



Research Article

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Differences in Recovery Progress After Pancreaticoduodenectomy in Elderly Versus Non-Elderly Patients Following Enhanced Recovery Programs: A Retrospective Cohort Study



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Abstract

Objective: The aims of this study were to analysis the efficacy of enhanced recovery program for elderly patients after pancreaticoduodenectomy (PD) and to compare postoperative recovery progress between elderly and non-elderly patients.

Methods: Consecutive patients undergoing PD in a tertiary hospital between January 2015 and February 2016 were included in current study. Ninety-eight patients matched inclusion and exclusion standard were divided into two groups according to their age (<60 vs. ≥60 years old), and both of the two groups were managed according to a special enhanced recovery program for PD. Fasting blood glucose (FBG) on postoperative day (POD) 1, 3 and 7, timing of first postoperative ambulatory episode, recovery of gastrointestinal function, complication, length of stay (LOS) and postoperative LOS were compared between groups.

Result: The study finally included 98 patients, with 49 elderly patients in group A and 49 non-elderly patients in group B. The FBG on POD 1, 3 and 7 in group A were significantly lower than those in group B (9.23 ± 3.18 , 6.67 ± 0.94 and 6.49 ± 1.07 vs 11.96 ± 3.45 , 7.18 ± 1.36 and 7.07 ± 1.32 mmol/L, $p=0.000$, 0.034 and 0.019). The timing of first postoperative ambulatory episode and recovery of gastrointestinal function, including the time to first flatus and time to bowel movement, did not reach significant differences between the two groups (51.45 ± 14.65 , 67.82 ± 19.26 , and 80.49 ± 31.80 vs. 55.92 ± 17.72 , 71.02 ± 17.15 and 83.08 ± 23.09 hours, $p=0.177$, 0.387 and 0.646). Length of stay (LOS) and postoperative LOS were similar between two groups (21.51 ± 7.96 and 15.31 ± 7.09 vs. 22.22 ± 12.42 and 16.81 ± 12.10 days; $p = 0.735$ and 0.484). Complications after PD did not differ between groups (22 vs 25 ; $\chi^2 = 0.368$, $p = 0.686$).

Conclusion: Outcomes after implementation of enhanced recovery program in elderly and non-elderly patients after PD was of no difference. However, elderly patients were usually along with higher stress level compared with the non-elderly counterparts after PD even with enhanced recovery program.

Keywords: Pancreaticoduodenectomy; Enhanced Recovery; Elderly Patients; Stress Hyperglycemia

Abbreviations: FBG: Fasting blood glucose; POD: Postoperative Day; LOS: Length of Stay; NSAIDs: Non-Steroidal Anti-Inflammatory Drugs; ERAS: Enhanced Recovery After Surgery

Introduction

Pancreatic cancer is the 12th most common cancer in men and the 11th most common in women in 2012 worldwide [1]. There are 458.9 estimated new pancreatic cancer cases and 432.2 estimated pancreatic deaths in 2018 worldwide, age standardized rates of occurrence were 4.8 and 4.4 per a hundred thousand, respectively [2]. As pancreatic cancer is predominantly considered as a disease

of the elderly, nearly 90% of patients diagnosed after the age of 55 years [3]. Particularly, the incidence of rate increases with age, and the highest is in patients aged than 70 years [4]. In China, the diagnoses and deaths of pancreatic cancer every year have been beyond the cases in United State [5]. According to GLOBOCAN 2012, newly diagnosed pancreatic cancer cases account for 19.4%

and the death cases were 19.27% of all in the world, in particular, the morbidity and mortality of pancreatic cancer were relatively lower before age 40 years, and then were rapidly rising as the age going, reaching the peak value at 80 years old or older [6]. Nearly 76.1% pancreatic cancer concentrates on the elderly over 65 years old [7]. Pancreaticoduodenectomy (PD) is considered to be the main way to treat periampullary malignant tumor and the only way to provide long term survival [8]. Some scholars consider it acceptable to be conducted on elderly [9], even in patients aged over 80 years [10], while others believe that age is an independent risk factor affecting mortality after PD [11], elderly patients over 75 years or older should be cautious in selecting PD for them with pancreatic cancer [12]. A clinical trial with large sample conducted in United Kingdom concluded that the elderly had the similar perioperative outcomes compared with younger counterparts after PD in a tertiary center, so did the five-year survival [13]. Therefore, older patients with pancreatic or periampullary cancers should be considered for surgical resection.

