Pancreatic Surgery in the Older Population: A Single Institution’s Experience over Two Decades

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Objectives. Surgery is the most effective treatment for pancreatic cancer. However, present literature varies on outcomes of curative pancreatic resection in the elderly. The objective of the study was to evaluate age as an independent risk factor for 90-day mortality and complications after pancreatic resection.

Methods. Nine hundred twenty-nine consecutive patients underwent 934 pancreatic resections between March 1995 and July 2014 in a tertiary care center. Primary analyses focused on outcomes in terms of 90-day mortality and postoperative complications after pancreatic resection in these two age groups.

Results. Eventhough patients aged 75 years or older had significantly more postoperative morbidities compared with the younger patient group, the age group was not associated with increased risk of 90-day mortality after pancreatic resection.

Discussion. The study suggests that age alone should not preclude patients from undergoing curative pancreatic resection.

1. Introduction

The older population, defined as older than 65 years of age, is an important section of the United States (US) population [1]. The US 2010 census reported that the older population increased at a faster rate (15.7%) than the entire US population (9.7%) in the last decade [1]. This expanding older population has also been reported to have a higher incidence of pancreatic cancer. From 2008–2012, 39.6% of pancreatic cancers were diagnosed in patients older than 75 years of age [2]. The Surveillance, Epidemiology, and End Results program estimated that, in 2015, there were 48,960 new cases of pancreatic cancer and 40,560 people died of this disease [2]. Pancreatic cancer is the third leading cause of cancer death in the United States [2]. The 5-year survival rate for pancreatic cancer is 7.2% [2]. To date, surgery has proven to be the most effective treatment for pancreatic cancer. Despite the recent advances that have reduced the overall operative risks [3–6], there is still conflicting evidence regarding the outcomes of surgery in older patients.

The majority of the studies published on the topic have been retrospective, with small sample sizes, conducted at highly specialized, high-volume centers [4, 7–12]. Some studies have reported age to be a risk factor in postoperative morbidity after pancreatic resection [6, 11, 13–16], while others reported that increased age alone does not prohibit pancreatic surgery [7, 10, 12, 17]. Recently, Lee et al. reported that increased age is not a risk factor for postoperative mortality based on information from the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database [3]. However, NSQIP is a voluntary program, and it does not represent all hospitals in the US. Furthermore, the NSQIP database is built on a sample from a particular patient population, so it does not include the total number of patients treated at each participating institution. It is, therefore, difficult to correctly make a conclusion based on the current available findings.

The aim of this study was to compare the outcomes of pancreatic surgery, including 90-day morbidity and
3. Results.
The study sample included 934 pancreas resections in 929 different patients. To optimize clinical outcome after pancreatic resection, preoperative decisions were preceded by individualized evaluations for the entire cohort. Every patient's cardiologist and/or pulmonologist for those with a medical history of cardiac or pulmonary disease, respectively, were consulted prior to the procedure for optimization of medical conditions including hypertension and diabetes. Ultimately, the decision to offer surgery was made by the attending surgeon after reviewing subspecialist evaluations and preoperative testing results and by assessing each patient's functional status via evaluation of an individual's capacity to perform activities of daily living independently. Our primary analysis focused on comparing morbidity and 90-day mortality of older patients undergoing pancreatic surgery to those younger than 75 years of age.

3.1. Results.

The primary outcome measures were to compare morbidity and 90-day mortality in the postoperative period between patients aged 75 years or older and those younger than 75 years.

3.2. Discussion.

As the older population increases, there is an increasing demand for surgery in this older population. Outcomes of various surgical procedures, including PD, in patients aged 75 years or older, as compared to patients younger than 75 years, revealed a significantly higher proportion of patients aged 75 years or older experienced cardiac complications (17% versus 9%, \( p = 0.017 \)) and a significantly higher incidence of pancreatic ductal adenocarcinoma (42.6% versus 31%) as compared to patients younger than 75 years. Patients aged 75 years or older were more likely to have pylorus preserving pancreaticoduodenectomy as compared to standard PD (32.9% versus 29.5%) and standard PD (22.3% versus 19.8%). There was no significant difference between the two groups in terms of operating time as shown in Table 2. The frequency of patients aged 75 years or older requiring packed red blood cell transfusion was significantly higher than those younger than 75 years (48% versus 35%, \( p < 0.0009 \)).

