ORIGINAL ARTICLE

EARLY OUTCOME OF PANCREATICODUODENECTOMY IN SEPTUAGENARIANS AND OCTOGENARIANS IN NEPAL

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Abstract

Elderly population is growing because of increasing life expectancy. Decision-making for major surgery like pancreaticoduodenectomy in this group is challenging. Therefore, we evaluated the feasibility of this procedure by comparing perioperative outcomes in Septuagenarians and Octogenarians patients. From August 2017 to December 2019, 18 consecutive patients who underwent pancreaticoduodenectomy were enrolled. These patients were divided into two groups (group 1 – septuagenarians and group 2 – octogenarians). A comparative study between two groups was done regarding perioperative outcome and early complications. 18 patients were enrolled, 10 patients (55.6%) were septuagenarians (70-80 years) and 8 (44.4%) patients were Octogenarians (>80 years). There was no significant difference in the rate of surgical and medical complications between the two groups. Furthermore, there were no significant differences in risk factors, blood loss and operating time between the groups. Overall mortality in the study is 5.5%. Pancreaticoduodenectomy is feasible treatment option in septuagenarians and octogenarians with the help of multidisciplinary approach. Age alone should not be considered as decision maker for pancreaticoduodenectomy.

Keywords: pancreaticoduodenectomy, septuagenarians, octogenarians, early outcome**Introduction**

Population ageing, a phenomenon of increase in the proportion of population above certain age, is occurring globally. It rises with the increase life expectancy and decrease in fertility rates. Population aged 60 years and above is the fastest growing age group [1]. In 2015, there were 901 million people aged 60 or over, comprising 12% of the global population; by 2050, this age group will constitute nearly a quarter or more of the population. Census of 2011 of Nepal indicates that 5.28% of total population is aged above 65 years [2]. Consequently, more patients from this age group are expected to have any form of

malignancy and might be considered candidates for surgery. As per The Global Cancer Observatory, in Nepal the incidence of pancreatic cancer in 2018 was 1.9% of all malignancies (rank – 16) with a mortality of 2.3% of total cancer death [3]. More than 60% of patients diagnosed with a pancreatic malignancy are >65 years [4], and the incidence is expected to increase by 55% by 2030 and by 300% by 2050 [5].

In the year 1909, a complicated abdominal surgery, pancreaticoduodenectomy (PD), was done for the first time by Dr. Walther Kausch, and was later familiarized by Dr. Allen Whipple in 1930 [6]. PD is considered a major surgery

with high morbidity and mortality rate. In early eighty's PD had high mortality rate up to 25% but it has declined significantly in high volume center nowadays [7]. Today, most high-volume centers display a mortality of 1%-6% but the outcomes are plagued by morbidity as high as 35%-51% [8]. Considering the requirement of adjuvant therapy in these cases, the increased morbidity takes a toll in overall outcome of the patients.

The incidence of periampullary malignancies is rising because of increasing percentage of elderly population. Octogenarians carry fifty-fold higher risk of pancreatic cancer than early 40s population [9]. PD is the only definitive treatment option available for the periampullary malignancy. Due to multiple comorbid conditions, the decision to operate on octogenarians and elderly patients is difficult for both surgeons and patient's attendant. PD in elderly population had high morbidity and mortality in studies done by Sukhramwala P et al. [4] and Lightner AM et al. [10]. However, Tani M et al. [11] argued, saying PD can be done safely in advanced age even in octogenarians.

The literature on PD in the elderly patients is limited, and being a potentially morbid procedure, consideration of age as one of compounding factor of outcome is less studied. For these reasons we were keen to study the outcome of PD in septuagenarians and octogenarians' group of patients.

Materials and Methods

We conducted a comparative study between two groups of patients (septuagenarians – Group 1 and octogenarians – Group 2). Study was conducted at Kathmandu Medical College Teaching Hospital, Sinamangal, Kathmandu and Grande International Hospital, Dhapasi, Kathmandu, Nepal over a period of 28 months (2017 August – 2019 December). The study was conducted after due sanction of institutional ethics committee clearance. The same team of surgeons performed all surgeries.

All septuagenarians (>70 years) and octogenarians (>80 years) patients that undergone PD during the study period for different indications were included in the study. Patients taken up for PD but who have not

undergone PD due to locally advanced diseases detected peri-operative were excluded from the study.

Preoperative demographic and clinical data, surgical procedure, pathological diagnosis and postoperative course were collected prospectively from maintained data and analyzed. Continuous data are expressed as mean $\pm$ standard deviation (SD). Data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 16. Significance was tested using chi-square test; a p value of less than 0.05 was considered to be significant.

