

Systematic Review

*Corresponding author

Oliver Bellevue, MD

Section of Surgical Oncology
Swedish Medical Center
Swedish Cancer Institute
747 Broadway, 7 West, General Surgery
Seattle, WA 98122, USA
Tel. (510)301-3722
E-mail: oliver.bellevue@swedish.org

Volume 3 : Issue 1

Article Ref. #: 1000SROJ3116

Article History

Received: July 15th, 2016

Accepted: July 27th, 2016

Published: July 27th, 2016

Citation

Bellevue O, Johnson B, Feczko A, Ong F. Pancreatic cancer in the very elderly patient: Challenges and solutions. *Surg Res Open J.* 2016; 3(1): 4-12. doi: [10.17140/SROJ-3-116](https://doi.org/10.17140/SROJ-3-116)

Copyright

©2016 Bellevue O. This is an open access article distributed under the Creative Commons Attribution 4.0 International License (CC BY 4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Pancreatic Cancer in the Very Elderly Patient: Challenges and Solutions

Oliver Bellevue, MD*; Bennett Johnson, MD; Andrew Feczko, MD; Evan Ong, MD, MS, FACS

Section of Surgical Oncology, Swedish Medical Center, Swedish Cancer Institute, Seattle, WA, USA

ABSTRACT

Pancreatic cancer is responsible for a significant disease burden on the aging US population. The only chance at curing this highly morbid disease is surgical resection, however choosing appropriate surgical candidates in the elderly population remains challenging. We review the literature for appropriate treatment modalities to the elderly patient. Although significant literature exists in choosing appropriate surgical candidates as well as managing those not deemed fit for surgery, the medical community is not unified when approaching these patients. Further collaboration between the surgical, medical, and palliative communities will likely spawn better outcomes for less overall health care cost in the future.

KEYWORDS: Pancreatic cancer; Elderly; Palliative care; Chemotherapy.

ABBREVIATIONS: SEER: Surveillance, Epidemiology, and End Results; ASA: American Society of Anesthesiologists; ICU: Intensive Care Unit; ISGO: International Society of Geriatric Oncology; fTRST: Flemish version of the Triage Risk Screening Tool; VES-13: Vulnerable Elders Survey-13; QoL: Quality of Life; NCCN: National Comprehensive Cancer Network.

INTRODUCTION

Pancreatic cancer is the fourth leading cause of cancer related mortality with 44,000 American and 250,000 worldwide diagnoses annually.¹ A disturbing increase in the US incidence of pancreatic cancer has been noted in recent years. Surgical therapy remains the only chance at cure for early stage disease, but unfortunately only 9% of patients present with localized disease. The advanced age of diagnosis frequently complicates potential therapies due to comorbidities, frailty, or perceived risk. Although surgical morbidity has dramatically decreased, 5-year survival remains a dismal 7.8%. Current data from the Surveillance, Epidemiology, and End Results (SEER) Program reveals that only 31.7% of patients diagnosed with pancreatic cancer are under age 64, while 26.8% will be diagnosed between age 65-74, another 26.1% will be diagnosed between age 75-84, and 13.5% will be diagnosed at an age above 85. The average age at diagnosis is now 71 years of age.² With rising incidence in an aging population we have sought to review the best management strategy for elderly patients with pancreatic cancer.

The term “elderly” is inconsistently defined throughout the literature. Prior studies have used a range of ages from 65-90 years to demarcate “elderly”, but more recent literature stresses functional status over numerical age. Several scoring systems have been developed to predict outcomes in elderly patients with cancer diagnoses and include variables such as nutritional status, laboratory values, cardiopulmonary status, timed “get up and go” testing, and American Society of Anesthesiologists (ASA) status.^{3,4} Further confounding the discussion of the elderly patient with pancreatic cancer is the wide variety of pathology (pancreatic adenocarcinoma, neuroendocrine tumors, mucinous neoplasms, peri-ampullary or duodenal tumors) combined with anatomic considerations (lesions in the head vs. body vs. tail) and the implications for surgical resection, research, and outcomes. In our practice we do not define elderly at a

specific age, but rather take into account every patient's comorbidities, functional level, and nutritional status.

SURGICAL OUTCOMES

Outcomes after major abdominal operations are worse in the elderly. Two large US studies^{5,6} as well as one large Australian study⁷ have shown increased morbidity and mortality in older surgical patients. Interestingly, risk factors plateau at age 60, but surgical morbidity and mortality continues to increase linearly with age.⁵ For unknown reasons (referral bias, surgeon hesitancy), elderly patients are operated on less than their younger counterparts; peak surgical volume occurs in the fifth decade of life.⁵ The result is that many elderly patients are removed from the operative pool due to comorbidities, perceived risk, and referral basis.⁸ Operative complexity has been shown to predict mortality in the elderly.^{5,6} One group reported a 5% increase in mortality for every year increase above age 80.⁶ Long-term outcomes are not well studied in the elderly population, but evidence regarding functional outcomes suggests a 3-6 month minimum return to baseline functional status following major abdominal surgery.⁹ This has been verified in patients undergoing resection for pancreatic cancer.¹⁰ The substantial cognitive changes associated with general anesthesia^{11,12} are certainly compounded by prolonged hospitalizations or intensive care unit (ICU) stays.

Despite a tendency towards worse surgical outcomes in the elderly, surgical resection for pancreatic cancer remains the only treatment modality that offers complete cure. Surgeons have been compelled to push the age boundary in hopes of curing patients for over 60 years.¹³ A PubMed search was performed using the keywords "pancreatic cancer," "elderly," "resection," and "pancreaticoduodenectomy". All publications with original data of the surgical treatment of pancreatic cancer in the elderly within the last 15 years are included in Table 1.

The shortcomings of the above studies, as a whole, are important. All are retrospective, many have a small number of participants. Additionally, few authors include details on how their cohort was or was not selected for surgery. Many authors emphasize or only report 30-day mortality. Standardized definitions of morbidity are lacking. Overall there is a trend (especially in larger studies) toward slight increase in morbidity and mortality in the elderly, although authors universally conclude that a small increase in morbidity and mortality is acceptable when weighted against the risk of not pursuing the only curative therapy.

