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Surgical outcomes of pancreaticoduodenectomy in young patients: Case series study

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## **Surgical Outcomes of Pancreaticoduodenectomy in Young Patients: Case series study**

### **Abstract**

**Background:** Pancreaticoduodenectomy (PD) is a complex procedure for management periampullary neoplasms. The aim of our work is to report the surgical outcomes after PD in young adult (YA) (< 35 years) and to compare it to adult patients who underwent PD.

**Methods:** We retrospectively analyzed the data of all patients who underwent PD in the period from January 1993 to December 2016. The primary outcome was the rate of total postoperative complications. Secondary outcomes included postoperative pathology, exocrine and endocrine function and survival rate.

**Results:** 58/975 patients (5.9%) were YA and the majority of them were females. The incidence of post-operative complications in the YA was comparable to that in the adult group. Delayed gastric emptying developed significantly in adult group than YA group (0.008). The overall survival was significantly higher in the YA ( $P = 0.0001$ ). The most common pathology in the YA was adenocarcinoma (41.4%) and solid pseudopapillary tumor (SPT) (29.3 %). No significant difference as regards postoperative pancreatic exocrine and endocrine function in both groups.

**Conclusion:** PD in YA when performed in tertiary centers with good surgical experience is safe. The most common pathological diagnosis in the YA was adenocarcinoma followed by SPT.

**Key words:** Pancreaticoduodenectomy, periampullary neoplasms, pancreatic exocrine and endocrine function, solid pseudopapillary tumor, Delayed gastric emptying

## Introduction

Pancreaticoduodenectomy (PD), a complex radical procedure, is considered a cornerstone in the management of pancreatic head and periampullary neoplasms [1]. The procedure entails resection of the pancreatic head and performing a challenging pancreatic anastomosis which requires certain degree of surgical training and expertise. Due to the complexity of the procedure, a significant risk of morbidity and mortality exists. The incidence of post-operative complications after PD is reported to range from 20 to 40% [1-3].

Many studies were performed trying to identify factors increasing the risk of post-operative complications. These risk factors included patient's age, body mass index, pre-operative jaundice, intra-operative blood loss, consistency of the pancreas, pancreatic duct diameter, type of pancreatic reconstruction, use of somatostatin analogues and surgeon's experience [4-7].

As pancreatic and periampullary pathologies are uncommon in young populations, Pancreaticoduodenectomy (PD) is not a frequently performed procedure in pediatric and young adults [8-10]. In a statistical review performed by the National Cancer institute, the incidence of pancreatic tumors in young population (below 19 years) is 0.19 per million populations [11, 12].

Given this rare incidence in young adult population, the impact of young age on the short-term and long-term outcomes after PD is not well studied. In fact the literature is relatively deficient in this area with the largest published series to our knowledge only including 22 patients [13].

The aim of our work is to report the surgical outcomes after PD in young adult population (< 35 years) and to compare it to a cohort of adult patients who underwent PD at our institute at the same study period.

## Patients and Methods

After Institutional Review Board approval, we retrospectively analyzed the data of all patients who underwent PD at Gastro-intestinal Surgical Center, in the period from

January 1993 to December 2016. The hospital peri-operative records have had the policy of entering the data in a prospectively maintained database since 2000 and before 2000, the data were collected from the patients files. The data included demographic data, operative measuring the pancreatic and bile duct diameters intra-operatively and postoperative outcomes. It is a routine to record the history to rule out exocrine pancreas dysfunction. Patients under 35 years were defined as young adults according to previous studies [14, 15]. The adult cohort represents adult patients who underwent PD in the same study period at our institute. Patients data were collected in a web based hospital registry. **This case series study has been reported in line with the PROCESS criteria [16]**

#### Operative technique

All patients underwent a subtotal stomach preserving PD through a bilateral subcostal incision. The dissection was performed using diathermy with ligation of major vessels and recently, harmonic or ligasure was introduced and used in dissection. The bile duct and pancreatic diameters were measured by a ruler. Pancreatic texture was defined soft or firm according to the operating surgeon or the senior assisting surgeon. All patients underwent regional lymphadenectomy, which included resection of nodes to the right side of the superior mesenteric vessels, and inferior vena cava (retropancreatic, supradudenal, peripancreatic, hepatic artery, infrapyloric, subpyloric , hepatic artery, celiac).

Our Institutional policy on pancreatic reconstruction method included pancreatico-gastrostomy (PG), simple loop pancreatico-jejunostomy (PJ) and isolated loop PJ [17-20]. Duct to mucosa or invaginated type was performed. These techniques are described in details in previous papers (17-20). Biliary reconstruction was

performed by end-to-side hepaticojejunostomy HJ (retrocolic), Gastric reconstruction was performed by an antecolic end-to-side gastrojejunostomy GJ 30 cm distal to the HJ. The type of reconstruction depends on surgeon choice or on randomization in the randomized study [17-20].

#### Post-operative management

Post-operatively, all patients routinely received intra-venous antibiotics and proton pump inhibitors. Somatostatin analogues were administered routinely for 4 post-operative days (100  $\mu$ g octreotide subcutaneously every 8 hours). Vital parameters and drain outputs were recorded every hour for the first day then at a 4 hours interval afterwards.

Abdominal drains amylase levels were measured at the first, third and fifth post-operative days. Trans-abdominal ultrasonography was done only on clinical suspicion of any abdominal collections. In patients with smooth post-operative course oral intake was resumed on the 4th post-operative day.

#### Definition of complications

The severity of post-operative complications was graded according to the Dindo–Clavien complication classification system [21].

Regarding post-operative pancreatic fistula (POPF), the International Study Group for Pancreatic Fistula (ISGPF) definition was followed (high amylase content of the drainage fluid,  $>3$  times the upper normal serum value, at any time on or after 3rd postoperative day. POPF was graded according to the ISGPF into grade A, B and C according to the clinical course and the need for specific treatment or intervention [22].

Bile leak was defined according to the ISGPF as the presence of bile in the drained fluid persisting to post-operative day 4 [22]. As for delayed gastric emptying, the International Study Group of pancreatic Surgery (ISGPS) definition and grading was implemented [23].

Pancreatic exocrine function was evaluated by asking about the presence or absence of steatorrhea, presence of excess fat in the stool as a result of fat malabsorption (bulky stool that floats has pasty or greasy appearance, a foul smell, and it tends to stick on the sides of the toilet). Definition of pancreatic exocrine insufficiency is weak but there is a problem in detecting the fat in stool because the tests for detection unreliable postoperatively in our center so we depend on clinical history of steatorrhea. Endocrine function was assessed by measuring fasting blood glucose level (normal level : < 110 mg/dl). Diabetes mellitus (DM) was diagnosed based on World Health Organization study group on DM [24, 25].

Patients were followed up 1 week after discharge then at 1, 3, 6 months intervals.

### ***Assessments:***

The primary outcome was the rate of total postoperative complications. The severity of post-operative complications was graded according to the Dindo–Clavien complication classification system [21]. Secondary outcomes included total operative time (hours), hospital mortality, length of postoperative stay (days), time to resume oral intake, postoperative pathology, re-exploration, and survival rate.

### ***Statistical analysis***

Categorical variables are expressed as group percentages and were compared for independent samples using Chi-square test. Continuous data are presented as medians and were compared for independent samples using t test. Survival was calculated and plots constructed according to the Kaplan-Meier method and life table method. The log-rank test was used for comparison of survival according to type of pathology (adenocarcinoma group and solid pseudopapillary tumour). All statistical tests were 2-sided, and the significance level was set at <0.05. Statistical analyses were performed using SPSS version 17 (Chicago, IL).

## **Results**

### ***Patients' characteristics***

Patients` demographics and baseline data are represented in table 1,2. A total of 975 patients were included in this study. The young adult (YA) cohort (< 35 years) included 58 patients.

***Operative data*** is demonstrated in table 3.

### ***Early post-operative outcomes***

The overall incidence of post-operative complications in the YA cohort was 36.3 % which was comparable to that in the adult group (32.5 %). Delayed gastric emptying (DGE) developed significantly in adult group II than YA group (0.008). Diabetes has no significant impact on development of DGE in both groups (Table 3).

**Survival in both groups** is shown in Table 4 and Fig 1(a-d).

***Postoperative pathology*** is shown in table 5

The most common pathological diagnosis in the YA cohort was adenocarcinoma (41.4%) followed by solid pseudopapillary tumor (SPT) (29.3 %).