All patients received preoperative antibiotics (ceftriaxone plus metronidazole). All patients with obstructive jaundice were operated with bilirubin <18 mg/dL. A single team of surgeons did all surgical procedures. Surgical technique (classical and artery first method) is decided by surgical team based on case basis, depending on comfort level of surgeons. All patient received injectable Octreotide during operation (100 micrograms subcutaneously). Intra-ductal stenting or spatulation was not required for any patient and all anastomosis were mucosa to mucosa. Operating time and intraabdominal blood loss was recorded. Subhepatic abdominal drain was kept in all patients. None of the patients mandated feeding jejunostomy. Serum bilirubin and amylase with drain amylase were checked in postoperative day three and day five. Postoperative chest physiotherapy was routinely done. Ambulation and feeding were done based on patient's tolerance.

Patients were followed up till discharge. Postoperative complications and early postoperative survival (postoperative day 30 mortality) were considered as primary end points. The objective of this study is to evaluate indications, preoperative issues, intraoperative difficulty, early postoperative complications & mortality rate in elderly patients in a developing country as performed by a single unit of surgeons.

Results

We included a total of eighteen patients in this study group, out of which 10 were septuagenarians (>70) and 8 were octogenarians (>80). Among included patients, 12 were males

and 6 were females. Demographics and Performance status prior to surgery are listed in Table 1. No statistical difference seen in between two groups regarding comorbidities of patients (Table 2).

Due to raised bilirubin (>18 mg/dL), biliary drainage was done preoperatively in three patients in group 1. Out of these three patients, one underwent percutaneous trans-biliary drainage (PTBD) and two had undergone endoscopic retrograde cholangiopancreatography (ERCP) stenting.

All patients in Group 2 and 8 patients in Group 1 were considered resectable disease (Stage IIB and less) based on CT and taken up for upfront surgery. Two patients in Group 1 had borderline resectable disease with impingement of major vessels; thus, they were taken up for surgery after short course of neo-adjuvant chemotherapy (NACT). Out of 18 patients, 1 patient had undergone PD under epidural anesthesia as decided by our anesthesiologist because of chest issue.

S.N.	Characteristics	Group 1 (n=10)	Group 2 (n=8)
1.	Age (mean)	75.3 years	81.6 years
2.	Sex (Male: Female)	6:4	6:2
3.	Performance status (ECOG)		
	Grade 0	6	4
	Grade 1	4	3
	Grade 2	0	1
	Grade 3	0	0
	Grade 4	0	0
	Grade 5	0	0

Table 1 – Patient demographics and performance status

Comorbidity	Group 1 (10)	Group 2 (8)	p-value
a) Hypertension	6	5	0.67
b) Diabetes mellitus	4	4	0.67
c) Deranged KFT	2	3	0.41
d) Cerebrovascular accident (Previous stroke)	0	1	0.25
e) Cardiac Disease (Coronary artery stented)	1	1	0.86
f) Neo-adjuvant therapy	2	0	0.18

Table 2 – Patient Comorbidities

Patients in both groups underwent classical or artery first PD depending upon disease condition, preoperative findings and surgeon's comfort. Pancreatic stump was managed with

pancreatojejunostomy (mucosa to mucosa). Important peri-operative parameters including pancreatic texture, operating time and intra-op blood loss are listed in Table 3.

	Group 1(n=10)	Group 2(n=8)	p-value
1. Pancreatic texture			0.19
a) Soft:	4	1	
b) Firm to Hard:	6	7	
2. Duct size			
a) <3mm:	3	1	
b) >3mm:	7	7	
3. Surgical time	180 SD 50 minutes	240 SD minutes	
4. Blood loss	448 SD 260 mL	410 SD 112mL	

Table 3 – Operative details

There was no statistical significance noted between two groups regarding surgical

complications, medical complications and mortality (Table 4).

S.N.	Characteristics	Group 1 (N=10)	Group 2 (N=8)	p-value
1.	Surgical Complications			
a)	Post-operative pancreatic fistula (POPF)	3 (30%) Grade (a and b)	2 (25%) (Grade b)	0.81
b)	Delayed gastric emptying (DGE)	1 (10%)	1 (12.5%)	0.86
c)	Bile leak	1 (10%)	0	0.35
d)	Postoperative intra-abdominal hemorrhage (re-exploration)	1 (10%)	0	0.35
e)	Pseudoaneurysm (Gastroduodenal artery)	0	1 (12.5%)	0.25
f)	Surgical site infection (SSI)	Deep= 1 (10%) Superficial= 4 (40%)	Deep=0	59
2.	Medical complications			
b)	Respiratory insufficiency/Pneumonia	1 (10%)	2 (25%)	0.39
c)	Urinary tract infection	2 (20%)	3 (37.5%)	0.41
d)	Arrhythmia	0	1 (12.5%)	0.25
e)	Acute renal failure	1 (10%)	1 (12.5%)	0.86
f)	Cerebrovascular accident	0	0	-
g)	Mortality	0	1 (12.5%)	0.25

Table 4 – Postoperative surgical and medical complications

Postoperative pancreatic fistula (POPF) was defined as drain output of any measurable volume after POD 3 with amylase >3 times the serum amylase value. Postoperative delayed gastric emptying (DGE) was defined as a daily output greater than 500mL from nasogastric tube after postoperative day five.

