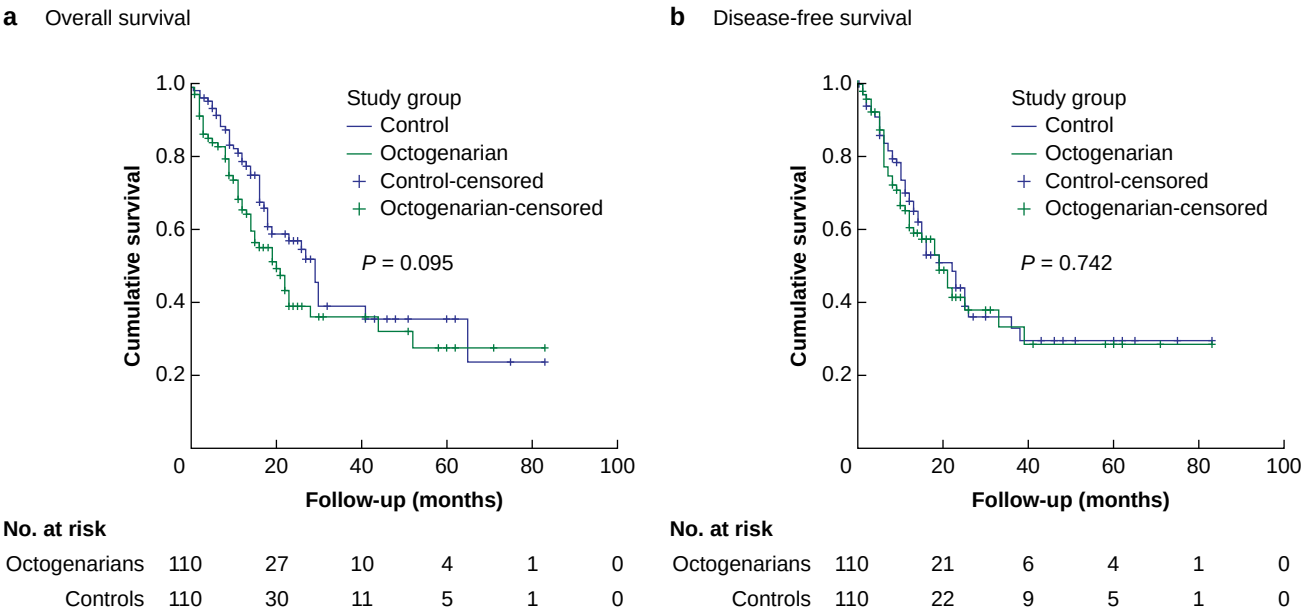

Fig. 1 Kaplan–Meier curves
a Overall survival and **b** disease-free survival.

