

World Journal of *Gastroenterology*

World J Gastroenterol 2018 February 21; 24(7): 767-876



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World Journal of Gastroenterology (*WJG*) is now indexed in Current Contents[®]/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch[®]), Journal Citation Reports[®], Index Medicus, MEDLINE, PubMed, PubMed Central and Directory of Open Access Journals. The 2017 edition of Journal Citation Reports[®] cites the 2016 impact factor for *WJG* as 3.365 (5-year impact factor: 3.176), ranking *WJG* as 29th among 79 journals in gastroenterology and hepatology (quartile in category Q2).

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NAME OF JOURNAL
World Journal of Gastroenterology

ISSN
ISSN 1007-9327 (print)
ISSN 2219-2840 (online)

LAUNCH DATE
October 1, 1995

FREQUENCY
Weekly

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World Journal of Gastroenterology
Baishideng Publishing Group Inc
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Pleasanton, CA 94588, USA
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Pleasanton, CA 94588, USA
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PUBLICATION DATE
February 21, 2018

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Retrospective Cohort Study

Elderly patients had more severe postoperative complications after pancreatic resection: A retrospective analysis of 727 patients

Ying-Tai Chen, Fu-Hai Ma, Cheng-Feng Wang, Dong-Bing Zhao, Ya-Wei Zhang, Yan-Tao Tian

Ying-Tai Chen, Fu-Hai Ma, Cheng-Feng Wang, Dong-Bing Zhao, Yan-Tao Tian, Department of Pancreatic and Gastric Surgery, National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China

Ya-Wei Zhang, Department of Surgery, Yale School of Medicine, New Haven, CT 06520, United States

ORCID number: Ying-Tai Chen (0000-0003-4980-6315); Fu-Hai Ma (0000-0003-2437-6881); Cheng-Feng Wang (0000-0002-2349-0415); Dong-Bing Zhao (0000-0002-3011-5277); Ya-Wei Zhang (0000-0001-5248-4754); Yan-Tao Tian (0000-0001-6479-7547).

Author contributions: Tian YT contributed to study conception and design; Ma FH, Chen YT and Zhang YW contributed to data acquisition, analysis and interpretation, and writing of the article; Wang CF, Zhao DB and Tian YT performed the operations.

Supported by National Natural Science Foundation of China, No. 81401947; Beijing Nova Program, No. xxjh2015A090.

Institutional review board statement: The study was reviewed and approved by the Cancer Hospital of the Chinese Academy of Medical Sciences.

Informed consent statement: All study participants provided informed written consent prior to study enrolment.

Conflict-of-interest statement: The authors declare that they have no conflicts of interest.

Data sharing statement: The original anonymized dataset is available upon request from the corresponding author at tyt67@163.com.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative

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Manuscript source: Unsolicited manuscript

Correspondence to: Yan-Tao Tian, MD, Professor, Department of Pancreatic and Gastric Surgery, National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, No. 17 Panjiayuan Nanli, Beijing 100021, China. tyt67@163.com
Telephone: +86-10-87787120
Fax: +86-10-87787120

Received: December 3, 2017

Peer-review started: December 4, 2017

First decision: December 20, 2017

Revised: January 3, 2018

Accepted: January 15, 2018

Article in press: January 15, 2018

Published online: February 21, 2018

Abstract

AIM

To examine the impact of aging on the short-term outcomes following pancreatic resection (PR) in elderly patients.

METHODS

A retrospective cohort study using prospectively collected data was conducted at the China National Cancer Center. Consecutive patients who underwent PR from January 2004 to December 2015 were identified

and included. 'Elderly patient' was defined as ones age 65 and above. Comorbidities, clinicopathology, perioperative variables, and postoperative morbidity and mortality were compared between the elderly and young patients. Univariate and multivariate analyses were performed using the Cox proportional hazard model for severe postoperative complications (grades IIIb-V).