PATIENT SELECTION AND THE NEED FOR A MULTI-DISCIPLINARY APPROACH

Careful patient selection and attention to risk factors may expand the pool of curable patients as well as limit surgical morbidity by restricting poor operative candidates. Numerous factors have been proven to predict post-operative outcomes—from concrete laboratory tests to more abstract attempts to quantify "frailty,"

"geriatrics," or the like. ASA class and serum albumin have been consistently identified as strong predictors of mortality in elderly patients.^{6,7} Serum albumin less than 30 g/L is associated with a 4 fold increased risk of 30 day mortality.⁷ These predictors have also been validated in oncology patients.³ Various scoring systems emphasizing "frailty" (mobility, physical strength, and nutritional status) have been shown to predict length of stay, readmission, post-operative complications, cardiac events, and discharge to a skilled nursing facility.^{25,26} A test of growing popularity, the timed "get up and go" test, was originally developed as a basic test of mobility.²⁷ In this test the administrator asks the patient to stand from a seated chair, walk 10 feet, and return to the same seated position. This simple, inexpensive test now has thorough community validation and was recently proven to predict mortality in geriatric patients receiving chemotherapy.²⁸ Additionally, it has also been shown to closely correlate with surgical and oncologic outcomes.³ Another predictive formula for elderly colorectal patients has been validated and is in wide use,⁴ however no scoring system yet exists specifically for patients with pancreatic neoplasm. Table 2 summarizes known risk factors that are germane to the pre-operative evaluation of elderly patients.

Given the variety of scoring systems, their lack of validation in this disease, and their inconsistent use, the role of geriatric medicine should not be underplayed. The International Society of Geriatric Oncology (ISGO) is the leading authority on health care screening and optimization in elderly oncology. Although not specific to pancreatic cancer, this review board demonstrated that peri-operative assessment with a comprehensive geriatric assessment, as well as assessments of fatigue and performance status and an anesthesiologist's evaluation of operative risk could predict a 50% increase in the relative risk of post-operative complications and extended hospital stays.²⁹ Subsequently, ISGO published updated consensus guidelines. This 2014 review found that geriatric assessment in older oncology patients had multiple benefits, including the ability to predict outcomes after oncologic treatment, identify those patients who were more likely to have adverse outcomes after treatment, and prevent under or over treating this population.³⁰

In spite of the benefits, referring all elderly patients to a geriatrician may prove too large a burden for the health care system to carry. Furthermore, without a consistent definition of elderly due to the heterogeneity of this population, the ISGO also endorses the use of screening tools to identify patients most in need of a geriatric assessment. Numerous screening tools exist, but the most studied are the G8, Flemish version of the Triage Risk Screening Tool (fTRST) and Vulnerable Elders Survey-13 (VES-13). Of these, the most studied and highest sensitivity (80%) of detecting a patient who would benefit from a comprehensive geriatric assessment was the G8. Importantly, screening tools have never been demonstrated to confer the benefits of a comprehensive geriatric assessment, but in resource-poor practices these tools may offer a cost-effective middle ground.^{31,32}

Study	Total N	Age	Summary of Findings	Median Survival	Long term Survival
Bathe et al ¹⁴	70	75	No difference in 30-day mortality (8.5%), significant increase in morbidity in elderly (31% v 63%). Measured endpoints for morbidity: gastric atony, pancreatic fistula, intra abdominal abscess, biliary fistula, wound infection, line sepsis, urinary tract infection, gastrointestinal bleeding, bladder injury, pneumothorax, suppurative thrombophlebitis, pylephlebitis, chylous ascites, respiratory insufficiency, pneumonia, cardiovascular, multiple organ failure, hyperglycemia, pulmonary embolism, renal insufficiency, seizure, delirium, gout.	24 months for patients less than 75 years old, and 9 months in those over 75.	5-year survival: 23% in patients less than 75 years old and 31% in those over 75.
Hodul et al ¹⁵	122	70	No difference in 30-day mortality (only one death in the younger cohort) or morbidity. Measured endpoints for morbidity: wound infection, abscess, anastomotic leak, cardiac, urinary tract infection.	Not reported.	Not reported.
Brozetti et al ¹⁶	166	70	Significant increase in 30-day mortality (4% v 11%) and significant increase in morbidity (46% v 49%) in the elderly. Measured endpoints for morbidity: pancreatic fistula, pancreatitis, biliary fistula, delayed gastric emptying, post-operative bleeding, sepsis, wound infection, urinary tract infection, pneumonia, cardiac, renal, or cerebrovascular disease.	Not reported.	Not reported.
Makary et al ¹⁷	2698	80/90	Significant increase in 30-day mortality and morbidity for patients aged 80-90 compared to those less than 80, but not significant for those greater than 90. Measured endpoints for morbidity: reoperation, small bowel obstruction, ulcer, delayed gastric emptying, pancreatic fistula, pancreatitis, cardiac, pneumonia, sepsis, intra-abdominal abscess, lymph leak, cholangitis, bile leak, wound infection.	40 months for patients less than 80 years old, 19 months for patients 80-90, and 15 months for patients over 90.	5-year survival: 43.1% for patients less than 80 years old, 24.4% in those 80-90 and 0% in those over 90.
Scurtu et al ¹⁸	70	75	No difference in 30-day mortality (0% v 6.2%) or morbidity. Measured endpoints for morbidity: pancreatic fistula, delayed gastric emptying, bleeding, intestinal occlusion, intraabdominal collection, abdominal wall sepsis, ulcer, biliary stenosis, sepsis, urinary infection, pneumopathy and pleural effusion, neurologic, pulmonary, diarrhea, thrombophlebitis.	20 months for all patients.	3-year survival: 33.1% in patients less than 75 years old and 27.7% in those over than 75.
Finlayson et al ¹⁹	23,518	70/80	Significant increase in 30-day mortality with increased age for all groups (7% v 9% v 16%). Morbidity not reviewed.	Not reported.	5-year survival: 16% in patients less than 80 years old, 11% in those over 80.
Riall et al ²⁰	3,736	60/70/80	Significant increase in 30-day mortality with increased age for all groups (2% v 6% v 7% v 11%). Morbidity not reviewed.	Not reported.	Not reported.
Ito et al ²¹	98	75	No difference in 30-day mortality (0% v 3.2%) or morbidity. Measured endpoints for morbidity: pancreatic fistula, delayed gastric emptying, liver abscess, wound infection, intra abdominal bleeding, respiratory insufficiency, intra abdominal collection, sepsis, bile leakage, or gastrointestinal bleeding.	Not reported.	3-year survival: 65.9% for patients less than 75 years old and 50.5% for those over 75.
Oguro et al ²²	561	80	Significant increase in morbidity and significant decrease in median survival. Measured endpoints for morbidity: pancreatic fistula, delayed gastric emptying, abscess, hemorrhage, pneumonia, ascites.	65 months in patients less than 80 years old and 43 months in those over 80.	5-year survival: 51% in patients less than 80 years old and 46% in those over 80.
Frakes et al ²³	193	70	No difference in mortality or morbidity. Measured endpoints for morbidity: Pancreatic leak, gastrojejunostomy leak, atrial fibrillation, pulmonary embolus, abscess, wound infection, wound dehiscence, anastomotic bleed, stricture, pancreatic fistula, enterocutaneous fistula, peritonitis.	23 months in patients less than 70 years old, 23.4 months in those 70-75, 16.1 months those 76-80, and 18.7 months in those over 80.	5-year survival: 26.7% in patients less than 70 years old, 23% in those 70-75, 0% in those 76-80, and 15.4% in those over 80.
Zhang et al ²⁴	216	70	No difference in mortality or morbidity. Measured endpoints for morbidity: Delayed gastric emptying, pancreatic fistula, abscess, pleural effusion, cardiac, pulmonary, neurologic, urinary infections.	14 months in those less than 70 and 20 months in those over 70.	5-year survival: 14.8% in those less than 70 and 21.6% in those over 70.

