HHS Public Access

Author manuscript

HPB (Oxford). Author manuscript; available in PMC 2018 May 01.

Published in final edited form as:

HPB (Oxford). 2017 May ; 19(5): 465–472. doi:10.1016/j.hpb.2017.01.017.

Utilization of preoperative endoscopic ultrasound for pancreatic adenocarcinoma

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Abstract

Background—Endoscopic ultrasound (EUS) is used for pancreatic adenocarcinoma staging and obtaining a tissue diagnosis. The objective was to determine patterns of preoperative EUS and the impact on downstream treatment.

Methods—The Surveillance, Epidemiology, and End Results (SEER) Medicare-linked database was used to identify patients with pancreatic adenocarcinoma. The staging period was the first staging procedure within 6 months of surgery until surgery. Logistic regression was used to determine factors associated with preoperative EUS. The main outcome was EUS in the staging period, with secondary outcomes including number of staging tests and time to surgery.

Results—2782 patients were included, 56% were treated at an academic hospital (n=1563). 1204 patients underwent EUS (43.3%). The factors most associated with receipt of EUS were: earlier year of diagnosis, SEER area, and a NCI or academic hospital (all $p < 0.0001$). EUS was associated with a longer time to surgery (17.8 days; $p < 0.0001$), and a higher number of staging tests (40 tests/100 patients; $p < 0.0001$).

Conclusions—Factors most associated with receipt of EUS are geographic, temporal, and institutional, rather than clinical/disease factors. EUS is associated with a longer time to surgery and more preoperative testing, and additional study is needed to determine if EUS is overused.

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INTRODUCTION

Pancreatic adenocarcinoma is a devastating disease with a 5-year survival rate of 6.0%.[1] Despite only 48,000 cases per year,[2] pancreatic adenocarcinoma is the 4th leading cause of cancer-related death in the United States.[3] Selecting appropriate treatment requires accurate assessment of disease extent, which often entails an extensive workup at significant cost. Historically, assessment of disease extent required surgery; however, improvement in cross-sectional imaging modalities, such as CT and MRI, has allowed for more accurate non-invasive evaluation of disease extent. Newer technologies, specifically endoscopic ultrasound (EUS), allows for assessment of locoregional disease characteristics, with the benefit of obtaining tissue for pathology. With an increased diagnostic armamentarium, the sequence and types of staging exams has become more important.

Pathologic tissue diagnosis is important in certain settings: if diagnostic uncertainty exists, if patients are reluctant to proceed with surgery without a pathologic diagnosis, uncertainty about willingness to undergo operative therapy depending on pathology, or for neoadjuvant therapy planning.[4–8] In the absence of other easily accessible sites, EUS offers a non-operative approach to tissue sampling.

Although there are potential benefits of EUS in certain patients, preoperative tissue diagnosis is not required for the majority of patients.[9,10] Therefore, there is concern that EUS may be overused,[8] especially in patients undergoing resection with curative intent.[11] This is important because of the associated costs, need for an invasive procedure, and the potential for procedure related complications. To address this issue, the International Study Group of Pancreatic Surgery (ISGPS) convened a consensus panel to discuss EUS use in operative candidates. The result was a 2014 guideline stating that pathologic diagnosis is not required prior to surgical resection for a solid pancreatic head mass in which malignancy is suspected,[10] suggesting that the role of EUS in the staging work up for these patients is limited.

Currently, the extent of preoperative EUS utilization, factors that impact use, and ISGPS guideline adherence are not well understood. Given these knowledge gaps, we set out to determine the extent of preoperative utilization for pancreatic adenocarcinoma staging. In addition, we aimed to elucidate predictors of preoperative EUS receipt, and describe the staging workup and time to treatment for patients who undergo surgical resection.

METHODS

Data Source

The Surveillance, Epidemiology and End Results (SEER) Medicare-linked database links cancer registry data to claims, enabling investigation of cancer care patterns in Medicare beneficiaries.[12] Data include demographics, disease characteristics, and treatment information, and the data cohort used in this study was from 2000 to 2007. The use of SEER Medicare-linked data use was approved by the Institutional Review Board.