Enhanced recovery after surgery (ERAS) are multi-model, interdisciplinary, evidence-based approaches to optimize patient outcome after surgery, and the core of ERAS is to decrease perioperative stress [8,14]. Studies have confirmed that length of stay in hospital and postoperative complications are reduced with the application of ERAS after PD [15-17], but those studies are failure to consider the influence of age factor. A retrospective study of Coolsen MM et al. [18] regarded that ERAS can be safely implemented in elderly after PD without differences in complication, postoperative length of stay in hospital, mortality, readmission rate and compliance compared with young generation. Partelli S et al. [19] also confirmed that an ERAS protocol seems to be feasible and safe in elderly after PD, even though it was not associated with improved postoperative outcomes. However, this study has not investigated specific progress of recovery after PD in elderly following ERAS, such as the first postoperative ambulatory episode, recovery of gastrointestinal function, stress hyperglycemia, which conduce to nursing work. So, this study aims to explore the differences in the recovery progress after PD in elderly and non-elderly patients following enhanced recovery programs.

Patients and Methods

Patients selection

Consecutive patients undergoing PD were collected in pancreatic center in the first affiliated hospital of Nanjing Medical University between January 2015 and February 2016. Inclusion standards were as follows: age >18 years old; no severe cardiopulmonary diseases; no history of diabetes. Exclusion standard: minimally invasive surgery; hyperlipidemia; with the history of hyperthyroidism or hypothyroidism, taking thyroid hormone; patients with autoimmune disease; record information missing. Ninety-eight patients matched inclusion and exclusion standard were divided into group A (< 60 years old) and group B (≥ 60 years old) according to the definition of elderly in China,

and patients in both groups were managed according to the local enhanced recovery program.

Methods

Both of the two groups accepted enhanced recovery program from admission to discharge, which is established according to Guidelines for perioperative care for pancreaticoduodenectomy, including preoperative counselling, preemptive analgesia, early enteral nutrition and scheduled mobilization, etc. All patients were supplied with parenteral nutrition or parenteral nutrition combined with enteral nutrition. Parenteral infusion rate was 40-70 drops per minutes, and the nutrient solution were shaken gently during the infusion. Patients with the postoperative random BG > 12mmol/L were given insulin intervention. The dose value of insulin subcutaneous dose was the value of BG minus 12u. Other insulin interventions were according to doctors' orders. All surgeries were performed by the same group of experienced pancreatic surgeons. Fasting blood glucose (FBG) on postoperative day (POD) 1,3 and 7, the first postoperative ambulatory episode, recovery of gastrointestinal function, including first flatus time and first defecation time, complication, postoperative length of stay (LOS) and total LOS were measured.

Specific nursing interventions in ERAS program were as following: Preoperative counselling: patients were given education on admission, including knowledge related to pain and pain-management; educate patients with history of smoking and drinking and encourage them to quit. Breath trainers and related education were provided to elderly and patients with smoking history for pulmonary exercises, which lasted until their discharges.

Multimodal analgesia: Pain is always managed according to analgesic ladder, and multimodal analgesia includes non-drugs and drugs analgesia.

Non-drugs analgesia: responsible nurse provides appropriate movies and light music for patients, and encourage patients to talk with family members in non-resting time, and cope with psychological problems regularly to relief psychological pressure. Drugs analgesia includes dealing with pre, postoperative and acute pain. Patients were treated with non-steroidal anti-inflammatory drugs (NSAIDs) for preemptive analgesia regularly preoperation. Patients were routinely given 40mg parecoxib by intravenous injection or 100mg flurbiprofen axetil by intravenous infusion on the day of surgery and in the first three days after surgery. Patients with acute pain with NSAIDs were provided with opioid analgesics according to pain score.

Early enteral nutrition: patients were provided with clear water with the assistant of night shift nurse and encouraged to drink a little water on the 1st post-operative day (POD1). All patients were asked to chew gum three times every day from POD1 until their gut ventilation and tried to consume liquid low-fat diet on POD3, after which they were gradually fed with semi-liquid diet, following by a normal diet.

Early scheduled mobilization: patients were encouraged to do physical activity in bed after surgery as much as they can, and the activity targets included sitting on bed for 1 hour on POD1, sitting for 4 hours on bed on POD2, followed by standing beside the bed with little movement on PDO3, and walking with walking aids thereafter.