Table 1: Outcomes after pancreatic resection in the elderly patient.

Study	Age	Risk Factor	Study Endpoint
Hamel et al ⁶	80	Most predictive factors: ASA, albumin, emergency surgery, functional status, and blood urea nitrogen.	30-day mortality
McNicol et al ⁷	70	ASA, albumin, emergency surgery, renal impairment, respiratory insufficiency.	30-day mortality
Makary et al ²⁶	65	Weight loss, grip strength, exhaustion, activity level, walking speed.	Post-operative complications, length of stay, and discharge to a skilled nursing facility.
Robinson et al ²⁵	65	Frailty score, defined by: Katz score, Timed up-and-go, Charlson Index, anemia, mini-cog, albumin, and a fall within 6 months.	Length of stay and 30-day readmission rate.

Table 2: Preoperative evaluation of the elderly surgical candidate.

Although the ISGO offers several compelling reviews, geriatric medicine is rarely involved or done so in a fragmented way. Even specific to the elderly patient with pancreatic cancer this discipline predicts major complications, including longer hospital stays, ICU admissions, and readmission.³³ Similarly, palliative care is also involved relatively late—after treatment failures have occurred. This may partially result from physicians consistently overestimating life expectancy in oncology patients.³⁴ In a recent study only 52% of patients with advanced stage pancreatic adenocarcinoma had received a palliative care consultation; however, this consult is associated with decreased use of chemotherapy within 30 days of death, a lower risk of ICU admission, multiple emergency department visits, and multiple hospitalizations.³⁵ This study was not focused solely on the elderly patient. Some authors have advocated that palliative care consults should replace surgical resection (although we find this approach rather limiting in good-risk operative candidates). Patients on palliative care were found to spend 50% of what is required for surgical treatment with estimated quality-adjusted life years equivalent across groups.³⁶ No centers have yet reported an automatic palliative care consult triggers at the time of diagnosis for patients of any age. Based on the above studies, such an early multi-specialty approach would likely decrease cost, increase surgical utility, and provide better outcomes. Shared decision making will become mandatory as cost containment becomes a higher priority.

PALLIATIVE INTERVENTIONS IN THE ELDERLY

Chemotherapy

Eighty percent of patients of any age present with anatomically unresectable disease, a trend that will continue unless an early tumor marker is found. Chemotherapy is considered first line treatment for un-resectable disease. Current National Comprehensive Cancer Network (NCCN) guidelines for pancreatic adenocarcinoma recommend single agent gemcitabine for patients with poor performance status or intensive chemotherapy regimen of 5-fluorouracil, oxaliplatin, irinotecan, leucovorin (FOLFIRINOX) for those with a good performance status.³⁷ Data for chemotherapy is directly applicable to the elderly population; in the hallmark study comparing FOLFIRINOX to gemcitabine for metastatic pancreatic cancer, 76 out of 342 patients were 65 years or older.³⁸

A recent Cochrane Review questions the necessity for

aggressive 5-fluorouracil based regimens (such as FOLFIRINOX) with the finding that mono-agent gemcitabine is non-inferior to 5-fluorouracil for survival. Gemcitabine also had significant clinical benefit given limited side effects and therefore has been used frequently in the elderly population. Additional agents in combination with either gemcitabine or 5-fluorouracil have shown some improvement in early response rates, but this has not translated into a survival benefit.³⁹ In the elderly patient, the best chemotherapy regimen will certainly focus on the quality of life (QoL), limiting toxicity, and reducing disease associated pain.

A PubMed search using the terms “pancreatic cancer,” “chemotherapy,” and “elderly” failed to reveal any study that prospectively assigned patients to a chemotherapeutic regimen based on their age or performance status; however, several studies have demonstrated the safety, feasibility, and survival advantage of chemotherapy when used in the palliative setting for the elderly patient. These studies are reviewed in Table 3.

Overall these studies have relatively few participants, although outcomes and conclusions are similar. Most investigators prohibit patients with poor performance status or a large number of comorbidities from receiving chemotherapy. Notably, when elderly patients with worse performance status are treated with palliative chemotherapy the median survival appears quite similar (3.9 months) compared to studies utilizing best supportive care (2.3–4.2 months). This comparison may prove flawed as many patients treated with best supportive care were assigned that modality based on poor performance status, frailty, or family’s wishes. Currently, there is no evidence to support or deny the use of chemotherapy over best supportive care in elderly patients with poor performance status. Additional studies that distinguish between locally advanced and metastatic disease are warranted as patients with metastatic disease appear to have significantly worse survival.