### ***Pancreatic exocrine and endocrine function***

No significant difference as regards postoperative pancreatic exocrine and endocrine function in both groups Table 6.

## Discussion

Surgical resection remains the gold standard in the management of peri-ampullary neoplasms [1,3, 26-28]. Due to the complexity of the procedure, the main concern is the significant incidence of post-operative morbidity and mortality. Since the introduction of pancreaticoduodenectomy, many modifications in the surgical techniques have been made in attempt to decrease the risk of the associated complications [29-31]. However, recent studies in the literature still report significant morbidity and mortality rates [32-35].

Due to the rarity of pancreatic head and peri-ampullary neoplasm in pediatric and young adult populations, most of reports in the literature address PD in adults with a minority of series in the young adults and pediatric population [11-13, 35, 36].

In this study we describe the largest series of PD in young adult population to our knowledge and comparing them to an adult cohort performed at our institute at the same study period.

After analysis of the patients' demographic characteristics we found that the number of females was significantly higher than males in the young adult group compared to the adult patients. A possible explanation is that the second most common pathology in our series is SPT which is known to be more common in females [37, 38]. This finding is similar to what Mansfield et al. [13] reported in their series of PD in 22 young adults where the females represented 54.5 % of their study group and the second common pathology was SPT (22.7 %).

Regarding patients' presentation pre-operatively we noticed that although 70.7 % of the YA group presented with obstructive jaundice, this percentage was significantly lower than that for the adult group (90.2 %) ( $P = 0.001$ ). Also the percentage of these patients requiring pre-operative drainage was lower in the YA group ( $P = 0.002$ ). This finding could also be explained by the large subset of patients with SPT in the YA group. This is similar to several reports in the literature stating the low incidence of obstructive jaundice in cases with SPT which is mostly due to the low malignant behavior of the tumor [37-41]. In contrary, in a study reported by Lindholm et al. [35] on 12 young patients, obstructive jaundice was the second most common presentation after abdominal pain (34 %), however, SPT represented only 3



cases in their series and of the 4 patients presenting with jaundice, 3 were diagnosed with recurrent disease.

The median mass size was significantly larger in the YA group. This could also be attributed to the higher incidence of SPT which tends to reach larger sizes than adenocarcinoma [42].

The comparable rates of overall complications in our study between both groups support the relative safety of PD in young adult patients. Previous reports in the literature estimates the incidence of morbidity and mortality rates of PD in adults to be 30-40 % and 1-3 % respectively [1-3, 42-44]. In our study, the complications rate in the YA group was 36.3 % which is consistent with previous reports regarding PD in young / pediatric patients [13, 35, 36, 39, 45]. However, the 30 days' hospital mortality rate in our series was 1.7 % (one patient) which is slightly higher than the 0 % mortality reported in previous small series pediatric reports [13, 35, 39].

DGE is a common morbidity after PD, its incidence ranged from 15- 44 %. It is not a life-threatening complication, but it is associated with prolonged postoperative stay, affecting quality of life, and increased total cost. DGE may be primary or secondary to presence of complications. Primary DGE appears as a multifactorial phenomenon that is associated with the patient's characteristics (age, sex, presence of diabetes, obesity), type of surgical resection, type of reconstruction and post-operative cares [18, 23]. In our study, delayed gastric emptying (DGE) developed significantly in adult group II than YA group and diabetes has no significant impact on development of DGE in both groups

POPF, which is considered an Achilles heel in PD, was thought to be significantly higher in young patients due to the softer texture of the pancreatic stump. In our series, although the YA group had higher incidence of soft pancreatic texture and POPF was the most common complication to occur (19 %), yet no statistically significant difference existing between both groups regarding POPF. This incidence is higher to what Mansfield et al. reported in their study (POPF, 4.5 %), however, in their study 6 patients (27.3 %) had chronic pancreatitis which may owe to more fibrotic texture of the pancreas with fewer leaks [13]. In YA the technique of pancreatic reconstruction is more difficult, challenging and need experience than in

adult because the pancreas more softer, less fibrotic, smaller, in thickness/ diameter [10].

Several studies reported that when using a novel technique based on axial specimen dissection with extensive tissue sampling and reporting margin involvement if tumour cells are present within 1 mm from the margin not 0 mm, the R1 rate increases markedly, from 20% to more than 70% [46-48]. The R1 rate is low in this study as the traditional techniques were used, the main pancreatic duct and CBD are probed and the specimen is sliced once or several times along the plain defined by both probes (bivalving and multivalving technique) or the pancreatic head is serially sliced along a plane perpendicular to the longitudinal axis of the pancreatic neck (bread loaf slicing technique) [46-48]. Recently, our pathologist shifted to axial specimen dissection with extensive tissue sampling

The overall median survival in our series was significantly better in the YA adult than adult group. This could be explained by the higher frequency of SPT in the YA group. However, in contrast to Mansfield report [13] the median survival of YA patients with pancreatic adenocarcinoma was significantly better than the adult cohort (34 and months respectively).

Many studies have found that exocrine pancreatic function after PD depends on several complex factors, including pre-existing obstructive pancreatitis by tumour, , the volume of remnant pancreatic parenchyma and degree of fibrosis, anastomotic stricture or swelling of the gastric mucosa that impair the flow of pancreatic juice, and possibly the type of pancreatic reconstruction as in pancreaticogastrostomy, reflux of gastric juice causes the inactivation of pancreatic enzymes and early pancreatic insufficiency [19,20,25]. In the current study, no significant difference as regards

development of postoperative pancreatic exocrine and endocrine dysfunction in both groups.

Although this is the largest series of PD in young patients to our knowledge, there are some study limitations. Firstly, the adult cohort collected from data base included all adult patients regardless their general health and co-morbidities. Secondly, this series was performed by different surgeons using 3 different techniques in pancreatic reconstruction. Thirdly, in this study definition of pancreatic exocrine insufficiency is very weak, as it depends on clinical development of steatorrhea or the need of exogenous pancreatic enzymes

Conclusion: The majority of patients in the YA who underwent PD were females. The incidence of pre-operative jaundice and pre-operative biliary drainage were significantly higher in the adult group. The overall incidence of post-operative complications in the YA was comparable to that in the adult group. DGE is significantly more in adult group than in YA. The overall survival in the YA was significantly higher than the adult group. The most common pathological diagnosis in the YA was adenocarcinoma followed by solid pseudopapillary tumor. No significant difference as regards postoperative pancreatic exocrine and endocrine function in both groups. This study concludes that PD in YA when performed in tertiary centers with good surgical experience is safe.

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**Figure Legend**

Fig (1a): Actuarial survival (Kaplan-Meier analysis) after PD for adenocarcinoma: influence of age

Fig (1b): Actuarial survival (life table analysis) after PD for adenocarcinoma : influence of age

Fig (1c): Actuarial survival (Kaplan-Meier analysis) after PD for Solid pseudopapillary tumour: influence of age

Fig (1d): Actuarial survival (life table analysis) after PD for Solid pseudopapillary tumour: influence of age