Statistical Analysis

The SPSS 20.0 software package was used for statistical analysis. Quantitative variables were showed in the form of average value ± standard deviation and analyzed using independent sample t test, including FBG, the first postoperative

ambulatory episode time, first flatus time first defecation time and LOS. Whether using glycerine enema or not and complication were analyzed using Chi-square test

Result

Demographic and intra operative variables

The study included 98 patients, including 49 elderly patients in group A and 49 non-elderly patients in group B. The mean age was 48.84 ± 10.17 years old in group A and 68.78 ± 5.99 in group B. The two groups were similar regarding to demographic profile and clinic-pathological factors (Table 1-4).

Table 1: Demographic and perioperative parameters in patients between the two groups.

Variables		Non-Elderly	Elderly	t or χ2	P
Sex	Male	23	28		
	Female	26	21	1.022	0.419
Smoking history	Yes	8	15		
	No	41	34	2.873	0.095
Drinking history	Yes	4	8		
	No	45	41	1.519	0.218
Education background	Illiteracy	6	10		
	Primary	9	10		
	Junior	12	8	2.072	0.723
	Senior	9	10		
	Undergraduate or more	13	11		
Pathology of disease	Benign	7	4	0.41	0.524
	Malignant	42	45		
BMI (kg/cm2)		22.90±2.82	23.43±3.20	-0.871	0.386
Preoperative Hb (g/L)		128.124±17.28	124.22±17.83	1.133	0.26
Preoperative FBG (mmol/L)		6.16±2.15	6.27±1.56	-0.288	0.774
Duration of surgery (min)		223.24±75.75	233.82±75.27	-0.693	0.49
Blood loss (mL)		209.39±206.60	281.63±230.83	-1.632	0.106

Ambulatory episode and recovery of gastrointestinal function

The timing of first postoperative ambulatory episode after surgery in group A and group B were not significantly different (51.45 ± 14.65 vs. 55.92 ± 17.72 hours, p=0.177). First flatus time in group A and B were 67.82 ± 19.26 and 71.02 ± 17.15 hours, and first defecation time in group A and B were 80.49 ± 31.80 and 83.08 ± 23.09 hours. There were 24 patients starting recovery gastrointestinal function with glycerine enema and 25 patients without in group A, while there were 29 patients starting recovery

gastrointestinal function with glycerine enema and 20 patients without in group B. The first postoperative ambulatory episode did not differ between the two groups (51.45 ± 14.65 and 55.92 ± 17.72 hours; t= - 1.361, p= 0.177). Recovery of gastrointestinal function, including the time of gut ventilation through anus and defecation did not differ between the two groups (67.82 ± 19.26 and 80.49 ± 31.80 vs 71.02 ± 17.15 and 83.08 ± 23.09; t= - 0.870, p= 0.387; t= - 0.463, p= 0.646;). Whether using glycerine enema to induce the time of gut ventilation and defecation did not differ in groups (χ2 =1.027, p = 0.311).

Table 2: The comparison of ambulatory episode and recovery of gastrointestinal function between the two groups.

h: hours

Groups	N	Ambulatory Episode(H)	Gut Ventilation(H)	Defecation(H)
A	49	51.45±14.65	67.82±19.26	80.49±31.80
B	49	55.92±17.72	71.02±17.15	83.08±23.09
t		-1.361	-0.87	-0.463
p		0.177	0.387	0.646

Table 3: The comparison of fasting blood glucose (FBG) in POD 1, 3 and 7 between the two groups(mmol/L).

Groups	N	FBG in POD1	FBG in POD3	FBG in POD7
A	49	9.23±3.18	6.67±0.94	6.49±1.07
B	49	11.96±3.45	7.18±1.36	7.07±1.32
t		-4.074	-2.151	-2.376
p		0	0.034	0.019

POD: postoperative day

Table 4: The comparison of postoperative complications and total LOS stay and LOS between the two groups.

Groups	N	Complications	Postoperative LOS(d)	LOS(d)
A	49	22	15.31±7.09	21.5±7.96
B	49	25	16.81±12.10	22.22±12.42
t or χ^2		0.368*	- 0.703#	- 0.339#
p		0.686	0.484	0.735

d: days, *: χ^2 , #: t

Fasting blood glucose in POD 1, 3 and 7

The FBG on POD 1, 3 and 7 in group A were 9.23 ± 3.18, 6.67 ± 0.94 and 6.49 ± 1.07 mmol/L, and the same blood sugar profiles in group B were 11.96 ± 3.45, 7.18 ± 1.36 and 7.07 ± 1.32 mmol/L. There were significant differences between group A and B in postoperative FBG on POD1, 3 and 7 (p=0.000, 0.034 and 0.019, respectively).