A comparison of postoperative morbidity and mortality is shown in Table 1. Patients aged 75 years or older had similar postoperative laboratory values except for the levels of INR (1.56 versus 1.80, \( p < 0.005 \)). There were a total of 45 deaths within the 90-day postoperative period, for an overall mortality of 4.8%. The 90-day mortality rate for patients younger than 75 years was 3.2% (31), compared with 5% (14) for patients aged 75 years or older (\( p = 0.09 \)). On multivariate analysis of preoperative factors associated with mortality (Table 3), age of 75 years or older was not associated with an increase in the likelihood of 90-day mortality (odds ratio 1.46; 95% confidence interval 0.74–2.87; \( p = 0.272 \)). Despite no significant difference in 90-day mortality, postoperative complications were more significantly seen in patients aged 75 years or older as compared to patients younger than 75 years. A significantly higher proportion of patients aged 75 years or older experienced cardiac complications (17% versus 9%, \( p = 0.0001 \)), pulmonary complications (15% versus 11%, \( p = 0.027 \)), respiratory failure (8.5% versus 5%, \( p = 0.013 \)), and renal insufficiency (5.5% versus 5%, \( p = 0.017 \)).
Table 1: Demographic details and postoperative morbidity.

| Characteristic                  | Age < 75 years (n = 737) | Age ≥ 75 years (n = 197) | p value |
|--------------------------------|--------------------------|--------------------------|---------|
| Females (%)                    | 54% (399)                | 49.2% (98)               | 0.26    |
| Race                           |                          |                          | 0.14    |
| Caucasian                      | 89% (655)                | 94.4% (188)              |         |
| Non-Caucasian                  | 11% (82)                 | 5.6% (9)                 |         |
| Cardiovascular history         |                          |                          |         |
| Hypertension                   | 56% (413)                | 66.8% (133)              | 0.001   |
| Cardiac disease                | 40% (294)                | 76% (151)                | 0.001   |
| Peripheral vascular disease    | 3.6% (27)                | 6% (13)                  | 0.069   |
| Pulmonary disease              | 8% (59)                  | 11% (21)                 | 0.23    |
| Tobacco use                    |                          |                          | 0.001   |
| Past                           | 41.5% (307)              | 53% (106)                |         |
| Active                         | 19% (140)                | 6% (12)                  |         |
| ECOG status                    |                          |                          | 0.001   |
| 0                              | 68.6% (517)              | 51.5% (103)              |         |
| 1                              | 27.7% (205)              | 40.5% (81)               |         |
| 2                              | 2.3% (17)                | 6% (12)                  |         |
| Pathology                      |                          |                          |         |
| Pancreatic ductal adenocarcinoma | 31% (229)              | 42.6% (84)               | 0.002   |
| Pancreatic cysts (IPMN, MCN, SCN) | 21.9% (162)           | 20.3% (40)               | 0.61    |
| Ampullary adenocarcinoma       | 6.5% (48)                | 11.1% (22)               | 0.03    |
| Miscellaneous neoplasm (GIST, RCC, sarcoma, etc.) | 2.5% (67)              | 8% (15)                  | 0.51    |
| Neuroendocrine tumors          | 13.7% (102)              | 5.5% (11)                | 0.002   |
| Cholangiocarcinoma             | 8.5% (62)                | 9% (18)                  | 0.74    |
| Benign (pseudocyst, pancreatitis, trauma) | 8.5% (67)              | 3.5% (7)                 | 0.013   |

Postoperative morbidity and mortality

|                          | Age < 75 years (n = 737) | Age ≥ 75 years (n = 197) | p value |
|--------------------------|--------------------------|--------------------------|---------|
| 90-day mortality         | 3.2% (31)                | 5% (14)                  | 0.09    |
| Mean number of ICU days  | 1.35 days                | 2.33 days                | 0.027   |
| (Range)                  | (0–59 days)              | (0–58 days)              |         |
| Clavien grade of complications (90 days) |                   |                          | 0.56    |
| (a) Minor (grades 1-2)   | 31% (227)                | 37% (73)                 |         |
| (b) Major (grades 3–5)   | 21% (157)                | 22% (78)                 |         |
| Pancreatic fistula       | 14.6% (108)              | 12% (24)                 | 0.123   |
| Grade A                  | 6.3% (47)                | 5% (10)                  |         |
| Grade B                  | 4.2% (31)                | 4.5% (9)                 |         |
| Grade C                  | 4.2% (31)                | 2.5% (5)                 |         |
| Postpancreatectomy hemorrhage | 5% (38)              | 2.5% (5)                 | 0.013   |
| Grade A                  | 1.2% (9)                 | 0% (0)                   |         |
| Grade B                  | 1.2% (9)                 | 1.5% (3)                 |         |
| Grade C                  | 2.7% (20)                | 1% (2)                   |         |

ECOG status: Eastern Cooperative Oncology Group (ECOG) performance status; IPMN: intraductal papillary mucinous neoplasm; SCN: serous cystic neoplasm; MCN: mucinous cystic neoplasms; GIST: gastrointestinal stromal tumors; RCC: renal cell cancer.

the older population, have become a subject of concern; however, limited data exist [4, 7–12, 17]. It has been well established in previous studies that PD could safely be performed for patients aged 70 years or older. However, PD becomes daunting with patients who are older than 80 years. Outcomes in octogenarians have been reported over the last few years. While some of these studies have reported age as a risk factor in postoperative morbidity after PD [6, 11, 13–16], others have shown that age does not prohibit surgery [7, 10, 12, 17, 18]. One of the most recent studies on the topic, based on the NSQIP database [3], specifically analyzed outcomes of patients older than 80 years for increased risk of complications and mortality. Even though the study had a large sample size, participation in the NSQIP database
Table 2: Operative details.