RESULTS

A total of 454 (63.4%) patients were < 65-years-old and 273 (36.6%) patients were ≥ 65-years-old, respectively. Compared to patients < 65-years-old, elderly patients had worse American Society of Anesthesiologists scores ($P = 0.007$) and more comorbidities (62.6% *vs* 32.4%, $P < 0.001$). Elderly patients had more severe postoperative complications (16.8% *vs* 9.0%, $P = 0.002$) and higher postoperative mortality rates (5.5% *vs* 0.9%, $P < 0.001$). In the multivariate Cox proportional hazards model for severe postoperative complications, age ≥ 65 years [hazard ratio (HR) = 1.63; 95% confidence interval (CI): 1.18-6.30], body mass index ≥ 24 kg/m² (HR = 1.20, 95%CI: 1.07-5.89), pancreaticoduodenectomy (HR = 4.86, 95%CI: 1.20-8.31) and length of operation ≥ 241 min (HR = 2.97; 95%CI: 1.04-6.14) were significant ($P = 0.010$, $P = 0.041$, $P = 0.017$ and $P = 0.012$, respectively).

CONCLUSION

We found that aging is an independent risk factor for severe postoperative complications after PR. Our results might contribute to more informed decision-making for elderly patients.

Key words: Pancreatectomy; Aged; Pancreatic cancer; Postoperative complications; Mortality

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Core tip: Pancreatic resection is the only treatment with curative potential for pancreatic cancer and periampullary cancer, and it is a useful treatment for other benign diseases. But, compromised physiological reserve and comorbidities may counterindicate pancreatic resection in elderly patients. We found that aging is an independent risk factor for severe postoperative complications (grades IIIb-V). The potential deleterious effect of age on severe complications translates to a need for improvement in surgical management of elderly patients undergoing pancreatic resection. Our results might contribute to informed decision-making for elderly patients.

Chen YT, Ma FH, Wang CF, Zhao DB, Zhang YW, Tian YT. Elderly patients had more severe postoperative complications after pancreatic resection: A retrospective analysis of 727 patients.

World J Gastroenterol 2018; 24(7): 844-851 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v24/i7/844.htm> DOI: <http://dx.doi.org/10.3748/wjg.v24.i7.844>

INTRODUCTION

The aging population worldwide is growing at a remarkable rate. It is predicted that the proportion of the population aged 65 or above, in developed and developing nations alike, will rise until at least 2050^[1]. The incidence of pancreatic and periampullary cancer is strongly age-related, and elderly patients represent 60% of all diagnosed cases^[2]. Pancreatic resection is the only treatment with curative potential for pancreatic and periampullary cancer, and it is a useful treatment for other benign diseases^[3]. Thus, pancreatic surgeons will increasingly face decisions on whether to perform a pancreatic resection on elderly patients.

Over the last decade, several reports described outcomes for pancreatic resection on elderly patients; however, the results are inconsistent. Some studies^[2,4-15] reported a positive association between age and the postoperative complications after pancreatic resections, whereas others^[3,16-27] found no association. Moreover, the majority of such studies were conducted in developed countries. For developing countries, the data was scarce. As such, we conducted a single-center, large-scale retrospective study to examine the association between age and postoperative complications after pancreatic resections in Chinese patients.

MATERIALS AND METHODS

Patients who underwent pancreatic resection at the Cancer Hospital of the Chinese Academy of Medical Sciences, China National Cancer Center from January 2004 to December 2015 were identified and included in the study. All pancreatic resections including pancreaticoduodenectomy ($n = 385$), distal pancreatectomy ($n = 281$) and middle-segment pancreatectomy ($n = 51$) were reviewed. The patients were divided into those at the age of 65-years-old or above and those younger than 65 years. The patients aged at 65-years-old or above were defined as "elderly patients". All study procedures were approved by the Institutional Review Board at the Cancer Hospital of the Chinese Academy of Medical Sciences.