Complications and length of hospital stay

There were 22 patients with complications in group A, including 7 cases with pancreatic fistula, 5 cases with infection, 5 cases with delayed gastric emptying, 5 cases with other complications. There were 25 patients with postoperative complications in group B, including 8 cases with pancreatic fistula, 6 cases with delayed gastric emptying, 5 cases infections, 3 cases with hemorrhage, and 3 cases with other complications. The distinguish between infection and normal fever after surgery, if Temperature is between 37.5 to 38.5 from POD1 to POD 3, with hemogram index normal or little high, then it will be concluded as normal fever after surgery, otherwise it will be considered as

infection. Postoperative LOS were 15.31 ± 7.09, 16.81 ± 12.10 days in group A and group B respectively. LOS were 21.51 ± 7.96, 22.22 ± 12.42 days in group A and group B respectively. Complications after PD did not differ between groups ($\chi^2 = 2.841$, p = 0.092). Both postoperative length of stay (LOS) and LOS did not differ between groups (t = - 0.703, p = 0.484; t=- 0.339 p= 0.735).

Discussion

Several studies on ERAS in PD have confirmed that enhanced recovery program appear to be feasible in PD, and it is associated with early recovery, reduced DGE and reduced length of hospital stay [15-17]. This study explores the effect of enhanced recovery on elderly patients after PD following enhanced recovery program and the differences in the recovery progress in elderly and non-elderly patients. There were no differences in length of hospital stay, complication, and mortality between elderly and non-elderly patients, which is similar to the study of Coolsen MM, however, there are some differences in the progress of recovery.

The results show that there was no difference in the first postoperative ambulatory episode time. The elderly had reduced immunologic function and decreased organ function with the manifestation of reduced physical fitness and decreased anti-stress capability, and the incidence of complication is higher in the elderly compared with younger patients [20]. Lin Liu et al. [21] found that the first postoperative ambulatory episode time in patients undergoing gastrointestinal surgery is 75.2 ± 6.2 hours, while this study shows that the first postoperative ambulatory episode time in elderly and younger patients undergoing PD following enhanced recovery program is 55.92 ± 17.72 and 51.45 ± 14.65 hours despite PD is more invasive than gastrointestinal surgery, and there is no difference between the two groups. The elderly accepted breathing training according to enhanced recovery program to increase physical fitness pre-operation and to prevent respiratory complication postoperative, which will increase physical fitness of elderly peri-operation. Patients were allowed to early ambulation on bed and early mobilization out of bed. Elderly patients themselves are not sensitive to pain, along with the application of multi-model of analgesia, the movement - related pain will be reduced, followed by more confidence and compliance in mobilization.

A study had reviewed 773 cases with pancreatic resection and considered that DGE is mainly found in the elderly [22]. Mechanical bowel preparation (MBP) may lead to dehydration and offset fluid and electrolyte balance, particularly in elderly. This study confirmed that there is no difference in the recovery of gastrointestinal function elderly and non-elderly patients following enhanced recovery program, which prompts that ERAS can effectively stimulate the recovery of gastrointestinal function of the elderly. In this study patients did not get MBP, and they were allowed to chew gum three times a day, which has been shown to be safe and beneficial in restoring gut after colorectal surgery.

Laxatives which has been showed to support early start of normal bowel function in pancreatic resection were used to patients without gut ventilation in 3 days after surgery.

There were differences in FBG in POD 1, 3 and 7 in the two groups. As patients were in the state of hyper-metabolism and metabolism inhibition after surgery and trauma, it often come to increased catabolism, negative nitrogen balance, poor wound healing and rising infection rate [23], followed by unstable homeostasis and increasing mortality, and hyperglycemia is the most distinctive feature [24]. The average FBG value in POD 1, 3 and 7 are higher in the elderly group than the younger group, so the intensity of stress is higher in the elderly. This is related to the functional decline of organs, poor physical fitness and decreased capacity of anti-stress, even with the enhanced recovery program.

Conclusion

There was no significant difference in elderly and non-elderly patients after PD in enhanced recovery program, Enhanced recovery program are appropriate to the elderly. However, elderly patients were usually along with higher stress level compared with the non-elderly counterparts after PD even with enhanced recovery program. Medical staff need to be more careful to the change of glucose in this period in elderly patients.

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