Table (1) : Demographic data and surgical outcome over 3 periods

Variables	Total (975)	First 10 years 1993-2002	Second 10 years 2003-2012	Last 5 years 2013-2016	P value
Number of cases	975	300	442	233	
Median age (years)	54 (12-88)	53	55	55	0.21
<35 years	58 (5.9%)	17 (5.7%)	24 (5.4%)	17 (7.3%)	0.6
>35 years	917 (94.1%)	283 (94.3%)	418 (94.6%)	216 (92.7%)	
Sex n (%)					0.31
Male	599 (61.4%)	190 (63.3%)	260 (58.8%)	149 (63.9%)	
Female	376 (38.6%)	110 (36.7%)	182 (41.2%)	84 (36.1%)	
Pre-operative biliary drainage n (%)	504 (51.7%)	163 (54.5%)	226 (51.1%)	(49.4%)	0.15
Cirrhosis	123 (12.6%)	28 (9.3%)	62 (14%)	33 (14.2%)	0.01
Type of reconstruction					0.0001
PG	769 (75.9%)	235 (78.3%)	417 (94.3%)	117 (50.2%)	
Simple PJ	160 (16.4%)	65 (21.7%)	25 (5.7%)	70 (30%)	
Isolated loop PJ	46 (4.7%)	0	0	46 (19.8%)	
Standard approach	883 (90.6%)	277 (92.3%)	388 (87.8%)	218 (93.6%)	0.004
Posterior approach	92 (9.4%)	23 (7.7%)	54 (12.2%)	15 (6.4%)	
Complete mesopancreatectomy	549	83 (27.7%)	233 (52.7%)	233 (100%)	0.0001
Laparoscopic assisted PD	9 (0.9%)	0	0	9	0.08
Complete laparoscopic PD	8 (0.8%)	0	0	8	
Hospital stay (days)	8 (5-71)	9	8	8	0.0001
Total postoperative complications	319 (32.7%)	120 (40%)	131 (29.6%)	68 (29.2%)	0.02
Pancreatic fistula	137 (14.1%)	45 (15%)	56 (12.7%)	36 (15.5%)	0.01
DGE	178 (18.3%)	76 (25.3%)	67 (15.2%)	35 (15%)	0.01
Bile leak	69 (7.1%)	39 (13%)	19 (4.3%)	11 (4.7%)	0.001
Hospital mortality	43 (4.4)	20 (6.6%)	15 (3.4%)	8 (3.4%)	0.006
Postoperative chemoradiotherapy	250 (25.6%)	0	132 (29.9%)	118 (50.6%)	0.01

Table (2) : Demographic and preoperative data

Variables	Total (975)	<35 years (58)	>35 years (917)	
Age (years) (median)	54 (12-88)	31 (12-35)	55 (36-88)	0.0001
Sex n (%)				
Male	599 (61.4%)	23 (39.7%)	576 (62.8%)	0.0001
Female	376 (38.6%)	35 (60.3%)	341 (37.2%)	
DM n (%)	140 (14.7%)	5 (8.6%)	135 (14.7%)	0.19
Abdominal pain n (%)	712 (73%)	47 (81%)	665 (72%)	0.06
Jaundice n (%)	868 (89%)	41 (70.7%)	827 (90.2%)	0.001
Pre-operative biliary drainage n (%)	504 (51.7%)	19 (32.8%)	485 (52.9%)	0.002
Preoperative serum albumin (gm%)	4 (3.2-5.2)	4.3 (3.2-5.2)	4 (3.3-5.1)	0.85
Preoperative serum bilirubin (mg%)	4 (0.5-38)	1.7 (0.5-38)	4 (0.5-38)	0.58
Preoperative CEA	6.4 (0.5-394)	5.2 (0.5-322)	6.4 (0.5-394)	0.51
Preoperative CA19-9	27 (0.5-1200)	34 (0.5-1080)	26 (0.5-1200)	0.02

Table (3) : Operative data

Variables	Total (975)	<35 years (58)	>35 years (917)	
Mass size (cm) median	3 (0.5-15)	4 (1-15)	3 (0.5-10)	0.001
< 2 cm	399 (4.9%)	19 (32.8%)	380 (41.4%)	0.15
> 2 cm	576 (59.1%)	39 (67.2%)	537 (58.6%)	
Pancreatic texture				
Soft	571 (58.6%)	37 (63.8%)	534 (58.2%)	0.52
Firm	404 (41.4%)	21 (36.2%)	383 (41.8%)	
Median pancreatic duct diameter	5 (1-15)	4 (1-12)	5 (1-15)	0.18
< 3 mm	292 (29.9%)	20 (34.5%)	272 (29.7%)	0.77
> 3mm	683 (70.1%)	38 (65.5%)	645 (70.3%)	
Pancreatic duct to posterior border(mm)				
< 3 mm	407 (41.7%)	16 (27.6%)	391 (42.6%)	0.02
> 3mm	568 (58.3%)	42 (72.4%)	526 (57.4%)	
Pancreatic stump mobilization (cm)	2 (1-4))	2 (1-3)	2 (1-4)	0.12
CBD diameter (mm)	15 (5-30)	13 (5-22)	16 (6-30)	0.003
Type of reconstruction				
PG	769 (78.9%)	46 (79.3%)	723 (78.8%)	0.26
Simple PJ	160 (16.4%)	7 (12.1%)	153 (16.7%)	
Isolated loop PJ	46 (4.7%)	5 (8.6%)	41 (4.5%)	
Operative time (hours)	5 (3.5-10)	5 (3.5-7)	5 (3.5-10)	0.21
Blood loss (cc)	500 (50-4000)	500 (50-4000)	500 (50-3000)	0.08

Table (4) : Postoperative data

Variables	Total (975)	<35 years (58)	>35 years (917)	
Hospital stay (days)	8 (5-71)	8 (5-60)	8 (5-71)	0.17
Time to oral intake (days)	5 (4-56)	5 (4-9)	5 (4-56)	0.002
Total amount of drainage (ml)	700 (40-35000)	650 (170-8000)	700 (40-35000)	0.06
Drain removal (days)	8 (4-71)	8 (4-60)	8 (5-71)	0.36
Total postoperative complications	319 (32.7%)	21 (36.3%)	298 (32.5%)	0.56
Dindo grade				
I	113 (11.6%)	9 (15.5%)	104 (11.3%)	0.91
II	96 (9.8%)	6 (10.3%)	90 (9.8%)	
III	67 (6.9%)	5 (8.6%)	62 (6.8%)	
IV and V	43 (4.4%)	1 (1.7%)	42 (7.4%)	
Severe complications ( $\geq$ III)				
Minor	209 (21.4%)	15 (25.9%)	194 (21.2%)	0.81
Major	110 (11.3%)	6 (10.3%)	104 (11.3%)	
Pancreatic fistula	137 (14.1%)	11 (19%)	126 (13.7%)	0.27
Grade A	67 (6.9%)	8 (13.8%)	59 (6.4%)	0.19
Grade B	47 (4.8%)	2 (3.4%)	45 (4.9%)	
Grade C	23 (2.4%)	1 (1.7%)	22 (2.4%)	
DGE	178 (18.3%)	3 (5.2%)	175 (19.1%)	0.008
Types of DGE				
Secondary DGE	151 (15.5%)	3 (5.2%)	148 (16.1%)	0.03
Primary DGE	27 (2.8%)	0	27 (2.9%)	
Pulmonary complications	46 (4.6%)	4 (6.9%)	42 (4.7%)	0.44
Bile leak	69 (7.1%)	2 (3.4%)	67 (7.3%)	0.28
Internal haemorrhage ( <b>Postoperative bleeding</b> )	25 (2.6%)	3 (5.2%)	22 (2.4%)	0.44
Pancreatitis	20 (2.1%)	0	20 (2.2%)	0.25
Bleeding PG	15 (1.5%)	2 (3.4%)	13 (1.4%)	0.24
Wound infection	49 (5%)	2 (3.4%)	47 (5.2%)	0.55
Re-operation	72 (7.4%)	5 (8.6%)	67 (7.5%)	0.75
Recurrence n (%)	89 (9.1%)	1 (1.7%)	88 (9.8%)	0.04
Hospital mortality	43 (4.4%)	1 (1.7%)	42 (4.7%)	0.46
Overall median survival (months)	24 (1-300)	35 (1-300)	24 (1-250)	0.0001
1-year	65%	81%	64%	
3-year	29%	72%	26%	
5-year	16%	58%	13%	
SPT median survival	232	280	114	0.05
1-year	95%	94%	100%	
3-year	95%	94%	100%	
5-year	95%	94%	100%	

