

## Supplementary Materials

**Table S1** – Descriptive statistics of the study population.

IQR: interquartile range; AST: aspartate aminotransferase; ALT: alanine aminotransferase; AP: alkaline phosphatase; GGT: gamma-glutamyl transferase; BR: bilirubin; CA 19.9: carbohydrate antigen 19.9; CEA: carcinoembryonic antigen; CPD: cephalic pancreaticoduodenectomy; DDP: distal pancreatectomy; TDP: total pancreatectomy; CT: chemotherapy; RT: radiotherapy

Variable	N=148
<b>Age</b>	
Median (IQR)	70 (61-76)
Min-Max	40-93
<b>Sex</b>	
Male	93 (62.8%)
Female	55 (37.2%)
<b>Arterial hypertension</b>	88 (59.5%)
<b>Dyslipidemia</b>	55 (37.2%)
<b>Type 2 Diabetes mellitus</b>	55 (37.2%)
Metformin	28 (18.9%)
<b>Past history of other cancers</b>	17 (11.5%)
<b>Abdominal pain</b>	64 (43.2%)
<b>Jaundice</b>	93 (62.8%)
<b>Charlson comorbidity index</b>	
Median (IQR)	5 (4-6)
Min-Max	0-11
<b>Preoperative sodium (mEq/L)</b>	
Median (IQR)	137.0 (135.0-140.0)
Min-Max	124.0-144.7
<b>Preoperative AST (U/L)</b>	
Median (IQR)	60.0 (28.0-131.0)
Min-Max	9-668
<b>Preoperative ALT (U/L)</b>	
Median (IQR)	72.0 (31.0-170.5)
Min-Max	7-922
<b>Preoperative AP (U/L)</b>	
Median (IQR)	278.5 (118.5-458.0)
Min-Max	38-2100
<b>Preoperative GGT (U/L)</b>	
Median (IQR)	250.5 (69.3-635.8)
Min-Max	10-3001
<b>Preoperative total BR (mg/dL)</b>	
Median (IQR)	8.4 (1.0-17.2)
Min-Max	0.2-31.7
<b>Preoperative direct BR (mg/dL)</b>	
Median (IQR)	8.7 (2.5-14.1)
Min-Max	0.4-347.0
<b>Preoperative albumin (g/dL)</b>	
Median (IQR)	3.7 (3.3-4.2)
Min-Max	1.7-41.0
<b>Preoperative CA 19.9 (U/mL)</b>	
Median (IQR)	225.8 (36.3-978.8)

Min-Max	2.0-23911.0
<b>Preoperative CEA (ng/mL)</b>	
Median (IQR)	3.3 (1.9-6.1)
Min-Max	0.6-179297.0
<b>Prolonged hospitalization (≥17 days)</b>	83 (56.1%)
<b>Type of Surgery</b>	
CPD	124 (83.8%)
DP	17 (11.5%)
TP	7 (4.7%)
<b>Clavien-Dindo</b>	
No complications	24 (16.2%)
I	21 (14.2%)
II	57 (38.5%)
IIIa	20 (13.5%)
IIIb	5 (3.4%)
IVa	2 (1.4%)
IVb	4 (2.7%)
V	13 (8.8%)
<b>Postoperative pancreatic fistula (POPF)</b>	
No	93 (62.8%)
BL	20 (13.5%)
B	12 (8.1%)
C	12 (8.1%)
<b>Delayed gastric emptying (DGE)</b>	
No	61 (41.2%)
A	44 (29.7%)
B	25 (16.9%)
C	16 (10.8%)
<b>Adjuvant treatment</b>	
No	58 (39.2%)
CT	46 (31.1%)
CT+RT	40 (27.0%)