Cohort Selection

Patients ≥66 years old were included with at least 1 year of Medicare Part A and B enrollment to accurately capture comorbidities. All patients had pathologically confirmed adenocarcinoma (based on ICD-O-3) and an ICD-9-CM for a major pancreatic resection: partial, distal, or total pancreatectomy (Supplement A).

Defining Diagnosis Date and Staging Period

SEER defines the diagnosis date as the date of definitive histology in the pancreatic cancer database, which is the date of surgery for this patient population. To ensure that the focus of interest was on the preoperative staging period, the date of diagnosis had to be redefined to prevent the date of diagnosis from also being considered as the date of surgery. The diagnosis date was redefined as the date of first staging test – computed tomography (CT), magnetic resonance imaging (MRI), EUS, endoscopic retrograde cholangiopancreatography (ERCP), or percutaneous transhepatic cholangiography (PTC) - within the 6 months prior to the date of surgery. The duration of the staging period extended to the date of surgery.

First Consultant Definition

To determine the first consulting service after diagnosis, the date of the first in/outpatient physician consultation code within 30 days of diagnosis was noted. Specialty of the consultant was obtained from the carrier claims file. Specialties included surgery, general medicine, gastroenterology, and medical oncology.

Patient Covariates

The following variables were included as covariates: age, sex, marital status, rural/urban residence, race, Charlson Comorbidity Index (CCI),[13] first consulting service, income, SEER area, education, diagnosis year, stage (regional, local, other), neoadjuvant chemotherapy (Supplement A), medical school affiliation, National Cancer Institute (NCI) affiliation, hospital size (number of beds), and receipt of ERCP and PTC. Disease manifestations within 6 months of diagnosis were captured using CPT codes for jaundice (782.4), pruritus (698.9), coagulopathy (286.7), and cholangitis (576.1).

Descriptive Statistics

Patients were divided into two groups: those who had EUS during the study period and those who did not. χ^2 and t-tests were used to differentiate between groups. All statistical analyses were performed using SAS 9.3 (SAS Institute, Cary NC).

Regression Analysis

Multivariable logistic regression modeling was used to determine variables associated with EUS receipt. Variables with p-value ≤0.10 on univariate analysis were included in the model. To examine the impact of EUS utilization on the time to surgery and the number of tests during the staging period, multivariable linear regression was employed. Backward stepwise selection was used to determine final variable inclusion in the linear regression model with a ≤0.10 threshold for inclusion. Those who received neoadjuvant chemotherapy were excluded

in the calculations for the time to surgery and number of staging tests, as these patients were likely to have increased time to surgery and diagnostic testing use.

RESULTS

Patient Population

The 2782 patients who met the inclusion criteria (Fig. 1) had an average age of 74.7±5.5 years. Demographic data are provided in Table 1. Year of diagnosis was evenly distributed over the study period. 72% had regional disease. 46% underwent surgery within 30 days of diagnosis, and 80% underwent pancreaticoduodenectomy or total pancreatectomy. While 56% of patients were treated at a hospital with medical school affiliation, only 22% were treated at a NCI-designated hospital.

Comparison of EUS to Non-EUS Group

43.3% (1204/2782) underwent EUS during the staging period. When examining the differences between those undergoing EUS or not, there was significant variation in frequency of EUS amongst the SEER areas ($p < 0.0001$, Supplement B). Patients who received EUS were more likely to have been treated at an academic medical center (Table 2), a NCI hospital, a larger hospital have a gastroenterologist as the first consultant and be treated later during the study period. Patients with EUS were also more likely to have received neoadjuvant chemotherapy, with 65% (62/96) of those undergoing neoadjuvant chemotherapy having an EUS.

Factors Associated with EUS Receipt

Multivariable logistic regression to examine the factors associated with receipt of EUS found that the factor most strongly associated with preoperative EUS was diagnosis later in the study period (Table 3). Other structural and demographic factors associated with significantly different odds of EUS receipt were SEER Area, NCI hospital, academic hospital, size of hospital, gastroenterology as the first consultant and income. Presence of jaundice (OR 0.55; $p < 0.0001$) and eventual resection (Distal pancreatectomy: OR 0.57; $p < 0.0001$, Other pancreatectomy OR 0.50; $p = 0.0044$) were associated with decreased likelihood of receiving EUS.