Table 2 Univariable Cox regression analysis for overall survival

Overall survival				
Parameters	**Univariable analysis: whole cohort**		**Univariable analysis: octogenarians subgroup**	
	OR (95% c.i.)	***P***	**OR (95% c.i.)**	***P***
Preoperative				
Age Indicator: control; < 80 years	1.410 (0.935–2.125)	0.101	—	—
Sex Indicator: female	1.001 (0.663–1.511)	0.996	0.928 (0.529–1.628)	0.793
ASA score Indicator: class 1	1.326 (0.905–1.945)	0.148	0.993 (0.556–1.774)	0.981
ECOG performance status Indicator: grade 1	1.126 (0.779–1.629)	0.527	1.040 (0.616–1.756)	0.884
ECOG groups Indicator: grades 0–1	1.172 (0.428–3.211)	0.757	1.392 (0.335–5.773)	0.649
Diabetes Indicator: no	1.709 (1.118–2.612)	0.013*	2.054 (1.154–3.654)	0.014*
COPD Indicator: no	0.502 (0.158–1.594)	0.242	0.507 (0.070–3.688)	0.502
Congestive heart failure Indicator: no	2.776 (0.864–8.914)	0.086	1.862 (0.244–14.208)	0.549
Myocardial infarction Indicator: no	1.746 (0.837–3.641)	0.138	1.402 (0.497–3.955)	0.523
Prior PCI/previous coronary surgery/angina Indicator: no	1.918 (0.918–4.005)	0.083	1.330 (0.318–5.571)	0.696
Hypertension Indicator: no	1.042 (0.667–1.629)	0.856	1.036 (0.572–1.878)	0.907
Impaired sensorium Indicator: no	7.052 (0.955–52.057)	0.055	NA	NA
Dementia Indicator: no	4.778 (0.654–34.885)	0.123	NA	NA
Peripheral vascular disease Indicator: no	1.680 (0.410–6.889)	0.471	0.048 (0–98692.140)	0.683
TIA / CVA Indicator: no	2.592 (1.186–5.665)	0.017*	1.683 (0.600–4.723)	0.323
Neurological deficit Indicator: no	17.073 (2.204–132.244)	0.007*	NA	NA
Connective tissue disease Indicator: no	0.047 (0–32.697)	0.361	0.046 (0–34.921)	0.363
Peptic ulcer disease Indicator: no	0.292 (0.040–2.116)	0.223	6.804 (0.890–52.025)	0.065
Liver disease Indicator: no	0.047 (0–8.606)	0.250	0.046 (0–53.310)	0.393
Hypercoagulability Indicator: no	2.307 (0.724–7.354)	0.158	1.985 (0.612–6.439)	0.254
Chronic kidney disease Indicator: stage 1	0.996 (0.927–1.069)	0.902	0.988 (0.908–1.075)	0.780
Biliary stent Indicator: no	0.813 (0.526–1.256)	0.350	0.485 (0.270–0.872)	0.016*
Steroid use prior to operation Indicator: no	1.841 (1.011–3.353)	0.046*	4.070 (2.020–8.197)	<0.001*
Preoperative haemoglobin	0.952 (0.846–1.071)	0.414	0.852 (0.698–1.042)	0.118
Preoperative bilirubin	1.001 (0.999–1.003)	0.183	1.001 (0.999–1.003)	0.163
Preoperative albumin	0.668 (0.502–0.890)	0.006*	0.482 (0.323–0.718)	<0.001*
Neoadjuvant chemotherapy Indicator: no	1.259 (0.309–5.126)	0.748	1.287 (0.176–9.398)	0.803
Neoadjuvant radiotherapy Indicator: no	0.048 (0–29.994)	0.355	0.049 (0–6709.6999)	0.616
Intraoperative				
Classical or PPPD Indicator: classical	0.819 (0.542–1.239)	0.344	0.635 (0.357–1.129)	0.122
Venous resection Indicator: no	1.113 (0.687–1.803)	0.664	1.083 (0.563–2.082)	0.811
Additional organ resection Indicator: no	0.610 (0.224–1.666)	0.335	0.266 (0.036–1.948)	0.192
Histopathological				
pT Indicator: pT1	1.408 (0.792–2.502)	0.244	1.452 (0.692–3.048)	0.324

(continued)

Table 2 (**continued**)

Overall survival				
Parameters	**Univariable analysis: whole cohort**		**Univariable analysis: octogenarians subgroup**	
	OR (95% c.i.)	***P***	**OR (95% c.i.)**	***P***
Lymph node ratio	8.654 (4.038–18.549)	<0.001*	16.928 (4.299–66.656)	<0.001*
Resection margin Indicator: R0	1.790 (1.161–2.762)	0.008*	2.291 (1.259–4.171)	0.007*
Perineural invasion Indicator: no	3.055 (1.239–7.533)	0.015*	2.881 (0.698–11.892)	0.143
Intravascular invasion Indicator: no	1.960 (1.087–3.532)	0.025*	3.353 (1.040–10.808)	0.043*
Postoperative				
Postoperative complications Indicator: no	1.125 (0.746–1.696)	0.575	0.933 (0.529–1.644)	0.810
Clavien–Dindo classification based on higher category recorded Indicator: grade I	0.989 (0.832–1.175)	0.897	0.926 (0.720–1.191)	0.551
Adjuvant chemotherapy Indicator: yes	1.763 (1.120–2.775)	0.014*	2.052 (1.115–3.775)	0.021*

*P values are significant. ECOG, Eastern Cooperative Oncology Group; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; TIA, transient ischaemic attack; CVA, cerebrovascular accident; PPP, pylorus preserving pancreatoduodenectomy; NA, not applicable.