**Table S2 – Descriptive statistics of pathological characteristics.**  
IQR: interquartile range

<b>Variable</b>		<b>N=148</b>
<b>Stage</b>	I	28 (18.9%)
	II	77 (52.0%)
	III	31 (20.9%)
	IV	12 (8.1%)
<b>T</b>	T1	14 (9.5%)
	T2	97 (65.5%)
	T3	37 (25.0%)
	T4	0 (0%)
<b>N</b>	N0	35 (23.6%)
	N1	79 (53.4%)
	N2	34 (23.0%)
<b>Metastases</b>	M0	133 (89.9%)
	M1	15 (10.1%)
<b>Resected lymph nodes</b>		
	Median (IQR)	18 (13-25)
	Min-Max	3-62
<b>Invaded lymph nodes</b>		
	Median (IQR)	2 (1-3)
	Min-Max	0-12
<b>Lymph nodes ratio</b>		
	Median (IQR)	009 (0.03-0.19)
	Min-Max	0.00-0.86
<b>Histological grade</b>		
	Well differentiated (G1)	49 (33.1%)
	Moderately differentiated (G2)	76 (51.4%)
	Poorly differentiated (G3)	12 (8.1%)
<b>Perineural invasion</b>		133 (89.9%)
<b>Lymphovascular invasion</b>		117 (79.1%)
<b>Resection margin</b>		
	R0	73 (49.3%)
	R1	66 (44.6%)
	R2	9 (6.1%)
<b>Tumor size (cm)</b>		
	Median (IQR)	3,2 (2.5-4.0)
	Min-Max	0.4-11.0

**Table S3** – Influence of other variables on overall survival (OS).

OS: overall survival; AST: aspartate aminotransferase; ALT: alanine aminotransferase; AP: alkaline phosphatase; GGT: gamma-glutamyl transferase; CEA: carcinoembryonic antigen; CPD: cephalic pancreaticoduodenectomy; POPF: postoperative pancreatic fistula; DGE: Delayed gastric emptying; CT: chemotherapy; RT: radiotherapy

Variable	Median OS (months)	<i>p</i>
<b>Age</b>		
<70	18	0.345
≥70	18	
<b>Sex</b>		
Male	18	0.749
Female	19	
<b>Dyslipidemia</b>		
No	18	0.698
Yes	17	
<b>Metformin</b>		
No	16	0.437
Yes	13	
<b>Past history of other cancers</b>		
No	18	0.337
Yes	18	
<b>Jaundice</b>		
No	17	0.075
Yes	20	
<b>Preoperative hyponatremia (&lt;135 mEq/L)</b>		
No	19	0.430
Yes	16	
<b>Preoperative AST</b>		
Normal	19	0.800
High (≥35 U/L)	17	
<b>Preoperative ALT</b>		
Normal	19	0.079
High (≥45 U/L)	17	
<b>Preoperative AP</b>		
Normal	20	0.956
High (≥120 U/L)	17	
<b>Preoperative GGT</b>		
Normal	21	0.382
High (≥55 U/L)	17	
<b>Preoperative hypoalbuminemia (&lt;3,5 g/dL)</b>		
No	18	0.632
Yes	17	
<b>Preoperative CEA</b>		
≤5 ng/mL	21	0.764
>5 ng/mL	17	
<b>Type of surgery</b>		
CPD	18	0.333
Others	18	
<b>Surgery duration</b>		
<7h	20	0.711
≥7h	18	
<b>Blood transfusion</b>		
No	17	0.851
Yes	19	
<b>POPF</b>		
No	18	0.788
Yes	20	
<b>POPF grade</b>		