The following factors were compared between two groups: demographic characteristics, smoking and alcohol consumption, body mass index (BMI), hemoglobin and serum albumin levels, American Society of Anesthesiologists (ASA) score, preoperative biliary drainage, comorbidities (diabetes, coronary artery

disease, hypertension, chronic obstructive pulmonary disease, hepatitis B), previous history of cancer, previous abdominal surgery, family history of cancer, surgical procedure, intraoperative data (operative time, intraoperative blood loss), pathologic data, postoperative hospital stay, cost, perioperative complications and perioperative mortality.

Perioperative mortality was defined as in-hospital death within 30 d after surgery. The specific complications studied include delayed gastric emptying, pancreatic fistula, bile leak, gastrointestinal hemorrhage, cholangitis, pneumonia, wound infection, urinary tract infection, intraabdominal abscess, central line infection, and cerebrovascular accident. Postoperative complications were defined according to the Clavien-Dindo classification, and severe complications were defined as complications grade IIIb and greater^[28,29]. Length of stay was calculated from the date of operation to the date of hospital discharge.

Statistical analysis

χ^2 tests (for categorical variables) or *t*-tests (for continuous variables) were used to examine the differences in patients' characteristics between the elderly and young groups. Univariate and multivariate Cox proportional hazards regression models were performed to identify independent predictors for severe postoperative complications (grades IIIb-V). A *P*-value of less than 0.05 was considered statistically significant. Statistical analyses were conducted using SAS software version 9.3 (SAS Institute Inc., Cary, NC, United States).

RESULTS

Patient demographics and comorbidities

Pancreatic resection was performed in 454 elderly patients (63.4%) and 273 young patients (36.6%). The elderly patients had significantly higher male:female ratio and alcohol consumption (Table 1). Compared to the young patients, the elderly patients had statistically higher preoperative ASA scores, with 48.4% of these patients within III/IV classes compared to 19.6% in the young patients (*P* = 0.007), and had a higher rate of preoperative biliary drainage (*P* = 0.011). The elderly patients had more comorbidities (62.6% vs 32.4%, *P* < 0.001). The incidences of diabetes, hypertension and coronary artery disease were significantly higher in elderly patients (Table 1). Depending on the primary tumor localization, pancreaticoduodenectomy (*n* = 385), middle-segment pancreatectomy (*n* = 51) or distal pancreatectomy (*n* = 281) were performed. The most common malignancies were pancreatic ductal adenocarcinoma in 45 (60.8%), and the rate of pancreatic ductal adenocarcinoma was higher in the elderly than in the young patients (*P* < 0.001).

Patient age and postoperative complications

Although overall complication rate was comparable

between two groups (39.6% vs 33%, *P* = 0.075), the incidence of postoperative severe complications (grades IIIb-V) was significantly higher in elderly patients (16.8% vs 9.0%, *P* = 0.002). Gastrointestinal hemorrhage and urinary tract infection was more frequent in the elderly patients. There was no significant difference in the incidence of delayed gastric emptying, pancreatic fistula, bile leak, cholangitis, pneumonia, wound infection, intraabdominal abscess, central line infection and cerebrovascular accident between the two groups. Postoperative mortality was significantly higher in the elderly patients (5.5% vs 0.9%, *P* < 0.001) (Table 2).

Patient age and operative variables/length of hospital stay

Age did not show a significant association with operative time, cost of hospitalization or postoperative hospital stay (Table 3). Intraoperative blood loss (median: 468 mL) was comparable between groups, whereas the number of individuals receiving blood transfusions was significantly greater among elderly patients (129/273 vs 169/454).