Table 3 Univariable Cox regression analysis for disease-free survival

Disease-free survival				
Parameters	**Univariable analysis: whole cohort**		**Univariable analysis: octogenarians subgroup**	
	OR (95% c.i.)	***P***	**OR (95% c.i.)**	***P***
Preoperative				
Age Indicator: control; < 80 years	1.070 (0.710–1.612)	0.746	—	—
Sex Indicator: female	0.931 (0.618–1.404)	0.735	1.202 (0.660–2.191)	0.548
ASA score Indicator: class 1	1.044 (0.720–1.515)	0.819	0.638 (0.347–1.172)	0.147
ECOG performance status Indicator: grade 1	1.086 (0.744–1.586)	0.668	1.160 (0.647–2.078)	0.618
ECOG groups Indicator: grades 0–1	2.217 (0.895–5.491)	0.085	14.351 (3.707–55.552)	<0.001*
Diabetes Indicator: no	1.496 (0.957–2.337)	0.077	1.637 (0.838–3.199)	0.149
COPD Indicator: no	0.953 (0.414–2.191)	0.909	0.578 (0.079–4.232)	0.590
Congestive heart failure Indicator: no	2.267 (0.710–7.234)	0.167	3.056 (0.384–24.307)	0.291
Myocardial infarction Indicator: no	1.539 (0.707–3.349)	0.277	0.960 (0.295–3.125)	0.946
Prior PCI / previous coronary surgery / angina Indicator: no	2.346 (1.167–4.717)	0.017*	2.071 (0.632–6.787)	0.229
Hypertension Indicator: no	1.357 (0.892–2.065)	0.154	1.218 (0.662–2.239)	0.526
Impaired sensorium Indicator: no	2.955 (0.408–21.415)	0.284	NA	NA
Dementia Indicator: no	19.769 (2.504–156.043)	0.005*	NA	NA
Peripheral vascular disease Indicator: no	1.485 (0.469–4.708)	0.501	1.724 (0.407–7.291)	0.459
TIA / CVA Indicator: no	1.965 (0.853–4.527)	0.113	2.067 (0.731–5.843)	0.171
Neurological deficit Indicator: no	0.049 (0–6E + 014)	0.873	NA	NA
Connective tissue disease Indicator: no	0.550 (0.076–3.975)	0.553	0.727 (0.098–5.371)	0.755

(continued)

Table 3 (**continued**)

Disease-free survival				
Parameters	**Univariable analysis: whole cohort**		**Univariable analysis: octogenarians subgroup**	
	OR (95% c.i.)	**P**	**OR (95% c.i.)**	**P**
Peptic ulcer disease Indicator: no	0.295 (0.041–2.119)	0.225	0.049 (0–8E + 011)	0.846
Liver disease Indicator: no	0.639 (0.157–2.598)	0.531	0.046 (0–43.892)	0.379
Hypercoagulability Indicator: no	2.287 (0.835–6.266)	0.108	1.808 (0.556–5.876)	0.325
Chronic kidney disease Indicator: stage 1	1.000 (0.975–1.025)	0.982	0.999 (0.975–1.025)	0.961
Biliary stent Indicator: no	1.099 (0.718–1.684)	0.663	0.608 (0.330–1.123)	0.112
Steroid use prior to operation Indicator: no	1.030 (0.473–2.245)	0.940	2.722 (1.128–6.569)	0.026*
Preoperative haemoglobin	0.911 (0.799–1.038)	0.161	0.938 (0.765–1.151)	0.540
Preoperative bilirubin	1.001 (0.999–1.002)	0.568	1.000 (0.998–1.003)	0.736
Preoperative albumin	0.708 (0.536–0.936)	0.015*	0.632 (0.410–0.972)	0.037*
Neoadjuvant chemotherapy Indicator: no	1.039 (0.256–4.228)	0.957	1.275 (0.174–9.336)	0.811
Neoadjuvant radiotherapy Indicator: no	0.457 (0.064–3.287)	0.437	0.048 (0–7921.938)	0.621
Intraoperative				
Classical or PPPD Indicator: classical	0.687 (0.453–1.042)	0.078	0.807 (0.441–1.475)	0.486
Venous resection Indicator: no	1.057 (0.652–1.713)	0.823	0.741 (0.341–1.607)	0.447
Additional organ resection Indicator: no	0.656 (0.241–1.787)	0.410	0.913 (0.220–3.798)	0.901
Histopathological				
pT Indicator: pT1	1.431 (0.829–2.473)	0.199	1.130 (0.575–2.221)	0.722
Lymph node ratio	7.881 (3.725–16.674)	<0.001*	20.937 (4.727–92.741)	<0.001*
Resection margin Indicator: R0	1.733 (1.129–2.660)	0.012*	0.807 (0.441–1.475)	0.486
Perineural invasion Indicator: no	4.202 (1.541–11.455)	0.005*	5.200 (0.714–37.868)	0.104
Intravascular invasion Indicator: no	2.599 (1.381–4.890)	0.003*	2.334 (0.912–5.973)	0.077
Postoperative				
Postoperative complications Indicator: no	1.288 (0.853–1.944)	0.228	1.201 (0.657–2.196)	0.552
Clavien–Dindo classification based on higher category recorded Indicator: grade I	1.143 (0.964–1.355)	0.124	1.162 (0.902–1.497)	0.245
Adjuvant chemotherapy Indicator: yes	1.090 (0.672–1.767)	0.727	0.791 (0.407–1.540)	0.491