Table (5) : Postoperative pathology

Variables	Total (975)	<35 years (58)	>35 years (917)	
Site of the tumour				
Ampullary tumour	306 (31.4%)	11 (19%)	295 (32.2%)	0.02
Pancreatic head mass	554 (56.8%)	42 (72.4%)	512 (55.8%)	
CBD duct tumour	37 (3.8%)	0	37 (4 %)	
Duodenal tumour	59 (6.1%)	5 (8.6%)	54 (5.9%)	
Uncinate process mass	19 (1.9%)	0	19 (2.1)	
Pathological diagnosis				
Solid pseudopapillary tumor SPT	20 (2.1%)	17 (29.3)	3 (0.3%)	0.0001
Chronic pancreatitis	23 (2.4%)	1 (1.7%)	22 (2.4%)	
Adenocarcinoma	812 (83.3%)	24(41.4%)	788 (85.9%)	
Neuroendocrine tumor	28 (2.9%)	6 (10.31%)	22 (2.4%)	
Benign cyst	12 (1.2%)	6 (10.3%)	6 (0.7%)	
Lymphoma	3 (0.3%)	1 (1.7%)	2 (0.3%)	
Adenoma with dysplasia	41 (42.1%)	2 (3.4)	39 (4.3%)	
Gastrointestinal stromal tumour (GIST)	2 (0.2%)	0	2 (0.2%)	
Glomus	1 (0.1%)	0	1 (0.1%)	
Adenosquamous	2 (0.2%)	0	2 (0.2%)	
Glomus	1 (0.1%)	0	1 (0.1%)	
Pleomorphic adenoma	1 (0.1%)	0	1 (0.1%)	
Undifferentiated carcinoma	20 (2.1%)	1 (1.7)	19 (2%)	
Adenomyoma	3 (0.3%)	0	3 (0.3%)	
Papillary cystadenocarcinoma	6 (0.6%)	0	6 (0.7%)	
Number of dissected lymph node	6 (0-40)	5 (0-18)	6 (0-40)	0.63
Number of lymph node infiltration	0 (0-14)	0 (0-3)	0 (0-14)	0.008
Perineural infiltration	172 (17.6%)	6 (10.3%)	166 (18.1%)	0.11
Perivascular infiltration	126 (12.9%)	5 (8.6%)	121 (13.2%)	0.28
Pancreatic safety margin				
R1	86 (8.8%)	7 (12.1%)	79 (8.8%)	0.68
R2	14 (1.4%)	1 (1.7%)	13 (1.4%)	

Table 6: Exocrine ad endocrine function

Variables	Total (975)	<35 years (58)	>35 years (917)	P value
Preoperative steatorrhae	203/975 (20.8%)	11/58 (19%)	192/917 (20.9%)	0.72
Postoperative steatorrhae	320/910 (35.2%)	16/56 (28.6%)	304/854 (35.6%)	0.28
Preoperative serum albumin	4 (3.2-5.2)	4.3 (3.2-5.2)	4 (3.3-5.1)	0.85
Postoperative serum albumin	3.8 (3.2-5.2)	4 (3.2-4.8)	3.8 (3.2-4.7)	0.56
Preoperative DM	140 (14.7%)	5 (8.6%)	135 (14.7%)	0.19
Postoperative DM	225/910 (24.7%)	13/56 (23.2%)	212/854 (24.8%)	0.79
Median preoperative fasting blood sugar	115	117.5	124	0.56
Median postoperative fasting blood sugar	120	114	120	0.76



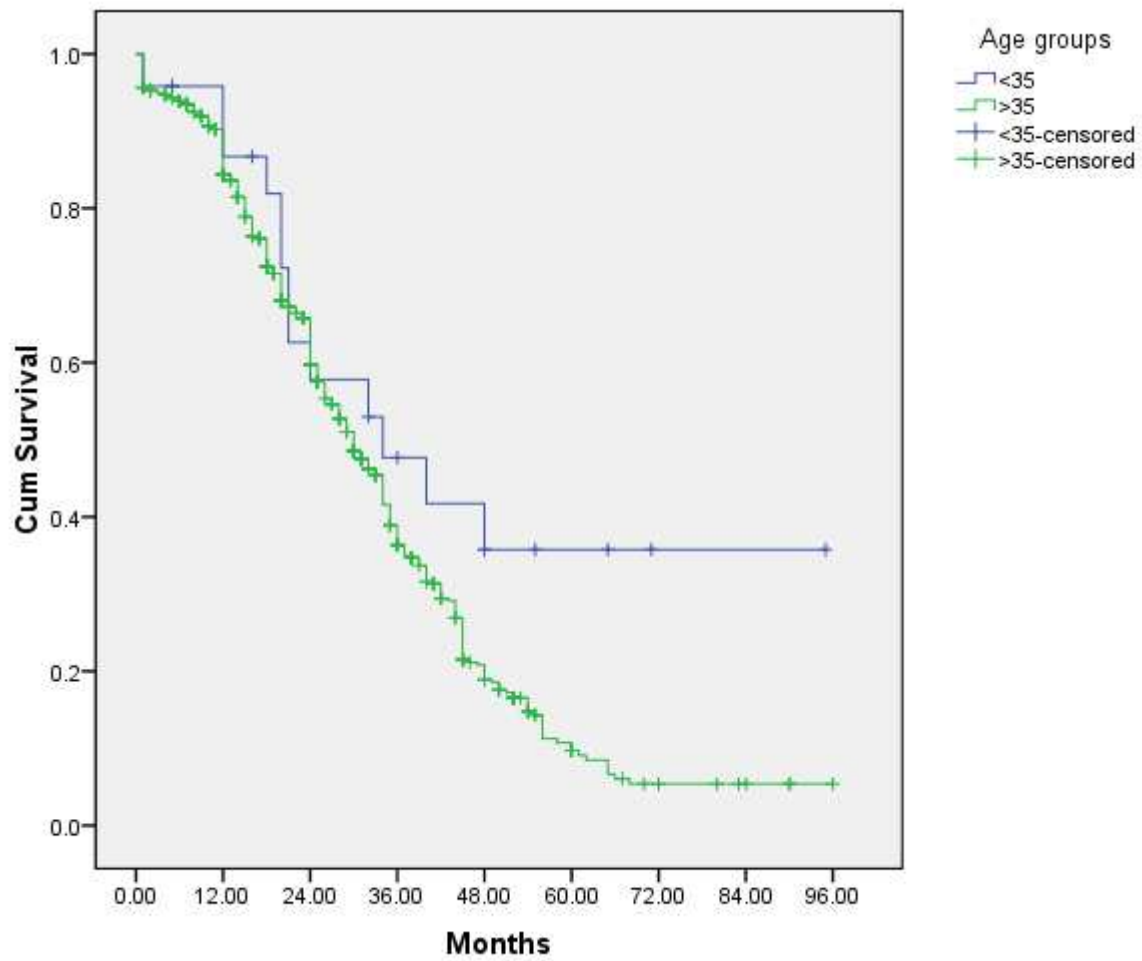


Fig (1a): Actuarial survival (Kaplan-Meier analysis) after PD for adenocarcinoma: influence of age

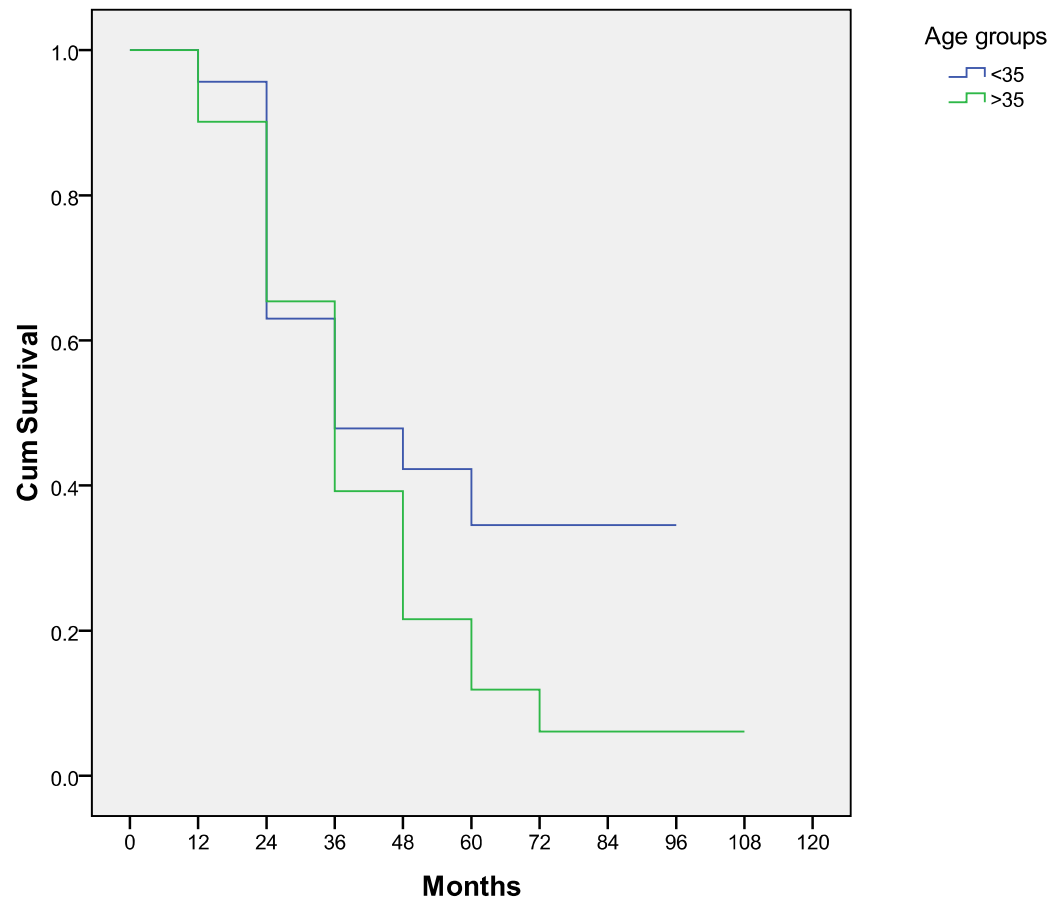


Fig (1b): Actuarial survival (life table analysis) after PD for adenocarcinoma :  
influence of age