BILIARY AND GASTRIC OUTLET BYPASS

The traditional operation to treat biliary and gastric outlet obstruction, an open double bypass, is of declining use given advances in endoscopic stenting.⁴⁷ The morbidity associated with a large operation is balanced against the durability of endoscopic interventions in patients with limited longevity. Biliary obstruction, with resultant puritis and fat mal-absorption, has been the topic of five randomized controlled studies. A recent meta-anal-

Study	Total N	Cohort	Variable	Median Survival (months)	Comments
Maréchal et al ⁴⁰	99	Elderly <70 vs >70	Age	7.9 vs 7.2	Gemcitabine and gemcitabine-based regimens. No significant difference in survival between groups.
Locher et al ⁴¹	38	Elderly >70	None (feasibility study)	7 vs 10	Longer survival in patients receiving second line 5-FU
Yamagishi et al ⁴²	66	<70 v >70 v best supportive care	Gemcitabine v best supportive care	10.2 vs 9.6 vs 4.2	No significant survival difference regardless of age when treated with gemcitabine
Matsumoto ⁴³	68	Elderly >65 years of age	Gemcitabine v best supportive care	7.6 vs 2.3	36% of patients treated with gemcitabine had grade 3 or 4 toxicity
Hentic et al ⁴⁴	38	Elderly >75 years of age	Gemcitabine v best supportive care	9.1 vs 2.9	23% of patients treated with gemcitabine had grade 3 toxicity
Berger et al ⁴⁵	53	Elderly >70 years of age	Any agent, ECOG<1 v ECOG>2	7.8 vs 3.9	81% gemcitabine monotherapy
Oziel-Taieb et al ⁴⁶	107	Elderly > 75	Locally advanced v metastatic disease	9.1 vs 4.7	Gemcitabine, 5-FU & cisplatin, or 5-FU alone

Table 3: Palliative chemotherapy in the elderly patient with pancreatic cancer. Survival differences are statically significant except where noted.

ysis examined these five studies and included 191 patients in the surgical arm and 188 patients in the endoscopic arm.⁴⁸ The review concludes that surgical palliation was safe, more durable than endoscopic treatment and should be offered first line to patients who are low surgical risk. A serious limitation of the above meta-analysis is the age of the studies included, with publication dates of 1986, 1988, 1989, 1994, and 2006. Advances in surgical, endoscopic, and anesthetic technique may well influence this older data. For example, self-expanding metal stents and concomitant duodenal stents are two technologies that have only recently been developed and were not reflected in older trials. Additionally, none of this data specifically targets the elderly patient.

A Cochrane review from 2006, found metal stents to have improved durability over older plastic stents.⁴⁹ The overall durability of surgical bypass was also reaffirmed. Similar results have been found in a more recent, albeit small retrospective study of 55 elderly patients (over 65 years old).⁵⁰ These authors similarly conclude that surgical palliation is superior to endoscopic stenting for malignant biliary obstruction even in spite of any increased surgical risk related to advanced age. They report no difference in morbidity or mortality, but better quality of life and longer survival in open bypass patients (mean 290 compared to 150 days).

Gastric outlet obstruction is a less frequent, but equally unpleasant complication with associated nausea, vomiting, cachexia and fatigue. Open gastrojejunostomy is the historic gold standard with newer modalities including laparoscopic gastrojejunostomy and endoscopic stenting. Survival averages 82 days once malignant gastric outlet obstruction presents.⁵¹ Studies uniformly indicate that endoscopic intervention results in decreased initial hospital stay and cost with a faster return to oral intake.⁵²⁻⁵⁴ Unfortunately the durability of endoscopic intervention is again inferior with frequent rate of re-intervention (11% vs. 48%, $p<0.01$).³⁷ Stenting has been proven to be equivalent in the elderly population with equal rates of success, complications, and oral intake.⁵⁵ For both biliary and gastric outlet ob-

struction, low risk patients should give consideration to surgical bypass, while those with decreased fitness or limited predicted survival should opt for endoscopic intervention.

PALLIATIVE WHIPPLE

Offering a palliative pancreaticoduodenectomy was popularized by a retrospective study from John's Hopkins in 1996 that found a survival advantage (mean 15 compared to 12 months) for patients that underwent pancreaticoduodenectomy with positive margins compared to patients that underwent a double bypass procedure at the time of an intended curative pancreaticoduodenectomy.⁵⁶ This notion has met significant controversy with multiple subsequent studies summarized in a meta-analysis that focused quality of life after each operation.⁵⁷ This meta-analysis concludes that patients recover faster from a double bypass procedure. In spite of a non-significant trend toward decreased survival in the double bypass group (6 vs. 7 months, $p=0.09$), this earlier return to baseline function and fewer long-term symptoms (specifically diarrhea) resulted in an overall improved quality of life in the bypass group. The controversy continues as newer studies delineate between an R1 resection (microscopically positive margins), an R2 (grossly positive margins) resection and a double bypass.⁵⁸ This data also concludes that a double bypass is associated with the least morbidity and the shortest survival. These authors have also concluded that this increased survival advantage (14-18 months compared to 9-13 months) outweighs the increased morbidity. R2 resections are associated with especially poor outcomes (7-10 month survival) and increased morbidity. Unfortunately, these studies appear underpowered as evidenced by the large range in survival after purportedly similar operations. None of these operations have been specifically studied in the elderly patient.

A NOVEL THERAPY: IRREVERSIBLE ELECTROPORATION

A novel therapy for the treatment of locally advanced disease is irreversible electroporation, or "NanoKnife," which acts through local electrical ablation of tumor cells. Early, small

studies are very promising. The largest to date includes 54 patients in a prospective, multicenter trial who underwent irreversible electroporation that were matched to 85 patients with similar pancreatic disease burden who underwent standard of care chemo-radiation. Overall survival improved in patients undergoing irreversible electroporation (20 vs. 13 months, $p=0.03$).⁵⁹ The oldest patient in this cohort was 80 years old, range 45-80 years. Another reported cohort includes 14 patients who underwent percutaneous irreversible electroporation. No deaths were attributed to the procedure; however two patients had complications (pneumothorax and pancreatitis). Two of these patients subsequently underwent R0 resection (Microscopically negative margins).⁶⁰ Ultrasound has also been successfully used to localize and treat with irreversible electroporation.⁶¹ In this study, five patients safely underwent irreversible electroporation and one went on to have R0 pancreaticoduodenectomy. Due to its potential as a minimally invasive therapy, irreversible electroporation may gain significantly utility in the elderly population if larger studies continue to validate its efficacy.