Staging Tests

The total group (excluding patients undergoing neoadjuvant therapy) underwent an average of 3.0 ± 1.7 tests, with the EUS group having more preoperative testing (3.8 ± 1.7 vs. 2.3 ± 1.3; $p < 0.0001$). When excluding EUS from the total number of tests there was still more testing in the EUS group (2.84 ± 1.65 vs. 2.34 ± 1.34; $p < 0.0001$). On multivariable regression, EUS was associated with 40 more tests/100 patients (Table 4). Hospital size, more patient comorbidity, NCI status, jaundice, and cholangitis were also associated with increased testing. Surgery as the first consultant was associated with decreased testing.

Time to Surgery

Time to surgery was longer in the group undergoing EUS (53.2 ± 41.9 vs. 33.8 ± 34.2; $p < 0.0001$). On multivariable regression, EUS accounted for 17.8 of the 19.5-day difference in the time to surgery (Table 4). Hospital size, jaundice, cholangitis, ERCP, MRI, and a NCI hospital were also significantly associated with increased time to surgery. The only disease related factor that decreased time to surgery was the presence of jaundice with Gastroenterology, Medicine, and Surgery consults prior associated with decreased time to surgery.

DISCUSSION

In this study of Medicare patients with pancreatic adenocarcinoma who ultimately underwent surgery, nearly half received preoperative EUS. Use of EUS appears to be most strongly associated with geographic and structural characteristics, and to a lesser degree, disease related variables. This suggests that EUS use is not standardized and, to the extent that guidelines suggest that its use may be unnecessary among patients undergoing resection with curative intent, it may be overused. Patients who underwent preoperative EUS had a longer time to surgery and a higher number of preoperative staging procedures.

When comparing our findings with previous data a number of interesting similarities are noted. For example EUS use in the outpatient setting has increased over time, from 3% in 1992–1995 compared to 17% in 2004–2007 in patients undergoing resection.[14] Our analysis found substantially higher rates of EUS use overall, likely due to our inclusion of both inpatient and outpatient procedures, as compared with the previous study, which only used outpatient codes. Additionally, previous data demonstrated higher EUS use at academic centers and urban areas, and the availability of EUS and fewer years in practice (of surgeons and gastroenterologists) were the only significant predictors of utilization.[15] Interestingly, only 14% of providers stated that EUS was an essential component of management. Our finding that the initial managing specialty impacted EUS use adds additional evidence that the recommendation for EUS is not driven by the clinical scenario alone.

It has been previously suggested that EUS may offer additional information about tumor resectability as a justification for its preoperative use. However, given the current literature, EUS is not superior to cross-sectional imaging for determining resectability and does not improve survival. This is reflected in the NCCN guidelines which suggest that high quality, pancreas protocol CT scan is the primary imaging technique, with EUS playing a secondary role in the assessment of resectability.[16] The primary study using multidetector CT demonstrated that CT was superior to EUS for determining resectability of the tumors that were ultimately resected.[17] Given the improvement in the CT technology since the majority of studies comparing EUS and CT, diagnostic accuracy of CT has likely improved. In addition, the best available SEER data has demonstrated that there is no improvement in survival for those patients that undergo EUS,[18] in contrast with the initial study examining this question.[19] Additionally, EUS can carry up to a 10% risk of complication including: pancreatitis, bleeding, and infection.[20] As EUS likely does not improve survival, and is inferior to CT for staging, its use in the preoperative setting may be unwarranted, a sentiment reflected in the ISGPS guidelines. Also, we do acknowledge that there are clinical

scenarios where preoperative EUS is clearly indicated. A high suspicion for pancreatic adenocarcinoma mimics, such as autoimmune pancreatitis or lymphoma, clearly requires further evaluation and pathologic assessment. EUS with FNA is often a very good diagnostic tool in this setting. However, given the rarity of these conditions (prevalence of less than 1 in 100,000 for autoimmune pancreatitis),[21] this does not account for the wide spread utilization, (nearly a 50% rate of preoperative EUS utilization), and is likely a very minor contributor to the overall use of EUS.

In this study, EUS was associated with an increased number of staging exams. Previous data have demonstrated this inefficiency with an average of three additional staging tests (total of 4),[11] which adds an additional test compared to the 2.96 for the total group in our study, with the increased testing representing a significant expenditure.[11] This, in the context of the recent ISGPS guidelines, suggests that EUS may contribute to healthcare inefficiency, with increased resource utilization.