<i>Biochemical leak</i>	24	
Grade B e C	13	0.082
<b>DGE</b>		
Grade A	21	
Grade B ou C	15	0.414
<b>Histological grade</b>		
Well differentiated	19	
Moderately/poorly differentiated	17	0.203
<b>Perineural invasion</b>		
No	30	
Yes	17	0.906
<b>Type of adjuvant treatment</b>		
CT	21	
CT+RT	21	0.785
<b>Local recurrence</b>		
No	19	
Yes	18	0.124
<b>Distant recurrence</b>		
No	18	
Yes	17	0.390
<b>Local and distant recurrence</b>		
No	18	
Yes	19	0.899
<b>Pulmonary recurrence</b>		
No	19	
Yes	17	0.480
<b>Hepatic recurrence</b>		
No	20	
Yes	15	0.127
<b>Pulmonary and hepatic recurrence</b>		
No	18	
Yes	21	0.739
<b>Peritoneal recurrence</b>		
No	19	
Yes	18	0.280

**Table S4** – Influence of other variables disease-free survival (DFS).

DFS: disease-free survival; AST: aspartate aminotransferase; ALT: alanine aminotransferase; AP: alkaline phosphatase; GGT: gamma-glutamyl transferase; CEA: carcinoembryonic antigen; CPD: cephalic pancreaticoduodenectomy; POPF: postoperative pancreatic fistula; DGE: delayed gastric emptying; CT: chemotherapy; RT: radiotherapy

Variable	Median DFS (months)	<i>p</i>
<b>Age</b>		
<70 years	10	
≥70 years	10	0.698
<b>Sex</b>		
Male	10	
Female	10	0.631
<b>Arterial hypertension</b>		
No	10	
Yes	10	0.331
<b>Dyslipidemia</b>		
No	10	
Yes	10	0.359
<b>Type 2 Diabetes mellitus</b>		
No	10	
Yes	9	0.244
<b>Metformin</b>		
No	10	
Yes	9	0.625
<b>Past history of other cancers</b>		
No	10	
Yes	7	0.537
<b>Abdominal pain</b>		
No	10	
Yes	10	0.140
<b>Jaundice</b>		
No	11	
Yes	10	0.851
<b>Preoperative hyponatremia (&lt;135 mEq/L)</b>		
No	10	
Yes	9	0.345
<b>Preoperative ALT</b>		
Normal	12	
High (≥45 U/L)	9	0.229
<b>Preoperative AP</b>		
Normal	12	
High (≥120 U/L)	10	0.352
<b>Preoperative GGT</b>		
Normal	12	
High(≥55 U/L)	10	0.366
<b>Preoperative hypoalbuminemia (&lt;3,5 g/dL)</b>		
No	10	
Yes	7	0.152
<b>Preoperative CEA</b>		
≤5 ng/mL	11	
>5 ng/mL	8	0.572
<b>Type of surgery</b>		
CPD	10	
Others	12	0.714
<b>Surgery duration</b>		
<7h	10	
≥7h	9	0.246
<b>Blood transfusion</b>		

	No	9	
	Yes	11	0.872
<b>Clavien-Dindo</b>			
	I, II, IIIa	10	
	IIIb, IV, V	6	0.500
<b>POPF</b>			
	No	10	
	Yes	8	0.345
<b>POPF grade</b>			
	<i>Biochemical leak</i>	10	
	Grade B e C	8	0.809
<b>DGE</b>			
	Grade A	10	
	Grade B ou C	6	0.442
<b>Stage</b>			
	I-II	10	
	III-IV	6	0.448
<b>T</b>			
	T1-2	10	
	T3-4	10	0.889
<b>Lymph nodes</b>			
	N0	12	
	N+	10	0.114
<b>Histological grade</b>			
	Well differentiated	10	
	Moderately/poorly differentiated	10	0.565
<b>Perineural invasion</b>			
	No	12	
	Yes	10	0.336
<b>Lymphovascular invasion</b>			
	No	11	
	Yes	10	0.723
<b>Resection margin</b>			
	R0	11	
	R1-2	8	0.119
<b>Tumor size (cm)</b>			
	≤2	13	
	>2	10	0.924
<b>Adjuvant treatment</b>			
	No	8	
	Yes	10	0.416
<b>Type of adjuvant treatment</b>			
	CT	10	
	CT+RT	10	0.999