PAIN MANAGEMENT

Severe abdominal pain is one of the most devastating consequences of end stage pancreatic cancer. As early as 1969, attempts at chemical splanchnicectomy have been described, although it was not until 1993 that the first prospective, randomized, double-blind, placebo controlled trial was performed in this population.⁶² Patients receiving alcohol ablation scored significantly lower on pain scores at 2, 4, 6 months and on final assessment. The average age of these patients was 64 years old. Another randomized trial compared celiac block to medical pain management (non-steroidal anti-inflammatory drugs and opiates) and found a significant decrease in analgesic use (specifically opiates) in patients receiving chemical splanchnicectomy.⁶³ The mean age of this study was 67 years in the group receiving the block and 63 years in the pharmacologic group. In contrast, a similarly designed trial found no significant decrease in the use of opiates, no difference in quality of life, or difference in survival, although patients undergoing splanchnicectomy did score consistently lower on pain scores.⁶⁴ A Cochrane review was undertaken in 2011 to determine the overall efficacy of this treatment and its influence on opiate use. A total of six randomized control trials (358 participants) were identified. The results found a statistically significant decrease not only in pain scores but also in opiate use in patients undergoing splanchnicectomy.⁶⁵ Given the minimal reported side effects of chemical splanchnicectomy and the large potential benefit of decreasing opiate use in the vulnerable elderly population this treatment modality ought to be employed when feasible.

RESOURCE UTILIZATION

Hospital resource utilization for elderly patients undergoing pancreaticoduodenectomy has only once been studied in the literature.⁶⁶ Via single institution retrospective review, patients undergoing pancreaticoduodenectomy were compared based on

age (less than 70 years old, 70-80 years, and greater than 80 years). This study included 99 total patients. Both groups aged 70-80 and above 80 were associated with significantly higher hospital charges. The youngest cohort charged \$22,073 less than the middle cohort and \$34,373 less than those patients over 80 years of age. This initial study bears further validation and may well prove highly significant as health care cost meets containment.

CONCLUSION

The best management strategy for elderly patients with pancreatic cancer depends on a variety of factors including pathology, anatomic resectability, patient comorbidity and overall fitness. When and how to best proceed with resection is best determined as a multidisciplinary conversation with early inclusion of palliative care, geriatrics, oncology and surgical specialties. Innovative prognostic factors such as genomic sequencing will play a larger role in counseling and treating the elderly patient. Improvements in determining a patient's true "age" reflected by the ability to safely undergo a major operation or chemotherapy treatment must be made. Although a wealth of data exists, it remains underutilized. Mitigating peri-operative risk will undoubtedly call for increasing consolidation of patients into high volume centers to allow for standardization and access to all needed specialties. Palliation will best be treated in a similar setting. Increasing demands on the health care system are guaranteed with the aging US population.

CONFLICTS OF INTEREST

None of the above authors have any disclosures.

REFERENCES

1. Yeo TP, Lowenfels AB. Demographics and epidemiology of pancreatic cancer. *Cancer J*. 2012; 18(6): 477-484. doi: [10.1097/PPO.0b013e3182756803](https://doi.org/10.1097/PPO.0b013e3182756803)
2. Surveillance Epidemiology and End Results. SEER Fact Sheets: Pancreas. Web site. <http://seer.cancer.gov/>. Accessed July 15, 2016.
3. Huisman MG, Audisio RA, Ugolini G, et al. Screening for predictors of adverse outcome in onco-geriatric surgical patients: A multicenter prospective cohort study. *Eur J Surg Oncol*. 2015; 41(7): 844-851. doi: [10.1016/j.ejso.2015.02.018](https://doi.org/10.1016/j.ejso.2015.02.018)
4. Tran Ba Loc P, du Montcel ST, Duron JJ, et al. Elderly POSSUM, a dedicated score for prediction of mortality and morbidity after major colorectal surgery in older patients. *Br J Surg*. 2010; 97(3): 396-403. doi: [10.1002/bjs.6903](https://doi.org/10.1002/bjs.6903)
5. Turrentine FE, Wang H, Simpson VB, Jones RS. Surgical risk factors, morbidity, and mortality in elderly patients. *J Am Coll Surg*. 2006; 203(6): 865-877. doi: [10.1016/j.jamcoll](https://doi.org/10.1016/j.jamcoll)