Our study also found that significant variation exists in the use of EUS among SEER areas (Supplement B), thus contributing another example to the growing literature documenting otherwise unexplained geographic variation in the healthcare delivery.[22–35] For example, a previous study using SEER data to examine preoperative biliary stenting led the authors to conclude that “stenting was done based on provider preference and not on the characteristics of patients or tumors.”[14] Though we were unable to determine the underlying cause of geographic variation, there are a number of possible explanations. First, EUS use may reflect the availability of specialized EUS practitioners. Surgeon preference or lack of guideline availability during the study could also account for this variation. Finally, the results may reflect a larger trend of preoperative test overutilization, which has been widely documented.[14,36–40] Further study is warranted to examine the factors that influence preoperative pancreatic adenocarcinoma staging modalities.

We found the time to surgery is longer in the EUS group, with EUS accounting for the majority of the delay. Admittedly, data derived from administrative datasets cannot be directly compared to data from primary sources, and the time to surgery as defined herein may not be directly applied to the clinical setting, however the relative difference between the groups is informative. Similarly, Jinkins *et al* found that increased time to surgery with additional procedures was demonstrated by a study which showed a 7 day delay to surgery in those who underwent biliary stenting (24.2 vs. 17.2 days; $p < 0.0001$).[14] Despite the fact that current data suggest increased time to surgery is not associated with worse survival,[41,42] these studies may not to capture all relevant variables, especially for a procedure that may not add significant clinical value preoperatively. The Institute of Medicine (IOM) report *Crossing the Quality Chasm,* states that timely delivery of care is critical to providing high quality care.[43] Timely care is defined as “reducing waits and sometimes harmful delays for those who received and those who give care,”[43] which applies to the nearly three week delay to surgery in our study group. Further, this delay is likely to contribute to patient anxiety, quality of life, and other patient-centered outcomes. Efficient and patient-centered care delivery is particularly important in this group, as testing is often invasive and survival is limited. Finally, EUS use may be discordant with the remaining IOM aims – safe, effective, efficient, equitable care. The findings of this study are unique in the fact that they suggest

that EUS is not effective or efficient, and the geographic variation suggests that EUS is not used equitably.

This study has several important limitations. First, the database date of diagnosis is difficult to determine as it is listed as the date of surgery. This required us to redefine the date of diagnosis based on a diagnostic test, which likely varies based on clinical presentation. However, the earliest of these tests within 6 months was deemed an appropriate surrogate for diagnosis date. In addition, when determining which patients underwent EUS we included all CPT codes that included an EUS with or without a biopsy, and did not distinguish between these groups. This decision was made because many of the CPT codes are very similar between procedures, and as with any coding data there is potential for the coders to inadvertently code a similar procedure but not exact procedure. To address this potential limitation of coding data we cast a broad net to obtain all patient with EUS to describe the overall utilization, without a further distinction between EUS alone and EUS with FNA. Second, as with any retrospective study, there is potential for unmeasured confounding.[44] Administrative data, in particular, lacks several important potential confounders – such as granularity in demographic variables and treatment center variables. While a lack of randomization implies that causality cannot be firmly established, the association with geography and contextual factors, and lack of strong association with disease and clinical factors suggests that this variation is not driven primarily by clinical indication. Additionally, the ISGPS guidelines were released years after the data used in the study. Clearly, we cannot make conclusions related to the impact of these guidelines on past EUS utilization during this study period, however discussion of the guidelines was used to frame the current treatment landscape. Further, the main goal of this study was not to investigate guideline adherence, but to describe the extent of EUS utilization in the years preceding these guidelines to act as a basis for future study into how these guidelines impacted EUS utilization in the years following. Finally, we included all pancreatic tumors regardless of location. This is unlikely to have a major impact on the findings since EUS can image the entire pancreas. Further, tumor location does not appear to affect the accuracy of EUS/FNA diagnosis.[45]