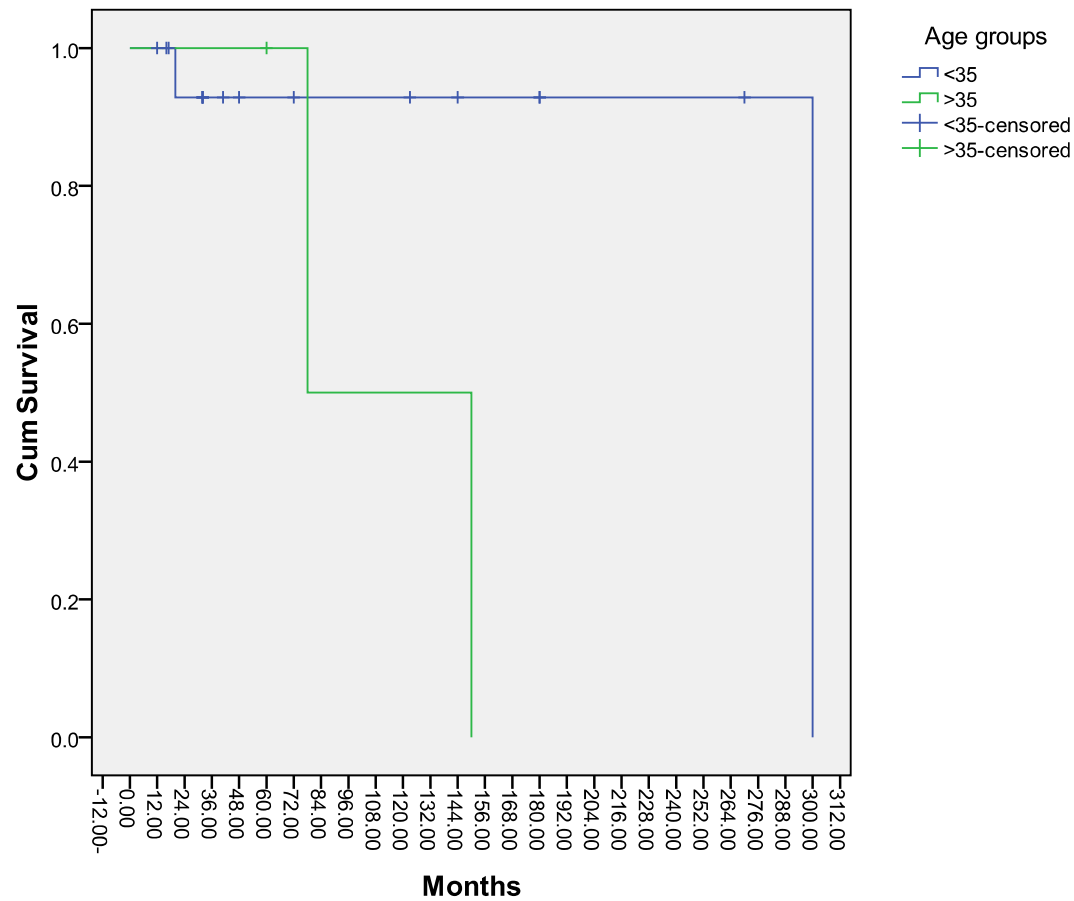


Fig (1c): Actuarial survival (Kaplan-Meier analysis) after PD for Solid pseudopapillary tumour: influence of age

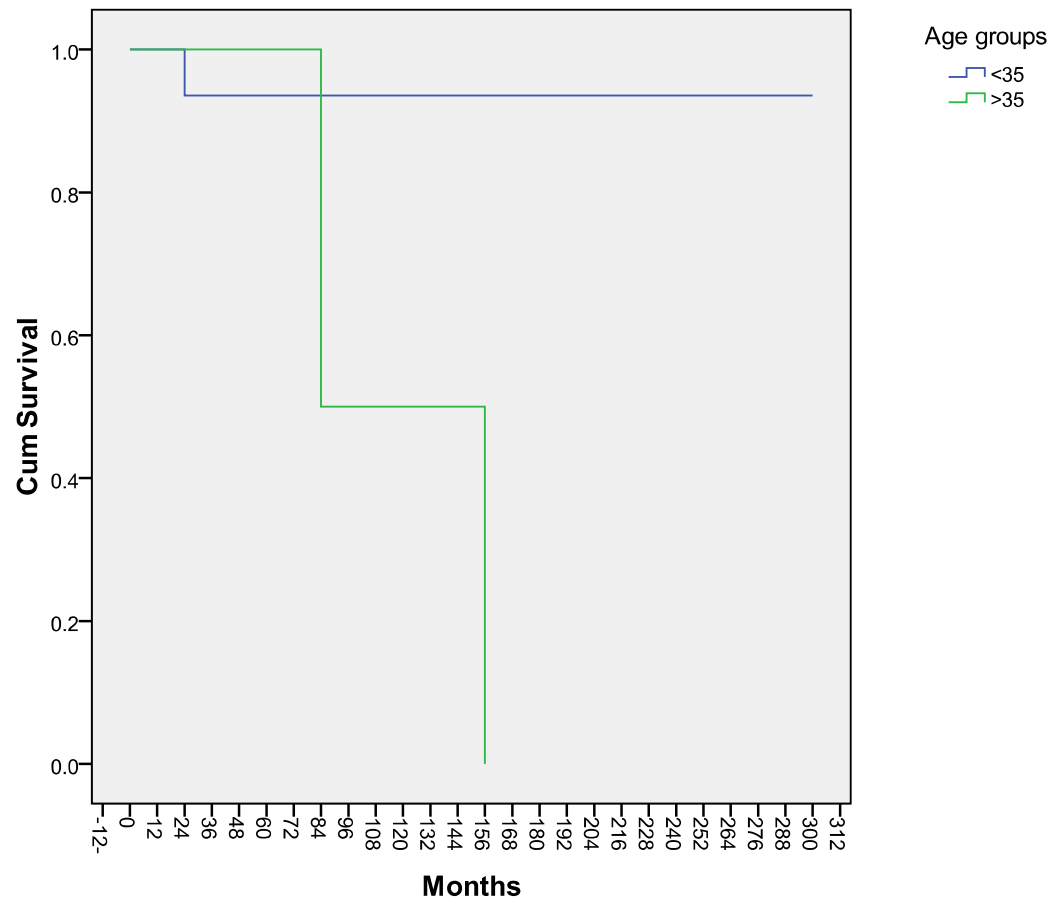


Fig (1d): Actuarial survival (life table analysis) after PD for Solid pseudopapillary tumour: influence of age

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### Please state any conflicts of interest

No

### Please state any sources of funding for your research

No

### Please state whether Ethical Approval was given, by whom and the relevant Judgement's reference number

Approved by local ethical committee

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### **Author contribution**

Please specify the contribution of each author to the paper, e.g. study design, data collections, data analysis, writing. Others, who have contributed in other ways should be listed as contributors.