surg.2006.08.026

6. Hamel MB, Henderson WG, Khuri SF, Daley J. Surgical outcomes for patients aged 80 and older: morbidity and mortality from major noncardiac surgery. *J Am Geriatr Soc.* 2005; 53(3): 424-429. doi: [10.1111/j.1532-5415.2005.53159.x](https://doi.org/10.1111/j.1532-5415.2005.53159.x)
7. McNicol L, Story DA, Leslie K, et al. Postoperative complications and mortality in older patients having non-cardiac surgery at three Melbourne teaching hospitals. *Med J Aust.* 2007; 186(9): 447-452. Web site: <https://www.mja.com.au/journal/2007/186/9/postoperative-complications-and-mortality-older-patients-having-non-cardiac>. Accessed July 14, 2016
8. Bilimoria KY, Mentrem DJ, Ko CY, Stewart AK, Winchester DP, Talamonti MS. National failure to operate on early state pancreatic cancer. *Ann Surg.* 2007; 246(2): 173-180. doi: [10.1097/SLA.0b013e3180691579](https://doi.org/10.1097/SLA.0b013e3180691579)
9. Lawrence VA, Hazuda HP, Cornell JE, et al. Functional independence after major abdominal surgery in the elderly. *J Am Coll Surg.* 2004; 199(5): 762-772. doi: [10.1016/j.jamcollsurg.2004.05.280](https://doi.org/10.1016/j.jamcollsurg.2004.05.280)
10. Lightner AM, Glasgow RE, Jordan TH, et al. Pancreatic resection in the elderly. *J Am Coll Surg.* 2004; 198(5): 697-706. doi: [10.1016/j.jamcollsurg.2003.12.023](https://doi.org/10.1016/j.jamcollsurg.2003.12.023)
11. Deiner S, Silverstein JH. Postoperative delirium and cognitive dysfunction. *Br J Anaesth.* 2009; 103(Suppl 1): i41-i46. doi: [10.1093/bja/aep291](https://doi.org/10.1093/bja/aep291)
12. Abildstrom H, Rasmussen LS, Rentowl P, et al. Cognitive dysfunction 1-2 years after non-cardiac surgery in the elderly. ISPOCD group. International Study of Post-Operative Cognitive Dysfunction. *Acta Anaesthesiol Scand.* 2000; 44(10): 1246-1251. doi: [10.1034/j.1399-6576.2000.441010.x](https://doi.org/10.1034/j.1399-6576.2000.441010.x)
13. Ferfuson G. Pancreatico-duodenectomy: Operation on two elderly patients. *Br Med J.* 1954.
14. Bathe OF, Levi D, Caldera H, et al. Radical resection of periampullary tumors in the elderly: Evaluation of long-term results. *World J Surg.* 2000; 24(3): 353-358. doi: [10.1007/s002689910056](https://doi.org/10.1007/s002689910056)
15. Hodul P, Tansey J, Golts E, et al. Age is not a contraindication to pancreaticoduodenectomy. *Am Surg.* 2001; 67(3): 270-275. Web site: <http://search.proquest.com/openview/878ad5e8812d22375068082eb6aae539/1?pq-origsite=gscholar>. Accessed July 15, 2016
16. Brozzetti S, Mazzoni G, Miccini M, et al. Surgical treatment of pancreatic head carcinoma in elderly patients. *Arch Surg.* 2006; 141(2): 137-142. doi: [10.1001/archsurg.141.2.137](https://doi.org/10.1001/archsurg.141.2.137)
17. Makary MA, Winter JM, Cameron JL, et al. Pancreaticoduodenectomy in the very elderly. *J Gastrointest Surg.* 2006; 10(3): 347-356. doi: [10.1016/j.gassur.2005.12.014](https://doi.org/10.1016/j.gassur.2005.12.014)
18. Scurtu R, Bachellier P, Oussoultzoglou E, Rosso E, Maroni R, Jaeck D. Outcome after pancreaticoduodenectomy for cancer in elderly patients. *Gastrointest Surg.* 2006; 10(6): 813-822. doi: [10.1016/j.gassur.2005.12.010](https://doi.org/10.1016/j.gassur.2005.12.010)
19. Finlayson E, Fan Z, Birkmeyer JD. Outcomes in octogenarians undergoing high-risk cancer operation: A national study. *J Am Coll Surg.* 2007; 205(6): 729-734. doi: [10.1016/j.jamcollsurg.2007.06.307](https://doi.org/10.1016/j.jamcollsurg.2007.06.307)
20. Riall TS, Reddy DM, Nealon WH, Goodwin JS. The effect of age on short-term outcomes after pancreatic resection: A population-based study. *Ann Surg.* 2008; 248(3): 459-467. doi: [10.1097/SLA.0b013e318185e1b3](https://doi.org/10.1097/SLA.0b013e318185e1b3)
21. Ito Y, Kenmochi T, Irino T, et al. The impact of surgical outcome after pancreaticoduodenectomy in elderly patients. *World J Surg Oncol.* 2011; 9: 102. doi: [10.1186/1477-7819-9-102](https://doi.org/10.1186/1477-7819-9-102)
22. Oguro S, Shimada K, Kishi Y, et al. Perioperative and long-term outcomes after pancreaticoduodenectomy in elderly patients 80 years of age and older. *Langenbecks Arch Surg.* 2013; 398(4): 531-538. doi: [10.1007/s00423-013-1072-7](https://doi.org/10.1007/s00423-013-1072-7)
23. Frakes JM, Strom T, Springett GM, et al. Resected pancreatic cancer outcomes in the elderly. *J Geriatr Oncol.* 2015; 6(2): 127-132. doi: [10.1016/j.jgo.2014.11.005](https://doi.org/10.1016/j.jgo.2014.11.005)
24. Zhang D, Gao J, Li S, et al. Outcome after pancreaticoduodenectomy for malignancy in elderly patients. *Hepatogastroenterology.* 2015; 62(138): 451-454. Web site: <http://europepmc.org/abstract/med/25916080>. Accessed July 14, 2016
25. Robinson TN, Wu DS, Pointer L, Dunn CL, Cleveland JC Jr, Moss M. Simple frailty score predicts postoperative complications across surgical specialties. *Am J Surg.* 2013; 206(4): 544-550. doi: [10.1016/j.amjsurg.2013.03.012](https://doi.org/10.1016/j.amjsurg.2013.03.012)
26. Makary MA, Segev DL, Pronovost PJ, et al. Frailty as a predictor of surgical outcomes in older patients. *J Am Coll Surg.* 2010; 210(6): 901-908. doi: [10.1016/j.jamcollsurg.2010.01.028](https://doi.org/10.1016/j.jamcollsurg.2010.01.028)
27. Podsiadlo D, Richardson S. The timed "Up & Go": A test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc.* 1991; 39(2): 142-148. doi: [10.1111/j.1532-5415.1991.tb01616.x](https://doi.org/10.1111/j.1532-5415.1991.tb01616.x)
28. Soubeyran P, Fonck M, Blanc-Bisson C, et al. Predictors of early death risk in older patients treated with first-line chemotherapy for cancer. *J Clin Oncol.* 2012; 30(15): 1829-1834. doi: [10.1200/JCO.2011.35.7442](https://doi.org/10.1200/JCO.2011.35.7442)