Despite the lack of clear indication for preoperative EUS for patients with resectable pancreatic cancers, a large and growing population of patients is undergoing EUS preoperatively. Factors most strongly associated with receipt of EUS are related to geographic and institutional factors, and year of diagnosis, as opposed to clinical or disease factors, which suggest there may be unwanted variation. Additionally, patients with EUS had a longer time to surgery and more staging tests, pointing to the fact that EUS utilization may have downstream effects. While clinical value is better demonstrated through clinical trials, this study suggests the increasing use of preoperative EUS may represent an opportunity for improvement in the efficiency and patient-centeredness of perioperative care for patients undergoing pancreatectomy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Research Support: NIH T32 - 5T32CA090217-12

Additional support was provided by the Health Innovation Program, the UW School of Medicine and Public Health from The Wisconsin Partnership Program, and the Community-Academic Partnerships core of the University of Wisconsin Institute for Clinical and Translational Research (UW ICTR) through the National Center for Advancing Translational Sciences (NCATS), grant UL1TR000427. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors. The authors acknowledge the efforts of the National Cancer Institute; the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc.; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database.

The collection of cancer incidence data used in this study was supported by the California Department of Public Health as part of the statewide cancer reporting program mandated by California Health and Safety Code Section 103885; the National Cancer Institute's Surveillance, Epidemiology and End Results Program under contract HHSN261201000140C awarded to the Cancer Prevention Institute of California, contract HHSN261201000035C awarded to the University of Southern California, and contract HHSN261201000034C awarded to the Public Health Institute; and the Centers for Disease Control and Prevention's National Program of Cancer Registries, under agreement # U58DP003862-01 awarded to the California Department of Public Health. The ideas and opinions expressed herein are those of the author(s) and endorsement by the State of California Department of Public Health, the National Cancer Institute, and the Centers for Disease Control and Prevention or their Contractors and Subcontractors is not intended nor should be inferred. The authors acknowledge the efforts of the National Cancer Institute; the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc.; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database.

References

1. Howlader, N., Noone, AM., Krapcho, M., Garshell, J., Neyman, N., Altekruse, SF., Kosary, CL., Yu, M., Ruhl, J., Tatalovich, Z., Cho, H., Mariotto, A., Lewis, DR., Chen, HS., Feuer, EJ., Cronin, KA. SEER Cancer Statistics Review (CSR). Bethesda, MD: 1975–2010. http://seer.cancer.gov/csr/1975_2010/
2. SEER stat fact sheets: pancreas cancer. 2014. http://seer.cancer.gov/statfacts/html/pancreas.html
3. Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics. CA Cancer J Clin. 2014; 64(1):9–29. http://dx.doi.org/10.3322/caac.21208. [PubMed: 24399786]
4. Săftoiu A, Vilmann P. Role of endoscopic ultrasound in the diagnosis and staging of pancreatic cancer. J Clin Ultrasound. 2009; 37(1):1–17. http://dx.doi.org/10.1002/jcu.20534. [PubMed: 18932265]
5. Hunt GC, Faigel DO. Assessment of EUS for diagnosing, staging, and determining resectability of pancreatic cancer: a review. Gastrointest Endosc. 2002; 55(2):232–237. http://dx.doi.org/10.1067/mge.2002.121342. [PubMed: 11818928]
6. Atiq M, Bhutani MS, Ross WA, et al. Role of endoscopic ultrasonography in evaluation of metastatic lesions to the pancreas: a tertiary cancer center experience. Pancreas. 2013; 42(3):516–523. http://dx.doi.org/10.1097/MPA.0b013e31826c276d. [PubMed: 23211369]
7. El Hajj II, LeBlanc JK, Sherman S, et al. Endoscopic ultrasound-guided biopsy of pancreatic metastases: a large single-center experience. Pancreas. 2013; 42(3):524–530. http://dx.doi.org/10.1097/MPA.0b013e31826b3acf. [PubMed: 23146924]
8. Gloor B, Todd KE, Reber HA. Diagnostic workup of patients with suspected pancreatic carcinoma: the University of California-Los Angeles approach. Cancer. 1997; 79(9):1780–1786. [Accessed 26 August] http://www.ncbi.nlm.nih.gov/pubmed/9128996. [PubMed: 9128996]
9. Clarke DL, Clarke BA, Thomson SR, Garden OJ, Lazarus NG. The role of preoperative biopsy in pancreatic cancer. HPB. 2004; 6(3):144–153. http://dx.doi.org/10.1080/13651820410030862. [PubMed: 18333068]