Risk factors for severe postoperative complications (grades IIIb-V) in elderly patients

Univariate Cox proportional hazards regression models identified the following risk factors for severe postoperative complications (grades IIIb-V): age \geq 65 (*P* = 0.002), BMI \geq 24 kg/m² (*P* = 0.012), ASA score III/IV (*P* = 0.038), PD (*P* < 0.001), and length of operation (\geq 241 min) (*P* = 0.004). In multivariate analysis, independent factors were age \geq 65 years [*P* = 0.010; odds ratio (OR) = 1.63; 95% confidence interval (CI): 1.18-6.30], BMI \geq 24 kg/m² (*P* = 0.041; OR = 1.20; 95%CI: 1.07-5.89), PD (*P* = 0.017; OR = 4.86; 95%CI: 1.20-8.31), and length of operation (*P* = 0.12; OR = 2.97; 95%CI: 1.04-6.14) (Table 4).

DISCUSSION

Pancreatic resection is recognized as a highly invasive surgery. Despite recent advances in surgical technique, devices and perioperative care, elderly patients undergoing pancreatic resection remain a challenge, mainly due to compromised physiological reserve and comorbidities, which may negatively impact the postoperative outcomes^[27].

In our study, we found that the incidence of severe postoperative complications (grades IIIb-V) was significantly higher in elderly patients (16.8% vs 9.0%, *P* = 0.002), although the overall complication rate was comparable between the two groups (39.6% vs 33%, *P* = 0.075). Recently, centers in developed countries have started to report their results after pancreatic resection in the elderly. The majority of studies reported statistically higher postoperative complication rates

Table 1 Demographic, comorbidity, operation type, and pathology data in patients grouped according to age

Variable	< 65 yr, n = 454	≥ 65 yr, n = 273	Total, n = 727	P value
Sex				
Male	202	159	361	
Female	252	114	366	
Male:female ratio	0.8	1.4	1.0	0.0003
Mean BMI in kg/m ²	23.1	23.4	23.2	0.351
Smoking				0.129
Never	323	180	503	
Ever	130	93	223	
Mean smoking amount. in packs/yr	50	53	51	0.127
Mean smoking time in yr	22.1	26.1	23.7	0.101
Alcohol				0.017
Never	367	200	567	
Ever	87	73	160	
Mean preoperative TBIL in μmol/L	31.4	42.8	36.3	0.134
Preoperative serum albumin in g/L	39.7	37.8	38.9	0.111
ASA category III + IV	89	77	166	0.007
Preoperative biliary drainage	51	49	100	0.011
Comorbidity				
Patients with any comorbidity	147	171	318	< 0.001
Diabetes	89	73	162	0.025
Coronary artery disease	18	57	75	< 0.001
Hypertension	77	63	140	0.043
COPD	11	12	23	0.141
HBV	26	9	35	0.138
HCV	11	4	15	0.379
Previous history of cancer	3	6	9	0.070
Previous abdominal surgery	61	37	98	0.964
Family history of cancer	49	50	99	0.004
Operation type				
Pancreaticoduodenectomy	232	153	385	0.196
Distal pancreatectomy	169	112	281	0.308
Middle-segment pancreatectomy	43	8	51	0.0008
Pathology data				
Pancreatic duct adenocarcinoma	94	101	195	< 0.001
Others ¹	360	172	532	

¹Distal bile duct adenocarcinoma, ampulla adenocarcinoma, gall bladder adenocarcinoma, duodenal adenocarcinoma, intraductal papillary mucinous neoplasm, neuroendocrine neoplasm, pancreatic metastasis, solid pseudopapillary tumor, benign neoplasm, pancreatitis. ASA: American Society of Anesthesiologists; BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; HBV: Hepatitis B virus; HCV: Hepatitis C virus; TBIL: Total bilirubin.