29. Audisio RA, Pope D, Ramesh HS, et al. Shall we operate? Preoperative assessment in elderly cancer patients (PACE) can help. A SIOG surgical task force prospective study. *Crit Rev Oncol Hematol*. 2008; 65(2): 156-163. doi: [10.1016/j.critrevonc.2007.11.001](https://doi.org/10.1016/j.critrevonc.2007.11.001)
30. Wildiers H, Heeren P, Puts M, et al. International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. *J Clin Oncol*. 2014; 32(24): 2595-2603. doi: [10.1200/JCO.2013.54.8347](https://doi.org/10.1200/JCO.2013.54.8347)
31. Decoster L, Van Puyvelde K, Mohile S, et al. Screening tools for multidimensional health problems warranting a geriatric assessment in older cancer patients: An update on SIOG recommendations. *Ann Oncol*. 2015; 26(2): 288-300. doi: [10.1093/annonc/mdu210](https://doi.org/10.1093/annonc/mdu210)
32. Sullivan R, Alatiser OI, Anderson BO, et al. Global cancer surgery: Delivering safe, affordable, and timely cancer surgery. *Lancet Oncol*. 2015; 16(11): 1193-1224. doi: [10.1016/S1470-2045\(15\)00223-5](https://doi.org/10.1016/S1470-2045(15)00223-5)
33. Dale W, Hemmerich J, Kamm A, et al. Geriatric assessment improves prediction of surgical outcomes in older adults undergoing pancreaticoduodenectomy: A prospective cohort study. *Ann Surg*. 2014; 259(5): 960-965. doi: [10.1097/SLA.0000000000000226](https://doi.org/10.1097/SLA.0000000000000226)
34. Amano K, Maeda I, Shimoyama S, et al. The accuracy of physicians' clinical predictions of survival in patients with advanced cancer. *J Pain Symptom Manage*. 2015; 50(2): 139-146. doi: [10.1016/j.jpainsymman.2015.03.004](https://doi.org/10.1016/j.jpainsymman.2015.03.004)
35. Jang RW, Krzyzanowska MK, Zimmermann C, Taback N, Alibhai SMH. Palliative care and the aggressiveness of end-of-life care in patients with advanced pancreatic cancer. *J Natl Cancer Inst*. 2015; 107(3): pii: dju424. doi: [10.1093/jnci/dju424](https://doi.org/10.1093/jnci/dju424)
36. Ljungman D, Hylander A, Lundholm K. Cost-utility estimations of palliative care in patients with pancreatic adenocarcinoma: A retrospective analysis. *World J Surg*. 2013; 37(8): 1883-1891. doi: [10.1007/s00268-013-2003-z](https://doi.org/10.1007/s00268-013-2003-z)
37. National Comprehensive Cancer Network (NCCN). 2015. http://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf
38. Conroy T, Desseigne F, Ychou M, et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. *N Engl J Med*. 2011; 364: 1817-1825. doi: [10.1056/NEJMoa1011923](https://doi.org/10.1056/NEJMoa1011923)
39. Gurusamy KS, Kumar S, Davidson BR, et al. Resection versus other treatments for locally advanced pancreatic cancer. *Cochrane Database Syst Rev*. 2014; 2: CD010244. doi: [10.1002/14651858.CD010244.pub2](https://doi.org/10.1002/14651858.CD010244.pub2)
40. Maréchal R, Demols A, Gay F, et al. Tolerance and efficacy of gemcitabine and gemcitabine-based regimens in elderly patients with advanced pancreatic cancer. *Pancreas*. 2008; 36(3): e16-e21. doi: [10.1097/MPA.0b013e31815f3920](https://doi.org/10.1097/MPA.0b013e31815f3920)
41. Locher C, Fabre-Guillevin E, Brunetti F, et al. Fixed-dose rate gemcitabine in elderly patients with advanced pancreatic cancer: An observational study. *Crit Rev Oncol Hematol*. 2008; 68(2): 178-182. doi: [10.1016/j.critrevonc.2008.06.010](https://doi.org/10.1016/j.critrevonc.2008.06.010)
42. Yamagishi Y, Higuchi H, Izumiya M. Gemcitabine as first-line chemotherapy in elderly patients with unresectable pancreatic carcinoma. *J Gastroenterol*. 2010; 45(11): 1146-1154. doi: [10.1007/s00535-010-0258-9](https://doi.org/10.1007/s00535-010-0258-9)
43. Matsumoto K, Miyake Y, Kato H, et al. Effect of low-dose gemcitabine on unresectable pancreatic cancer in elderly patients. *Digestion*. 2011; 84(3): 230-235. doi: [10.1159/000330384](https://doi.org/10.1159/000330384)
44. Hentic O, Dreyer C, Rebours V, et al. Gemcitabine in elderly patients with advanced pancreatic cancer. *World J Gastroenterol*. 2011; 17(30): 3497-3502. doi: [10.3748/wjg.v17.i30.3497](https://doi.org/10.3748/wjg.v17.i30.3497)
45. Berger AK, Abel U, Komander C, et al. Chemotherapy for advanced pancreatic adenocarcinoma in elderly patients (≥70 years of age): A retrospective cohort study at the National Center for Tumor Diseases Heidelberg. *Pancreatol*. 2014; 14(3): 211-215. doi: [10.1016/j.pan.2014.03.004](https://doi.org/10.1016/j.pan.2014.03.004)
46. Oziel-Taieb S, Faure M, Gilabert M, et al. Treatment of pancreatic adenocarcinoma in elderly patients over 75 years of age: A retrospective series of 129 patients. *J Gastrointest Cancer*. 2015; 47(1): 15-19. doi: [10.1007/s12029-015-9774-4](https://doi.org/10.1007/s12029-015-9774-4)
47. Kneuert PJ, Cunningham SC, Cameron JL, et al. Palliative surgical management of patients with unresectable pancreatic adenocarcinoma: Trends and lessons learned from a large, single institution experience. *J Gastrointest Surg*. 2011; 15(11): 1917-1927. doi: [10.1007/s11605-011-1665-9](https://doi.org/10.1007/s11605-011-1665-9)
48. Glazer ES, Hornbrook MC, Krouse RS. A meta-analysis of randomized trials: immediate stent placement vs. surgical bypass in the palliative management of malignant biliary obstruction. *J Pain Symptom Manage*. 2014; 47(2): 307-314. doi: [10.1016/j.jpainsymman.2013.03.013](https://doi.org/10.1016/j.jpainsymman.2013.03.013)
49. Moss AC, Morris E, MacMathuna P. Palliative biliary stents for obstructing pancreatic carcinoma. *Cochrane Database Syst Rev*. 2006; (1): CD004200. doi: [10.1002/14651858.CD004200.pub2](https://doi.org/10.1002/14651858.CD004200.pub2)
50. Hwang SI, Kim HO, Son BH, et al. Surgical palliation of unresectable pancreatic head cancer in elderly patients. *World J Gastroenterol*. 2009; 15(8): 978-982. doi: [10.3748/wjg.15.978](https://doi.org/10.3748/wjg.15.978)
51. van Hooft JE, Dijkgraaf MG, Timmer R, et al. Independent