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Table (1) : Demographic data and surgical outcome over 3 periods

Variables	Total (975)	First 10 years 1993-2002	Second 10 years 2003-2012	Last 5 years 2013-2016	P value
Number of cases	975	300	442	233	
Median age (years)	54 (12-88)	53	55	55	0.21
<35 years	58 (5.9%)	17 (5.7%)	24 (5.4%)	17 (7.3%)	0.6
>35 years	917 (94.1%)	283 (94.3%)	418 (94.6%)	216 (92.7%)	
Sex n (%)					0.31
Male	599 (61.4%)	190 (63.3%)	260 (58.8%)	149 (63.9%)	
Female	376 (38.6%)	110 (36.7%)	182 (41.2%)	84 (36.1%)	
Pre-operative biliary drainage n (%)	504 (51.7%)	163 (54.5%)	226 (51.1%)	(49.4%)	0.15
Cirrhosis	123 (12.6%)	28 (9.3%)	62 (14%)	33 (14.2%)	0.01
Type of reconstruction					0.0001
PG	769 (75.9%)	235 (78.3%)	417 (94.3%)	117 (50.2%)	
Simple PJ	160 (16.4%)	65 (21.7%)	25 (5.7%)	70 (30%)	
Isolated loop PJ	46 (4.7%)	0	0	46 (19.8%)	
Standard approach	883 (90.6%)	277 (92.3%)	388 (87.8%)	218 (93.6%)	0.004
Posterior approach	92 (9.4%)	23 (7.7%)	54 (12.2%)	15 (6.4%)	
Complete mesopancreatectomy	549	83 (27.7%)	233 (52.7%)	233 (100%)	0.0001
Laparoscopic assisted PD	9 (0.9%)	0	0	9	0.08
Complete laparoscopic PD	8 (0.8%)	0	0	8	
Hospital stay (days)	8 (5-71)	9	8	8	0.0001
Total postoperative complications	319 (32.7%)	120 (40%)	131 (29.6%)	68 (29.2%)	0.02
Pancreatic fistula	137 (14.1%)	45 (15%)	56 (12.7%)	36 (15.5%)	0.01
DGE	178 (18.3%)	76 (25.3%)	67 (15.2%)	35 (15%)	0.01
Bile leak	69 (7.1%)	39 (13%)	19 (4.3%)	11 (4.7%)	0.001
Hospital mortality	43 (4.4)	20 (6.6%)	15 (3.4%)	8 (3.4%)	0.006
Postoperative chemoradiotherapy	250 (25.6%)	0	132 (29.9%)	118 (50.6%)	0.01



Table (2) : Demographic and preoperative data

Variables	Total (975)	<35 years (58)	>35 years (917)	
Age (years) (median)	54 (12-88)	31 (12-35)	55 (36-88)	0.0001
Sex n (%)				
Male	599 (61.4%)	23 (39.7%)	576 (62.8%)	0.0001
Female	376 (38.6%)	35 (60.3%)	341 (37.2%)	
DM n (%)	140 (14.7%)	5 (8.6%)	135 (14.7%)	0.19
Abdominal pain n (%)	712 (73%)	47 (81%)	665 (72%)	0.06
Jaundice n (%)	868 (89%)	41 (70.7%)	827 (90.2%)	0.001
Pre-operative biliary drainage n (%)	504 (51.7%)	19 (32.8%)	485 (52.9%)	0.002
Preoperative serum albumin (gm%)	4 (3.2-5.2)	4.3 (3.2-5.2)	4 (3.3-5.1)	0.85
Preoperative serum bilirubin (mg%)	4 (0.5-38)	1.7 (0.5-38)	4 (0.5-38)	0.58
Preoperative CEA	6.4 (0.5-394)	5.2 (0.5-322)	6.4 (0.5-394)	0.51
Preoperative CA19-9	27 (0.5-1200)	34 (0.5-1080)	26 (0.5-1200)	0.02

Table (3) : Operative data

Variables	Total (975)	<35 years (58)	>35 years (917)	
Mass size (cm) median	3 (0.5-15)	4 (1-15)	3 (0.5-10)	0.001
< 2 cm	399 (4.9%)	19 (32.8%)	380 (41.4%)	0.15
> 2 cm	576 (59.1%)	39 (67.2%)	537 (58.6%)	
Pancreatic texture				
Soft	571 (58.6%)	37 (63.8%)	534 (58.2%)	0.52
Firm	404 (41.4%)	21 (36.2%)	383 (41.8%)	
Median pancreatic duct diameter	5 (1-15)	4 (1-12)	5 (1-15)	0.18
< 3 mm	292 (29.9%)	20 (34.5%)	272 (29.7%)	0.77
> 3mm	683 (70.1%)	38 (65.5%)	645 (70.3%)	
Pancreatic duct to posterior border(mm)				
< 3 mm	407 (41.7%)	16 (27.6%)	391 (42.6%)	0.02
> 3mm	568 (58.3%)	42 (72.4%)	526 (57.4%)	
Pancreatic stump mobilization (cm)	2 (1-4))	2 (1-3)	2 (1-4)	0.12
CBD diameter (mm)	15 (5-30)	13 (5-22)	16 (6-30)	0.003
Type of reconstruction				
PG	769 (78.9%)	46 (79.3%)	723 (78.8%)	0.26
Simple PJ	160 (16.4%)	7 (12.1%)	153 (16.7%)	
Isolated loop PJ	46 (4.7%)	5 (8.6%)	41 (4.5%)	
Operative time (hours)	5 (3.5-10)	5 (3.5-7)	5 (3.5-10)	0.21
Blood loss (cc)	500 (50-4000)	500 (50-4000)	500 (50-3000)	0.08

Table (4) : Postoperative data

Variables	Total (975)	<35 years (58)	>35 years (917)	
Hospital stay (days)	8 (5-71)	8 (5-60)	8 (5-71)	0.17
Time to oral intake (days)	5 (4-56)	5 (4-9)	5 (4-56)	0.002
Total amount of drainage (ml)	700 (40-35000)	650 (170-8000)	700 (40-35000)	0.06
Drain removal (days)	8 (4-71)	8 (4-60)	8 (5-71)	0.36
Total postoperative complications	319 (32.7%)	21 (36.3%)	298 (32.5%)	0.56
Dindo grade				
I	113 (11.6%)	9 (15.5%)	104 (11.3%)	0.91
II	96 (9.8%)	6 (10.3%)	90 (9.8%)	
III	67 (6.9%)	5 (8.6%)	62 (6.8%)	
IV and V	43 (4.4%)	1 (1.7%)	42 (7.4%)	
Severe complications ( $\geq$ III)				
Minor	209 (21.4%)	15 (25.9%)	194 (21.2%)	0.81
Major	110 (11.3%)	6 (10.3%)	104 (11.3%)	
Pancreatic fistula	137 (14.1%)	11 (19%)	126 (13.7%)	0.27
Grade A	67 (6.9%)	8 (13.8%)	59 (6.4%)	0.19
Grade B	47 (4.8%)	2 (3.4%)	45 (4.9%)	
Grade C	23 (2.4%)	1 (1.7%)	22 (2.4%)	
DGE	178 (18.3%)	3 (5.2%)	175 (19.1%)	0.008
Types of DGE				
Secondary DGE	151 (15.5%)	3 (5.2%)	148 (16.1%)	0.03
Primary DGE	27 (2.8%)	0	27 (2.9%)	
Pulmonary complications	46 (4.6%)	4 (6.9%)	42 (4.7%)	0.44
Bile leak	69 (7.1%)	2 (3.4%)	67 (7.3%)	0.28
Internal haemorrhage ( <b>Postoperative bleeding</b> )	25 (2.6%)	3 (5.2%)	22 (2.4%)	0.44
Pancreatitis	20 (2.1%)	0	20 (2.2%)	0.25
Bleeding PG	15 (1.5%)	2 (3.4%)	13 (1.4%)	0.24
Wound infection	49 (5%)	2 (3.4%)	47 (5.2%)	0.55
Re-operation	72 (7.4%)	5 (8.6%)	67 (7.5%)	0.75
Recurrence n (%)	89 (9.1%)	1 (1.7%)	88 (9.8%)	0.04
Hospital mortality	43 (4.4%)	1 (1.7%)	42 (4.7%)	0.46
Overall median survival (months)	24 (1-300)	35 (1-300)	24 (1-250)	0.0001
1-year	65%	81%	64%	
3-year	29%	72%	26%	
5-year	16%	58%	13%	
SPT median survival	232	280	114	0.05

1-year	95%	94%	100%	
3-year	95%	94%	100%	
5-year	95%	94%	100%	
Adenocarcinoma median survival	30	34	30	0.05
1-year	65%	63%	65%	
3-year	23%	42%	22%	
5-year	8%	35%	6%	