*P values are significant. ECOG, Eastern Cooperative Oncology Group; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; TIA, transient ischaemic attack; CVA, cerebrovascular accident; PPP, pylorus preserving pancreatoduodenectomy; NA, not applicable.

(OR = 0.625; c.i. = 0.446–0.876; $P = 0.006$), lymph node ratio (OR = 6.383; c.i. = 2.713–15.020; $P < 0.001$) and perineural invasion (OR = 7.022; c.i. = 1.684–29.281; $P = 0.007$) as independent predictors of DFS. Of note, age was not significant.

In an effort to identify predictors of mortality that can be used to council octogenarian patients, separate multivariable analyses were performed within that subgroup for all parameters and for preoperative parameters only. Amongst preoperative parameters low ECOG (OR = 15.053; c.i. = 3.552–63.794; $P < 0.001$) and preoperative albumin levels (OR = 0.588; c.i. = 0.381–0.907; $P = 0.016$) were independent predictors of DFS. When the postoperative parameters were also included in the model, lymph node ratio (OR = 10.704; c.i. = 2.148–53.338; $P = 0.004$) was also a significant predictor as shown in *Table S2*.

Discussion

The elderly comprises the fastest expanding portion of Western society and this shift in the population demographics is depicted in the patients being diagnosed with and assessed for treatment for PDAC. Cancer outcomes have taken large strides as a result of centralization and high-volume units bringing together multidisciplinary expertise and advances in perioperative and oncological management[18,19]. These overall improvements in time-dependent mortality have also been observed in the elderly, where risk of mortality before and after 2000 has almost halved[20]. Nonetheless, the elderly population appears to be disadvantaged due to selection bias for aggressive oncological treatment pathways. The reason behind this is the concern over the fitness

of this subset of patients and their ability to withstand the effects of systemic treatment and the stress of surgical resection. Furthermore, even if this is achieved, doubt still rests in any oncological benefit that may be produced in respect to the patients' life expectancy in the 9th decade of their life. The elderly are at a higher risk of mortality from both non-PDAC cancers and non-cancer-related causes[21,22]. Therefore, the propriety of curative treatment needs to take the patient's remnant life expectancy, as well as quality of life, into consideration[23]. Discerning any survival benefit to octogenarians treated for PDAC from the current literature is difficult. This is due to the small proportion of the elderly patients being included within studies or where the age cut-off excludes a significant proportion of elderly patients[24,25]. A vast majority of the literature uses age cut-offs much lower than 80 years to define the 'elderly' and yet the median age of patients presenting with PDAC is 72 years, where only 7 per cent are under 50 years[26–28].