in the group they defined as elderly patients when compared to young patients. Lahat *et al*^[8] reported that elderly patients (age ≥ 70 years) had more postoperative complications (41% vs 29%, $P = 0.01$), longer hospital stays (26.2 d vs 19.7 d, $P < 0.0001$) and higher incidences of perioperative mortality (5.4% vs 1.4%, $P = 0.01$). Adham *et al*^[2] found that elderly patients had higher postoperative mortality rates (12.9% vs 3.9%, $P = 0.04$) and demonstrated age ≥ 70 years [hazard ratio (HR) = 3.5; 95%CI: 1.3-9.3] as an independent predictor of postoperative mortality. Ayman *et al*^[14] showed that the incidence of complications was higher in elderly patients (25.9% in patients aged < 65 years, 36.8% in those aged at 65 to 69 years, and 37.5% in those aged ≥ 70 years, $P = 0.006$) and postoperative hospital mortality was comparable. Kow *et al*^[10] found that morbidity rate in elderly patients was higher (56% vs 44%, $P = 0.04$) for age ≥ 70 years, but the mortality rate was comparable (0% vs 3%,

$P = 0.28$). Riall *et al*^[5] described increasing age as an independent risk factor for mortality after pancreatic resection by using a large population-based cohort. Another population-based study^[15] in the Netherlands found that postoperative length of stay in hospital was longer and morbidity rate was higher (56% vs 44%, $P = 0.04$) among elderly patients, and also showed that elderly patient groups (≥ 70 years) exhibited a higher short-term mortality risk compared to patients under 70-years-old. Several studies did not show a statistical difference in overall morbidity or mortality rates between the older and younger groups. Our study is one of the largest studies, and our data is consistent with those from population-based studies.

Beside age, we also found BMI ≥ 24 kg/m², pancreaticoduodenectomy and length of operation ≥ 241 min (median) were independent risk factors for severe postoperative complications (grades IIIb-V). Taken together, age alone should not be the only

Table 2 Postoperative complications in patients grouped according to age

Complication	< 65 yr, n = 454	≥ 65 yr, n = 273	Total, n = 727	P value
Patients with any complication	150 (33.0)	108 (39.6)	258 (35.5)	0.075
Patients with severe complication (grades III b-V)	41 (9.0)	46 (16.8)	87 (12.0)	0.002 ^a
Pancreatic fistula	72 (15.9)	55 (20.1)	127 (17.5)	0.140
Delayed gastric emptying	45 (9.9)	35 (12.8)	80 (11.0)	0.225
Bile leak	15 (3.3)	14 (5.1)	29 (4.0)	0.224
Reoperation	12 (2.6)	11 (4.0)	23 (3.2)	0.301
Readmission	4 (0.9)	1 (0.4)	5 (0.7)	0.416
Gastrointestinal hemorrhage	9 (2.0)	13 (4.8)	22 (3.0)	0.034 ^a
Wound infection	18 (4.0)	12 (4.4)	30 (4.1)	0.777
Cholangitis	6 (1.3)	5 (1.8)	11 (1.5)	0.585
Urinary tract infection	12 (2.6)	16 (5.9)	28 (3.9)	0.029 ^a
Pneumonia	7 (1.5)	10 (3.7)	17 (2.3)	0.067
Intraabdominal abscess	13 (2.9)	7 (2.6)	20 (2.8)	0.811
Bacteremia	7 (1.5)	9 (3.3)	16 (2.2)	0.118
Central line infection	12 (2.6)	10 (3.7)	22 (3.0)	0.437
Pulmonary embolus	0 (0)	1 (0.4)	1 (0.1)	0.197
Deep venous thrombosis	1 (0.2)	3 (1.1)	4 (0.5)	0.121
Arrhythmia	10 (2.2)	11 (4.0)	21 (2.9)	0.154
Cerebrovascular accident	1 (0.2)	1 (0.4)	2 (0.3)	0.716
Mortality	4 (0.9)	15 (5.5)	19 (2.6)	< 0.001 ^a

Data are presented as n (%). ^aStatistical significance.