## (5) : Postoperative pathology

Variables	Total (975)	<35 years (58)	>35 years (917)	
Site of the tumour				
Ampullary tumour	306 (31.4%)	11 (19%)	295 (32.2%)	0.02
Pancreatic head mass	554 (56.8%)	42 (72.4%)	512 (55.8%)	
CBD duct tumour	37 (3.8%)	0	37 (4 %)	
Duodenal tumour	59 (6.1%)	5 (8.6%)	54 (5.9%)	
Uncinate process mass	19 (1.9%)	0	19 (2.1)	
Pathological diagnosis				
Solid pseudopapillary tumor SPT	20 (2.1%)	17 (29.3)	3 (0.3%)	0.0001
Chronic pancreatitis	23 (2.4%)	1 (1.7%)	22 (2.4%)	
Adenocarcinoma	812 (83.3%)	24(41.4%)	788 (85.9%)	
Neuroendocrine tumor	28 (2.9%)	6 (10.31%)	22 (2.4%)	
Benign cyst	12 (1.2%)	6 (10.3%)	6 (0.7%)	
Lymphoma	3 (0.3%)	1 (1.7%)	2 (0.3%)	
Adenoma with dysplasia	41 (42.1%)	2 (3.4)	39 (4.3%)	
Gastrointestinal stromal tumour (GIST)	2 (0.2%)	0	2 (0.2%)	
Glomus	1 (0.1%)	0	1 (0.1%)	
Adenosquamous	2 (0.2%)	0	2 (0.2%)	
Glomus	1 (0.1%)	0	1 (0.1%)	
Pleomorphic adenoma	1 (0.1%)	0	1 (0.1%)	
Undifferentiated carcinoma	20 (2.1%)	1 (1.7)	19 (2%)	
Adenomyoma	3 (0.3%)	0	3 (0.3%)	
Papillary cystadenocarcinoma	6 (0.6%)	0	6 (0.7%)	
Number of dissected lymph node	6 (0-40)	5 (0-18)	6 (0-40)	0.63
Number of lymph node infiltration	0 (0-14)	0 (0-3)	0 (0-14)	0.008
Perineural infiltration	172 (17.6%)	6 (10.3%)	166 (18.1%)	0.11
Perivascular infiltration	126 (12.9%)	5 (8.6%)	121 (13.2%)	0.28
Pancreatic safety margin				
R1	86 (8.8%)	7 (12.1%)	79 (8.8%)	0.68
R2	14 (1.4%)	1 (1.7%)	13 (1.4%)	

Table 6: Exocrine ad endocrine function

Variables	Total (975)	<35 years (58)	>35 years (917)	P value
Preoperative steatorrhae	203/975 (20.8%)	11/58 (19%)	192/917 (20.9%)	0.72
Postoperative steatorrhae	320/910 (35.2%)	16/56 (28.6%)	304/854 (35.6%)	0.28
Preoperative serum albumin	4 (3.2-5.2)	4.3 (3.2-5.2)	4 (3.3-5.1)	0.85
Postoperative serum albumin	3.8 (3.2-5.2)	4 (3.2-4.8)	3.8 (3.2-4.7)	0.56
Preoperative DM	140 (14.7%)	5 (8.6%)	135 (14.7%)	0.19
Postoperative DM	225/910 (24.7%)	13/56 (23.2%)	212/854 (24.8%)	0.79
Median preoperative fasting blood sugar	115	117.5	124	0.56
Median postoperative fasting blood sugar	120	114	120	0.76

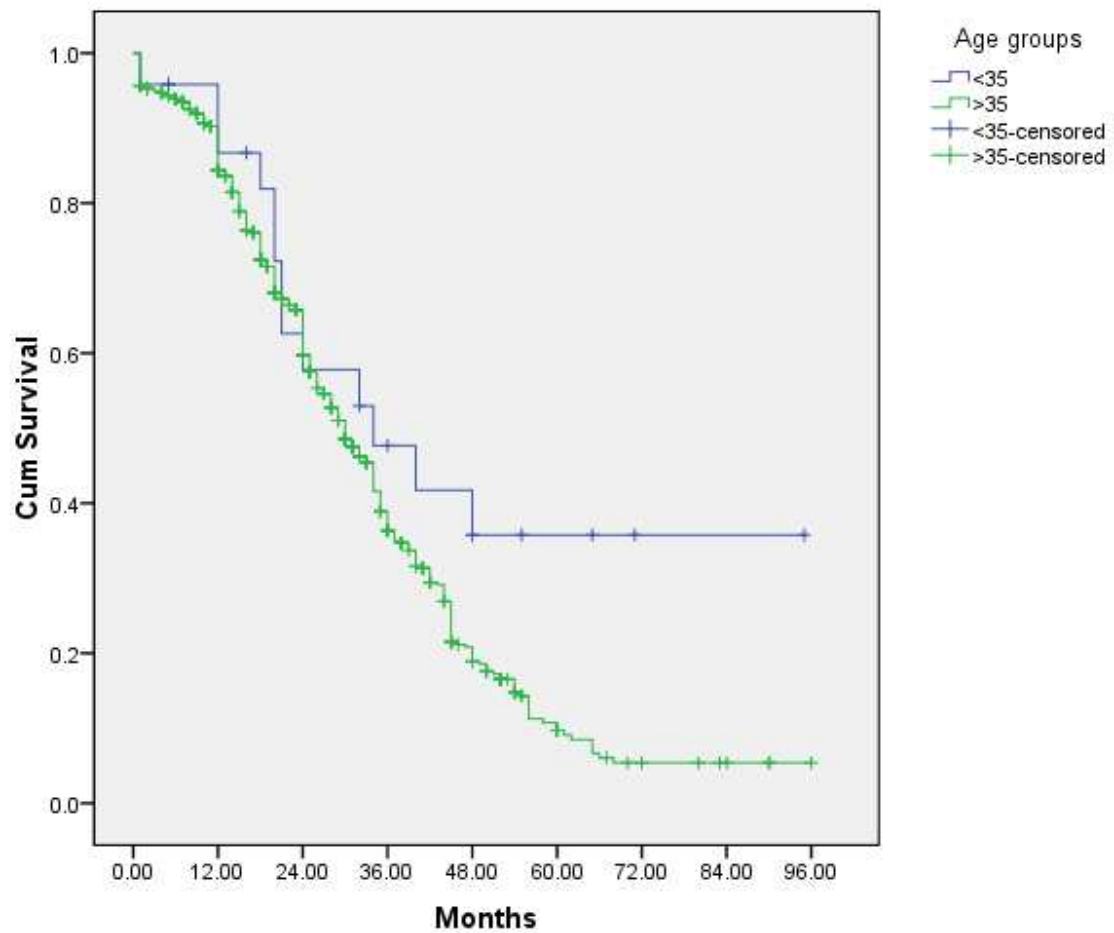


Fig (1a): Actuarial survival (Kaplan-Meier analysis) after PD for adenocarcinoma: influence of age