The elderly are frequently affected by reduced physiological reserve from chronic co-morbidities[29–31]. Compounded by PDAC-induced malnutrition, this may result in frailty syndrome and thus a reduced capacity to withstand major stress such as undergoing a PD[32]. Evidence suggests that in well selected octogenarians, perioperative complications[15,21–23] and 30-day and index admission mortality are comparable with younger controls[15]. Ninety-day mortality though was higher (9 per cent *versus* 3 per cent) and co-morbidities such as previous cerebrovascular event or history of dementia were identified as independent predictors, pointing to a general decline with possible failure to reverse this in the community after hospital discharge. On the contrary, age was not an independent predictor of mortality in any multivariable model[15]. Therefore, meticulous assessment and patient selection is of paramount importance when surgical treatment is considered[33]. Additional specialized tests, such as pulmonary function tests, cardiopulmonary exercise testing and echocardiography[33,34], use of frailty scoring systems[35] and assessment of sarcopenia[36,37] should all be carefully considered in the preoperative assessment, accepting their limitations.

With regards to oncological outcomes, OS has been reported as shorter in elderly patients undergoing pancreatic resections, however, the treatment selection bias with regards to receiving standard therapies, such as venous resection and adjuvant chemotherapy, was also highlighted[20]. On the other hand, in subgroup analysis of cohorts that receive adjuvant treatment, no difference in survival was reported[38]. A study of nonagenarians showed that an OS of 20.4 months could be achieved with multimodal therapy, however, 70 per cent of the study group did not receive multimodal therapy[39]. In this study, OS was defined as the time from the date of diagnosis to death rather than from the date of surgery to death. The rationale behind this choice stands in the inclusion of patients who received preoperative chemotherapy, as well as taking into account the differences in the time between diagnosis and surgery or first treatment among the patients. Any disease progression or stability during this time is also a measure of disease biology that primarily affects OS. There was no significant difference in OS or DFS between octogenarians and controls. The recorded OS in the octogenarian subgroup of 20 months is consistent with the range of 15–30 months in the published literature[40,41]. Similarly, there is also no demonstrable difference in DFS between the elderly and younger groups where use of adjuvant therapy has been shown to be an independent prognostic variable[41,42]. On risk analysis, history of cardiac co-morbidities and low preoperative albumin were identified as independent predictors of both OS and DFS. High lymph node ratio and perineural were also identified as predictors of oncological outcomes (OS and DFS respectively). The significance of low preoperative albumin levels persisted after analysis of only preoperative variables. Low albumin levels may indicate a status of relative malnutrition which would predispose the patient to prolonged hospitalization and recovery[43] and in turn reduce the opportunity to be offered any adjuvant treatment. Similarly, cardiac history may prevent or limit the use of systemic treatment due to the described chemotherapy-related cardiotoxicities[44]. The fact that elderly patients are in general less likely to receive any systemic treatment has been documented by various studies[45] (possibly due to the concerns regarding tolerability of multiagent regimens), even though evidence supports their safety and efficacy resulting in comparable survival to younger cohorts[8,46,47]. Elderly patients are more likely to receive reduced doses of adjuvant chemotherapy and only in the presence of lymph-node-positive disease[40], a treatment selection bias which is not present in younger patients[22].

Limitations of this study include its retrospective nature and the consequent inability to also assess parameters that have not been captured such as frailty and quality of life, type of systemic treatment and follow-up. Details of cause of death after hospital discharge were lacking, hence the inability for any non-cancer-related mortality to be assessed. Nonetheless, this is a multicentre study over a 10-year interval on a large cohort of patients that are underrepresented in the published surgical literature for the management of PDAC. Matching for the extent of surgery was also utilized to account for any possible intraoperative selection bias for utilizing a more radical surgical technique.

In summary, octogenarians with PDAC of the head and uncinate process benefit from comparable oncological outcomes to younger patients with surgical treatment after careful preoperative assessment and patient selection, which should be the focus of future studies.

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The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS Open* online.

Data availability

The data sets generated during and/or analysed during the present study are available from the corresponding author on reasonable request.

Author contributions

Rupaly Pande (Data curation, Formal analysis, Writing—original draft), Joseph Attard (Data curation, Formal analysis, Writing—review & editing), Bilal Al-Sarireh (Data curation, Writing—review & editing), Ricky Bhogal (Data curation, Writing—review &

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