Table 3 Association among operative difficulty, postoperative hospital stay and cost with age

Variable	< 65 yr, n = 454	≥ 65 yr, n = 273	Total, n = 727	P value
Mean operative time in min	239.8	247.5	243.1	0.330
Mean intraoperative blood loss in mL	461.0	479.1	468.0	0.650
Blood transfusion, n	169	129	298	0.008
Mean postoperative hospital stay in d	21.1	22.7	21.9	0.150
Mean cost in RMB	76411	73610	74717	0.790

Table 4 Univariate and multivariate Cox proportional hazards models for severe postoperative complications (grades III b-V)

Variable	Subgroup	Univariate	Multivariate	
		P value	P value	HR (95%CI)
Medical risk factors				
Age in yr	< 65 vs ≥ 65	0.002	0.010	1.63 (1.18-6.30)
BMI	< 24 kg/m ² vs ≥ 24 kg/m ²	0.012	0.041	1.20 (1.07-5.89)
ASA classification	I / II vs III / IV	0.038	0.271	-
Surgical risk factors				
Pancreaticoduodenectomy	Yes vs No	< 0.001	0.017	4.86 (1.20-8.31)
Length of operation	< 241 min vs ≥ 241 min (median)	0.004	0.012	2.97 (1.04-6.14)

ASA: American Society of Anesthesiologists; BMI: Body mass index; CI: Confidence interval; HR: Hazard ratio.

contraindication to pancreatic resection. It is important for surgeons to recognize that elderly patients have higher severe postoperative complications. In order to allow the proper selection of those patients best suited for surgery, a more comprehensive evaluation of the comorbidities, BMI, complexity of the surgical procedure and type of surgical procedure is required.

The age groups studied vary among the published studies. Some studies^[10,19] set 65-years-old as the cut-off for elderly patients, while others set the ages of 70 years^[2,8,13,15,21,23,25,27], 75 years^[3,18,22] or even 80 years^[7,11,16,20] as cut-offs. We accepted the age

of 65 years as a definition of elderly. Compared to patients aged < 65 years, those elderly patients had statistically higher preoperative ASA scores and more comorbidities, such as diabetes, hypertension and coronary artery disease. In the present series, the elderly patients had a higher rate of preoperative biliary drainage ($P = 0.011$), which is in line with a previous study^[21] that found most physicians might reduce the threshold of acceptable preoperative bilirubin in the elderly, fearing the well-known impact of sustained jaundice on nutritional status and renal function in elderly patients. The elderly patients also

had a higher rate of pancreatic duct adenocarcinoma; this could be explained by age-dependent biological differences.

The study has several strengths. First, to our knowledge, this is one of the largest studies in developing countries evaluating the effect of age on short-term outcomes after pancreatic resection. Second, our study used the Clavien-Dindo classification system to classify the complications associated with pancreatic resection, and we found that aging is an independent risk factor for severe postoperative complications (grades IIIb-V), which have negative effects on health-related quality of life, length of stay and resource utilization^[30,31]. Our study may provide a more realistic view of complications following pancreatic resection. As for the current study, there are several limitations. The retrospective nature of this study can be associated with selection bias. The study also took place over a 12-year period, during which advances in surgical technique, devices and perioperative care likely improved outcomes in elderly patients. In addition, all patients were analyzed from a single institution, so the findings may not be generalizable to other settings. The limited sample size makes it difficult to further perform subcategory analysis based on age.

In conclusion, increasing age is an independent risk factor for severe postoperative complications (grades IIIb-V) after pancreatic resection. Therefore, pancreatic surgery should be considered with caution in elderly patients. Our results may contribute to informed decision-making for elderly patients.

ARTICLE HIGHLIGHTS

Research background

Pancreatic resection is the only treatment with curative potential for pancreatic cancer and periampullary cancer, and it is also a useful treatment for other benign diseases. But, compromised physiological reserve and comorbidities may counterindicate pancreatic resection on elderly patients. Over the last decade, several reports described outcomes for pancreatic resection on elderly patients; however the results are inconsistent. Some studies reported a positive association between age and the postoperative complications after pancreatic resections, whereas others found no association. Moreover, the majority of such studies were conducted in developed countries. For developing countries, the data was scarce.