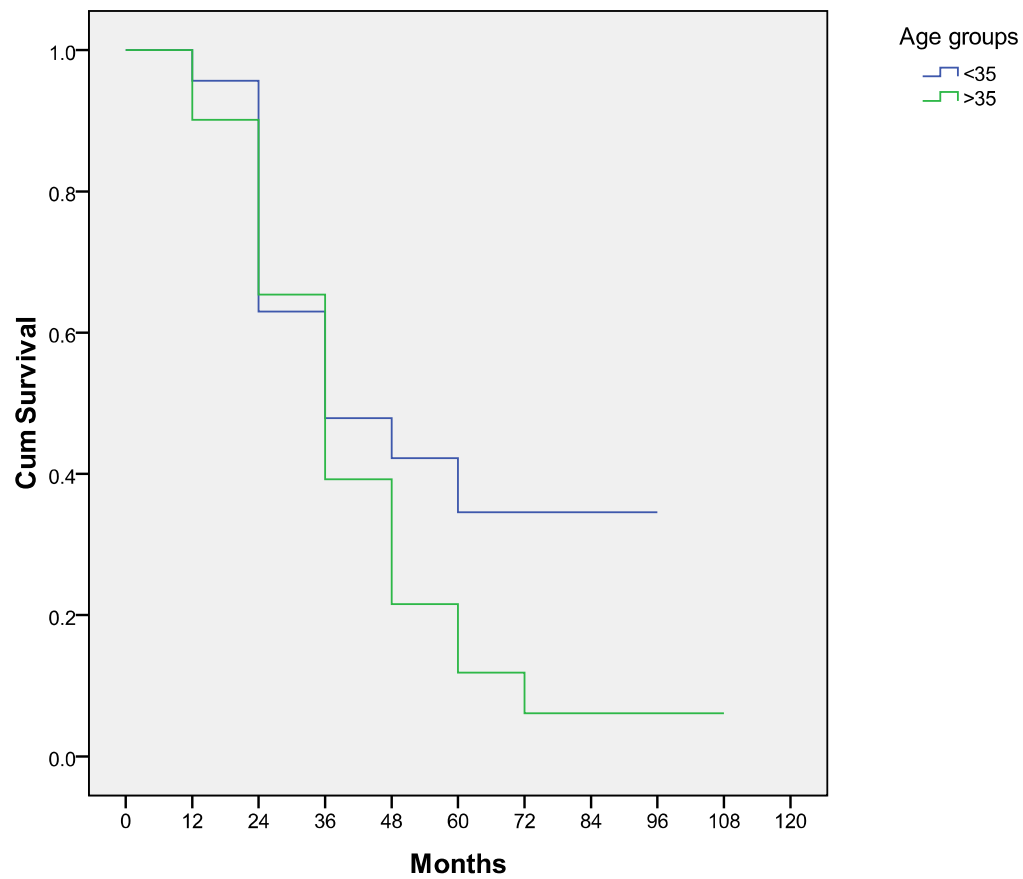


Fig (1b): Actuarial survival (life table analysis) after PD for adenocarcinoma : influence of age



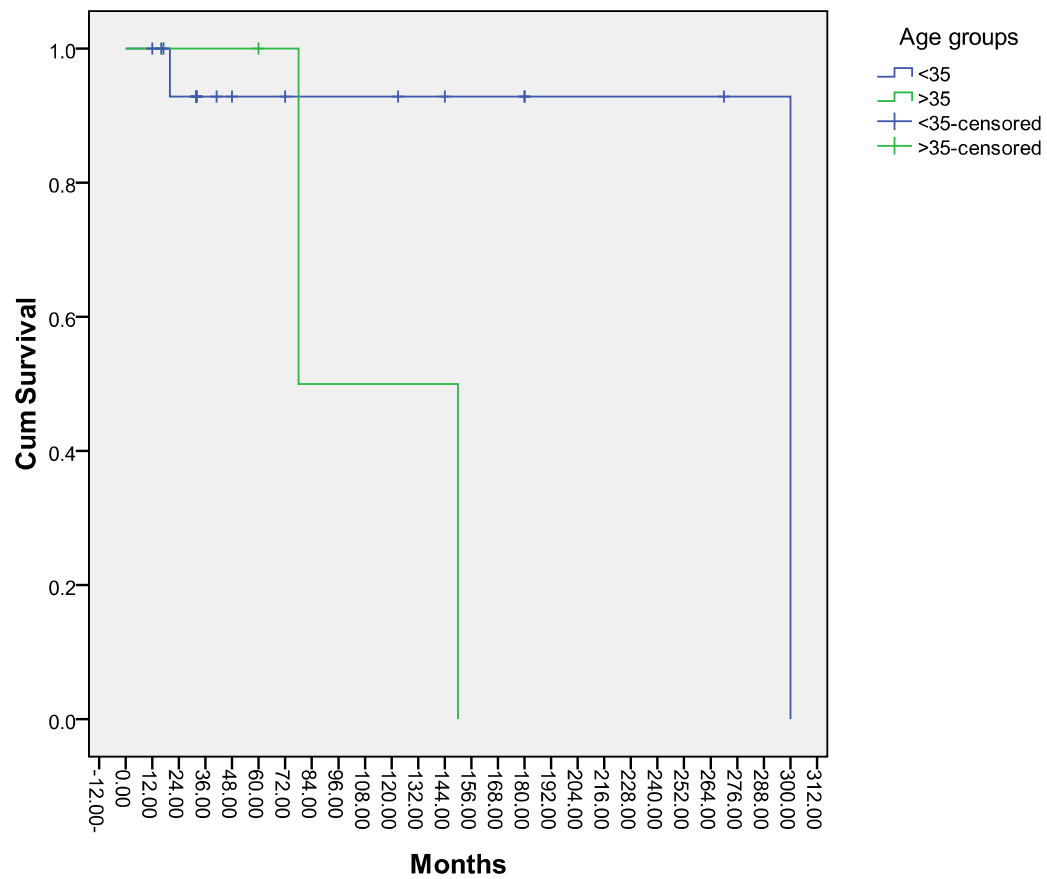


Fig (1c): Actuarial survival (Kaplan-Meier analysis) after PD for Solid pseudopapillary tumour: influence of age

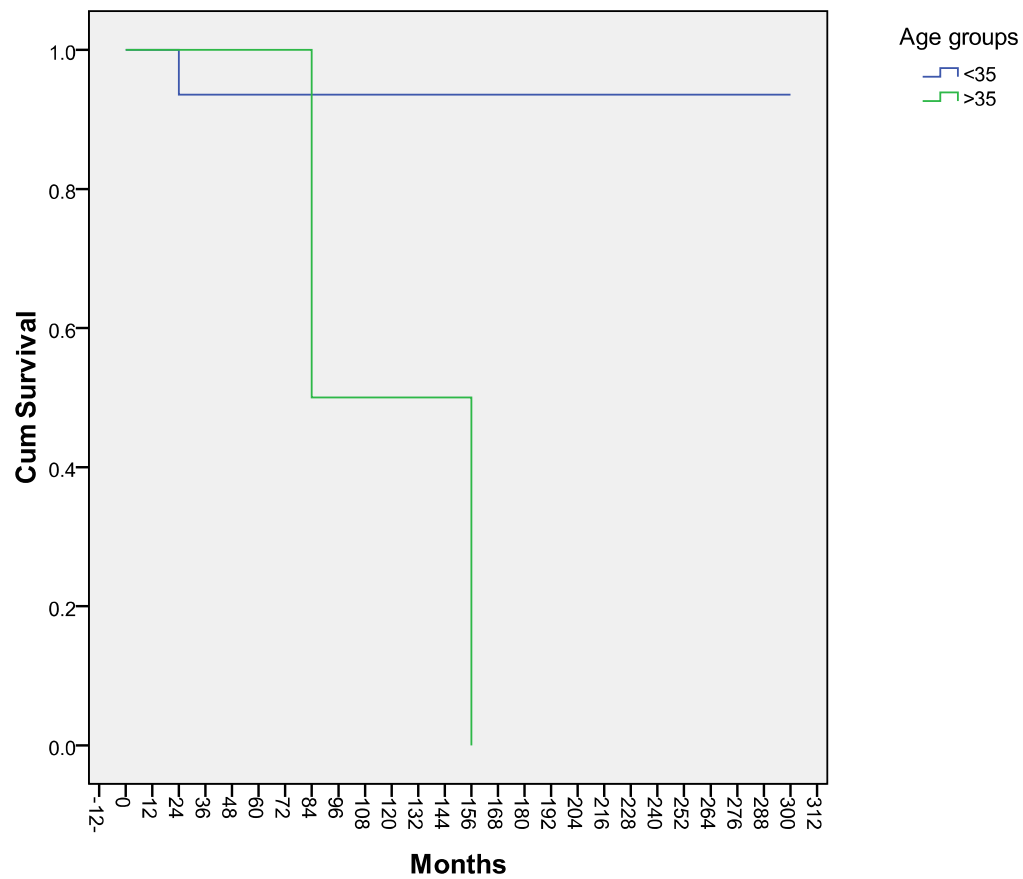


Fig (1d): Actuarial survival (life table analysis) after PD for Solid pseudopapillary tumour: influence of age

## **Surgical Outcomes of Pancreaticoduodenectomy in Young Patients: Case series study**

- The most common pathological diagnosis in the YA was adenocarcinoma followed by SPT.
- PD in YA when performed in tertiary centers with good surgical experience is relatively safe.
- The incidence of post-operative complications in the YA was comparable to that in the adult group.
- Delayed gastric emptying developed significantly in adult group II than YA group

## Surgical Outcomes of Pancreaticoduodenectomy in Young Patients Case series study

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