10. Asbun, HJ., Conlon, K., Fernandez-Cruz, L., et al. When to perform a pancreatoduodenectomy in the absence of positive histology? A consensus statement by the International Study Group of Pancreatic Surgery. Surgery. Jan. 2014 http://dx.doi.org/10.1016/j.surg.2013.12.032
11. Cooper M, Newman NA, Ibrahim AM, et al. Unnecessary tests and procedures in patients presenting with solid tumors of the pancreas. J Gastrointest Surg. 2013; 17(7):1218–1223. http://dx.doi.org/10.1007/s11605-013-2213-6. [PubMed: 23645419]
12. National Cancer Institute. SEER-Medicare: brief description of the SEER-Medicare Database. http://healthcaredelivery.cancer.gov/seermedicare/overview/
13. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987; 40(5):373–383. [Accessed 9 January 2014] http://www.ncbi.nlm.nih.gov/pubmed/3558716. [PubMed: 3558716]
14. Jinkins LJ, Parmar AD, Han Y, et al. Current trends in preoperative biliary stenting in patients with pancreatic cancer. Surgery. 2013; 154(2):179–189. http://dx.doi.org/10.1016/j.surg.2013.03.016. [PubMed: 23889947]
15. Ahmad NA, Kochman ML, Ginsberg GG. Practice patterns and attitudes toward the role of endoscopic ultrasound in staging of gastrointestinal malignancies: a survey of physicians and surgeons. Am J Gastroenterol. 2005; 100(12):2662–2668. http://dx.doi.org/10.1111/j.1572-0241.2005.00281.x. [PubMed: 16393217]
16. National Comprehensive Cancer Network. [Published 2016] Pancratic Adenocarinoma: NCCN Clinical Practice Guidelines in Oncology. https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf
17. DeWitt J, Devereaux B, Chriswell M, et al. Comparison of endoscopic ultrasonography and multidetector computed tomography for detecting and staging pancreatic cancer. Ann Intern Med. 2004; 141(10):753–763. [Accessed 12 April 2015] http://www.ncbi.nlm.nih.gov/pubmed/15545675. [PubMed: 15545675]
18. Parmar AD, Sheffield KM, Han Y, et al. Evaluating comparative effectiveness with observational data: endoscopic ultrasound and survival in pancreatic cancer. Cancer. 2013; 119(21):3861–3869. http://dx.doi.org/10.1002/cncr.28295. [PubMed: 23922148]
19. Ngamruengphong S, Li F, Zhou Y, Chak A, Cooper GS, Das A. EUS and survival in patients with pancreatic cancer: a population-based study. Gastrointest Endosc. 2010; 72(1):78–83. 83–2. http://dx.doi.org/10.1016/j.gie.2010.01.072. [PubMed: 20620274]
20. Yoshinaga S, Suzuki H, Oda I, Saito Y. Role of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) for diagnosis of solid pancreatic masses. Dig Endosc. 2011; 23(Suppl 1): 29–33. http://dx.doi.org/10.1111/j.1443-1661.2011.01112.x. [PubMed: 21535197]
21. Nishimori, I., Tamakoshi, A., Otsuki, M., Research Committee on Intractable diseases of the pancreas, Ministry of Health, Labour, and Welfare of Japan. Prevalence of autoimmune pancreatitis in Japan from a nationwide survey in 2002; J Gastroenterol. May. 2007 p. 6-8.http://dx.doi.org/10.1007/s00535-007-2043-y
22. Wennberg J, Gittelsohn. Small area variations in health care delivery. Science. 1973; 182(4117): 1102–1108. [Accessed 21 May 2015] http://www.ncbi.nlm.nih.gov/pubmed/4750608. [PubMed: 4750608]
23. Wennberg JE, Freeman JL, Culp WJ. Are hospital services rationed in New Haven or over-utilised in Boston? Lancet (London, England). 1987; 1(8543):1185–1189. [Accessed 18 June 2015] http://www.ncbi.nlm.nih.gov/pubmed/2883497.
24. Wennberg J, Gittelsohn A. Variations in medical care among small areas. Sci Am. 1982; 246(4): 120–134. [Accessed 18 June 2015] http://www.ncbi.nlm.nih.gov/pubmed/7079718. [PubMed: 7079718]
25. Wennberg, JE., Fisher, ES., Baker, L., Sharp, SM., Bronner, KK. Evaluating the efficiency of California providers in caring for patients with chronic illnesses. Health Aff (Millwood). 2005. http://dx.doi.org/10.1377/hlthaff.w5.526. Suppl Web:W5-526-543
26. Baker LC, Fisher ES, Wennberg JE. Variations in hospital resource use for Medicare and privately insured populations in California. Health Aff (Millwood). 2008; 27(2):w123–34. http://dx.doi.org/10.1377/hlthaff.27.2.w123. [PubMed: 18270221]