predictors of survival in patients with incurable malignant gastric outlet obstruction: A multicenter prospective observational study. *Scand J Gastroenterol*. 2010; 45(10): 1217-1222. doi: [10.3109/00365521.2010.487916](https://doi.org/10.3109/00365521.2010.487916)

52. Fiori E, Lamazza A, Volpino P, et al. Palliative management of malignant antro-pyloric strictures. Gastroenterostomy vs. endoscopic stenting. A randomized prospective trial. *Anticancer Res*. 2004; 24(1): 269-271.

53. Mehta S, Hindmarsh A, Cheong E, et al. Prospective randomized trial of laparoscopic gastrojejunostomy versus duodenal stenting for malignant gastric outflow obstruction. *Surg Endosc*. 2006; 20(2): 239-242. doi: [10.1007/s00464-005-0130-9](https://doi.org/10.1007/s00464-005-0130-9)

54. Jeurnink SM, Steyerberg EW, van Hooft JE, et al. Surgical gastrojejunostomy or endoscopic stent placement for the palliation of malignant gastric outlet obstruction (SUSTENT study): A multicenter randomized trial. *Gastrointest Endosc*. 2010; 71(3): 490-499. doi: [10.1016/j.gie.2009.09.042](https://doi.org/10.1016/j.gie.2009.09.042)

55. Mansoor H, Zeb F. Enteral stents are safe and effective to relieve malignant gastric outlet obstruction in the elderly. *J Gastrointest Cancer*. 2015; 46(1): 42-47. doi: [10.1007/s12029-014-9675-y](https://doi.org/10.1007/s12029-014-9675-y)

56. Lillemoe KD, Cameron JL, Yeo CJ, et al. Pancreaticoduodenectomy. Does it have a role in the palliation of pancreatic cancer? *Ann Surg*. 1996; 223(6): 718-725. Web site. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1235219/>. Accessed July 15, 2016

57. Schniewind B, Bestmann B, Kurdow R, et al. Bypass surgery versus palliative pancreaticoduodenectomy in patients with advanced ductal adenocarcinoma of the pancreatic head, with an emphasis on quality of life analyses. *Ann Surg Oncol*. 2006; 13(11): 1403-1411. doi: [10.1245/s10434-006-9172-z](https://doi.org/10.1245/s10434-006-9172-z)

58. Tol JA, Eshuis WJ, Besselink MG, et al. Non-radical resection versus bypass procedure for pancreatic cancer - a consecutive series and systematic review. *Eur J Surg Oncol*. 2015; 41(2): 220-227. doi: [10.1016/j.ejso.2014.11.041](https://doi.org/10.1016/j.ejso.2014.11.041)

59. Martin RC, McFarland K, Ellis S, et al. Irreversible electroporation in locally advanced pancreatic cancer: potential improved overall survival. *Ann Surg Oncol*. 2013; 20(Suppl 3): S443-S449. doi: [10.1245/s10434-012-2736-1](https://doi.org/10.1245/s10434-012-2736-1)

60. Narayanan G, Hosein PJ, Arora G, et al. Percutaneous irreversible electroporation for downstaging and control of unresectable pancreatic adenocarcinoma. *J Vasc Interv Radiol*. 2012; 23(12): 1613-1621. doi: [10.1016/j.jvir.2012.09.012](https://doi.org/10.1016/j.jvir.2012.09.012)

61. Månsson C, Bergenfeldt M, Brahmstaedt R, et al. Safety and preliminary efficacy of ultrasound-guided percutaneous irreversible electroporation for treatment of localized pancreatic

cancer. *Anticancer Res*. 2014; 34(1): 289-293. Web site. <http://ar.iiarjournals.org/content/34/1/289.long>. Accessed July 15, 2016.

62. Lillemoe KD, Cameron JL, Kaufman HS, et al. Chemical splanchnicectomy in patients with unresectable pancreatic cancer. A prospective randomized trial. *Ann Surg*. 1993; 217(5): 447-455. Web site. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1242819/>. Accessed July 15, 2016.

63. Okuyama M, Shibata T, Morita T, et al. A comparison of intraoperative celiac plexus block with pharmacological therapy as a treatment for pain of unresectable pancreatic cancer. *J Hepatobiliary Pancreat Surg*. 2002; 9(3): 372-375. doi: [10.1007/s005340200042](https://doi.org/10.1007/s005340200042)

64. Wong GY, Schroeder DR, Carns PE, et al. Effect of neurolytic celiac plexus block on pain relief, quality of life, and survival in patients with unresectable pancreatic cancer: a randomized controlled trial. *JAMA*. 2004; 291(9): 1092-1029. doi: [10.1001/jama.291.9.1092](https://doi.org/10.1001/jama.291.9.1092)

65. Arcidiacono PG, Calori G, Carrara S, et al. Celiac plexus block for pancreatic cancer pain in adults. *Cochrane Database Syst Rev*. 2011; (3): CD007519. doi: [10.1002/14651858.CD007519.pub2](https://doi.org/10.1002/14651858.CD007519.pub2)

66. Langan R, Huang C, Mao W, et al. Pancreaticoduodenectomy hospital resource utilization in octogenarians. *Am J Surg*. 2016; 211(1): 70-75. doi: [10.1016/j.amjsurg.2015.04.014](https://doi.org/10.1016/j.amjsurg.2015.04.014)