| Variable                                      | Age < 75 years (n = 737) | Age ≥ 75 years of age (n = 197) | p value |
|-----------------------------------------------|---------------------------|---------------------------------|---------|
| Operative procedure                           |                           |                                 | 0.39    |
| (a) Pancreaticoduodenectomy                   | 49.5% (365)               | 55.3% (109)                     |         |
| (b) Total pancreatectomy                      | 10% (74)                  | 12.6% (25)                      |         |
| (c) Distal pancreatectomy                     | 37% (274)                 | 30.9% (61)                      |         |
| (d) Central Pancreatectomy/enucleation        | 3% (24)                   | 1% (2)                          |         |
| Operative time (minutes)                      | 339                       | 348                             | 0.40    |
| Number of patients requiring blood transfusion perioperative* | 35% (260)                | 48% (95)                        | 0.0009  |
| Mean number of packed RBC transfused          | 1.42 units                | 1.75 units                      | 0.32    |
| Number of patients requiring blood transfusion during hospital stay in postoperative period | 26% (197)                | 32% (64)                        | 0.11    |
| Mean number of packed RBC transfused          | 0.96 units                | 0.83                            | 0.64    |

*up to 24 hours after surgery. RBC: red blood cells.

Table 3: Multivariate logistic regression analysis for preoperative factors associated with mortality.

| Variable                        | Odds ratio (95% confidence interval) | p value |
|---------------------------------|--------------------------------------|---------|
| Age of 75 years or older        | 1.46 (0.74–2.87)                     | 0.272   |
| Hypertension                    | 0.501 (0.228–1.09)                   | 0.084   |
| Diabetes mellitus               | 0.63 (0.33–1.20)                     | 0.161   |
| Coronary artery disease         | 0.479 (0.239–0.960)                  | 0.038   |
| Pulmonary disease               | 0.449 (0.196–1.02)                   | 0.058   |

is voluntary, so it does not represent all of the patients in the participating institutions, and not all hospitals in the US participate. Therefore, whether age plays a role in postoperative morbidity after PD or not remains a subject of further research.

This study has a large sample size and focuses on the population aged 75 years or older undergoing pancreatic resections at our tertiary center. We evaluated postpancreatic resection outcomes for patients aged 75 years and older as inconclusive evidence has been reported for octogenarians while good outcomes for septuagenarians have been well reported [7]. The results of the study are comparable to other studies reported on the topic [7, 10, 12, 17]. Overall mortality rate was 4.5%, closer to the mean of the 0–10% reported by the majority of the studies since 2000 [3, 19–22]. The incidence of postoperative fistula and hemorrhage is also comparable to previous studies [22–24]. Even though patients aged 75 years or older were more likely to have postoperative morbidities than their younger counterparts, 90-day mortality after pancreatic resection did not differ significantly. A higher incidence of postoperative complications in patients aged 75 years or older could also be explained by the higher incidence of preoperative morbidities in the same cohort as compared to the younger group. Comparable 90-day mortality could be reflective of the optimization of medical conditions prior to the procedure, low severity of postoperative complications in the older group, better postoperative care, or selection bias in terms of better health status prior to surgery. Despite the above, these findings suggest that age alone should not preclude patients from undergoing curative resection of pancreatic lesion.

This study is limited by its retrospective nature. By design, it spans over a time period of 20 years. Improved surgical techniques and advancements in perioperative care [4–6] have resulted in the surgeons offering PD to older patients at our tertiary center over the last 2 decades, and patients treated more recently may be doing better. Although it is well known that poor health status is associated with an increased risk of death and adverse outcomes [25, 26], this study cannot rule out selection bias as patients with overall better health status would have been selected for surgery based on ECOG scores (the included patients in the sample have ECOG scores between 0 and 2). In this study, occurrence of pancreatic ductal carcinoma (42.6% versus 31%) and solid pancreatic lesions (62.8% versus 54%) was more common in patients aged 75 years or older as compared to patients younger than 75 years, which could have influenced the outcomes as fibrotic pancreatic tissue is comparatively easier to resect. Lastly, even though the study has a large sample size, it is still underpowered for detecting minor differences between the two groups. It is also underpowered to determine preoperative risk factors in the older subgroup who have an increased number of ICU days or higher frequency of postoperative complications.
4. Conclusions

Focusing on the high-risk group of patients aged 75 years or older, this study reports that there is no significant difference in 90-day mortality despite higher postoperative complications in the subgroup. This study suggests that pancreatic resection could be a feasible option in selected older patients, and these patients should not be denied the opportunity of curative resection based on age alone.

Disclosure

Bhaumik Brahmbhatt and Abhishek Bhurwal are considered as co-first authors.

Competing Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

Authors’ Contributions

B. Brahmbhatt with A. Bhurwal contributed equally to data analysis and manuscript writing. F. J. Lukens, M. A. Buchanan, J. A. Stauffer, and H. J. Asbun contributed to data gathering and editing of manuscript. All authors gave final approval of the article.

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