Research motivation

The aging population worldwide is growing at a remarkable rate. It is predicted that the proportion of the population aged 65 or above, in developed and developing nations alike, will rise until at least 2050. The incidence of pancreatic and periampullary cancer is strongly age-related, and elderly patients represent 60% of all diagnosed cases. Pancreatic resection is the only treatment with curative potential for pancreatic and periampullary cancer, and it is also a useful treatment for other benign diseases. Thus, pancreatic surgeons will increasingly face decisions on whether to perform a pancreatic resection on elderly patients. As such, we conducted a single-center, large-scale retrospective study to examine the association between age and postoperative complications after pancreatic resections in Chinese patients.

Research objectives

The aim of this study is to examine the impact of aging on the short-term

outcomes following pancreatic resection in elderly patients.

Research methods

A retrospective cohort study using prospectively collected data was conducted at the Cancer Hospital of the Chinese Academy of Medical Sciences, China National Cancer Center. The patients were divided into those at the age of 65-years-old or above and those younger than 65 years. The patients aged at 65-years-old or above were defined as 'elderly patients'. The following factors were compared between two groups: demographic characteristics, smoking and alcohol consumption, body mass index (BMI), hemoglobin and serum albumin levels, American Society of Anesthesiologists (ASA) score, preoperative biliary drainage, comorbidities (diabetes, coronary artery disease, hypertension, chronic obstructive pulmonary disease, hepatitis B), previous history of cancer, previous abdominal surgery, family history of cancer, surgical procedure, intraoperative data (operative time, intraoperative blood loss), pathologic data, postoperative hospital stay, cost, perioperative complications and perioperative mortality.

Research results

Compared to patients < 65-years-old, elderly patients had worse ASA scores ($P = 0.007$) and more comorbidities (62.6% vs 32.4%, $P < 0.001$). Operative time, intraoperative blood loss, postoperative hospital stay and cost were comparable. Elderly patients had more severe postoperative complications (grades IIIb-V) (16.8% vs 9.0%, $P = 0.002$) and higher postoperative mortality rates (5.5% vs 0.9%, $P < 0.001$). In the multivariate Cox proportional hazards model for severe postoperative complications (grades IIIb-V), age ≥ 65 years, BMI ≥ 24 kg/m², pancreaticoduodenectomy and length of operation ≥ 241 min were significant.

Research conclusions

Increasing age is an independent risk factor for severe postoperative complications (grades IIIb-V) after pancreatic resection. Therefore, pancreatic surgery should be considered with caution in elderly patients. Our results may contribute to informed decision-making for elderly patients. Aging is an independent risk factor for severe postoperative complications after pancreatic resection. We found that aging is an independent risk factor for severe postoperative complications after pancreatic resection. Our results might contribute to more informed decision-making for elderly patients. We found that aging is an independent risk factor for severe postoperative complications (grades IIIb-V) after pancreatic resection. Our results might contribute to more informed decision-making for elderly patients.

The association between age and postoperative complications after pancreatic resections in Chinese patients is unknown. Our study used the Clavien-Dindo classification system to classify the complications associated with pancreatic resection, and we found that aging is an independent risk factor for severe postoperative complications (grades IIIb-V). Our study may provide a more realistic view of complications following pancreatic resection.

Elderly patients had more severe postoperative complications and higher postoperative mortality rates. Age ≥ 65 years is an independent risk factor for severe postoperative complications (grades IIIb-V) after pancreatic resection. Outcomes for pancreatic resection on elderly patients are inconsistent. This potential deleterious effect of age on severe complications needs improvement for surgical management of elderly patients undergoing pancreatic resection.

Research perspectives

We found that aging is an independent risk factor for severe postoperative complications (grades IIIb-V) after pancreatic resection. Our results might contribute to more informed decision-making for elderly patients.

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P- Reviewer: Araujo RLC, Boeckxstaens GE, Lee MW
S- Editor: Gong ZM **L- Editor:** Filipodia **E- Editor:** Huang Y





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ISSN 1007-9327