One patient required re-exploration on day of surgery, due to hemorrhagic drain output. On re-exploration, retroperitoneal bleeding site was noted which was managed. POPF and bile leak was managed non-surgically. One pseudoaneurysm detected on 8th postoperative day and was managed by endovascular coiling by radiologist. After coiling, patient recovered well. The rest of the other complications were managed non-surgically.

One patient in group 2 had to be re-intubated because of respiratory insufficiency with pneumonia on 16th POD of which he later died. Our mean postoperative hospital stay was 14.8 days (median) in group 1 and 19.9 days (median) in group 2.

Post-operative biopsy reported of 17 patients having malignant cause of obstructive jaundice while one patient in group 1 had benign biliary stricture. Histopathology report in group 1: 4 pancreatic adenocarcinomas, 3 ampullary carcinomas, 2 cholangiocarcinomas, and 1

benign stricture; whereas in group 2: 3 pancreatic adenocarcinomas, 2 ampullary carcinomas, and 3 cholangiocarcinomas.

Discussions

PD is considered a major surgery because of complications like intraoperative bleeding, postoperative intra-abdominal bleeding, postoperative pancreatic fistula, and sepsis. Due to these potential complications, a high-quality multispecialty management is required for the peri-operative management of these cases [12, 13, 14].

PD is justified in elderly as only treatment option available and age alone should not be considered a factor for a patient to be excluded from it [8]. In older studies, octogenarians had more pre-operative comorbidities compared to <80 years [12]. This might have had a compounding effect on outcome after surgery. In our study, the pre-operative comorbidity was comparable in the two study groups, leading to more reliable results.

Yeu et al. [13] noted age as important predictor of mortality in PD in low volume centers, but not in high volume centers. Other studies as well are consistent with age as an

independent risk factor for pre-operative mortality following PD [15,16]. In our study, 1 out of 18 (5.5 %) had died due to respiratory insufficiency.

The immediate postoperative surgical complication was comparable in both the study groups with no statistically significant difference. Clinically seen, medical complications were more severe in both groups. Pulmonary complications like pneumonia leading to respiratory insufficiency and prolonged ventilator support, UTI and arrhythmia were all found to be slightly more represented in the 80s age group, but did not bear any statistical significance ($p>0.05$). In our experience, overall morbidity was higher for octogenarians, which is 66.6%.

The average hospital stay for the 80s population was 5 days longer than the 70s age group. Comparing the overall post-operative complications, our data fares congruent with the study by Salvatore Paiella et al [17] and Hatzaras I et al [18] in which there did not seem to be an increase in morbidity in late elderly age group (>75 years). But our data contrasts with the meta-analysis done by Sukharamwala et al [4] in terms of morbidity and we did not find any increase in mortality per se.

The prolonged hospital stays subject the older 80s age group to some outcomes. The increased hospital stay leads to financial drainage that imposes further difficulty for the patient and family to consider further treatment, the post-operative adjuvant treatment is delayed, or even exempted due to increased frailty because of prolonged recovery period. But immediate post-operative morbidity was not affected by the increase in age.

A randomized study evaluating the feasibility of PD in older recipients is ethically unfeasible. The main limitation of this study was a small sample size. Subgroup analysis, predictors of poorer outcome and the effect of different tumor histology could not be studied due to the low sample size since some studies reflect higher complications due to CAD, less differentiated histology and positive margins [19]. Although a large multicentric study might be able to overcome this limitation, and we ourselves may be able to gather a larger caseload in future to devise a more precise conclusion, till then, in lack of a less morbid treatment option in elderly,

age itself cannot be considered as a contraindication of PD. In summary, this study demonstrates that septuagenarians and octogenarians' patients can successfully undergo PD with comparable mortality and morbidity. And in the lack of an alternative equally curative procedure, age by itself should not be used to limit PD.

Conclusion

Careful selection and a more measured approach are required in treating the older age group population. Apart from a slight prolonged hospital stay, there is no increase in mortality or morbidity in the two groups of population. With both groups showing equal outcomes, and with PD being the sole definite method with possibility of cure, PD can be performed with relative safety in the elderly.

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