27. Song Y, Skinner J, Bynum J, Sutherland J, Wennberg JE, Fisher ES. Regional variations in diagnostic practices. N Engl J Med. 2010; 363(1):45–53. http://dx.doi.org/10.1056/NEJMsa0910881. [PubMed: 20463332]
28. Welch WP, Miller ME, Welch HG, Fisher ES, Wennberg JE. Geographic variation in expenditures for physicians' services in the United States. N Engl J Med. 1993; 328(9):621–627. http://dx.doi.org/10.1056/NEJM199303043280906. [PubMed: 8429854]
29. O'Connor GT, Quinton HB, Traven ND, et al. Geographic variation in the treatment of acute myocardial infarction: the Cooperative Cardiovascular Project. JAMA. 1999; 281(7):627–633. [Accessed 18 June 2015] http://www.ncbi.nlm.nih.gov/pubmed/10029124. [PubMed: 10029124]
30. Sutherland JM, Fisher ES, Skinner JS. Getting past denial--the high cost of health care in the United States. N Engl J Med. 2009; 361(13):1227–1230. http://dx.doi.org/10.1056/NEJMp0907172. [PubMed: 19741220]
31. Zuckerman S, Waidmann T, Berenson R, Hadley J. Clarifying sources of geographic differences in Medicare spending. N Engl J Med. 2010; 363(1):54–62. http://dx.doi.org/10.1056/NEJMsa0909253. [PubMed: 20463333]
32. Newhouse JP, Garber AM. Geographic variation in Medicare services. N Engl J Med. 2013; 368(16):1465–1468. http://dx.doi.org/10.1056/NEJMp1302981. [PubMed: 23520983]
33. Bach PB. A map to bad policy--hospital efficiency measures in the Dartmouth Atlas. N Engl J Med. 2010; 362(7):569–73. discussion p 574. http://dx.doi.org/10.1056/NEJMp0909947.
34. Skinner J, Staiger D, Fisher ES. Looking back, moving forward. N Engl J Med. 2010; 362(7):569–74. http://dx.doi.org/10.1056/NEJMp1000448. discussion 574.
35. Zhang Y, Baik SH, Fendrick AM, Baicker K. Comparing local and regional variation in health care spending. N Engl J Med. 2012; 367(18):1724–1731. http://dx.doi.org/10.1056/NEJMsa1203980. [PubMed: 23113483]
36. Vogt AW, Henson LC. Unindicated preoperative testing: ASA physical status and financial implications. J Clin Anesth. 1997; 9(6):437–441. [Accessed 15 June 2015] http://www.ncbi.nlm.nih.gov/pubmed/9278827. [PubMed: 9278827]
37. Schein OD, Katz J, Bass EB, et al. The value of routine preoperative medical testing before cataract surgery. Study of Medical Testing for Cataract Surgery. N Engl J Med. 2000; 342(3):168–175. http://dx.doi.org/10.1056/NEJM200001203420304. [PubMed: 10639542]
38. Bryson GL, Wyand A, Bragg PR. Preoperative testing is inconsistent with published guidelines and rarely changes management. Can J Anaesth. 2006; 53(3):236–241. http://dx.doi.org/10.1007/BF03022208. [PubMed: 16527786]
39. Chung F, Yuan H, Yin L, Vairavanathan S, Wong DT. Elimination of preoperative testing in ambulatory surgery. Anesth Analg. 2009; 108(2):467–475. http://dx.doi.org/10.1213/ane.0b013e318176bc19. [PubMed: 19151274]
40. Benarroch-Gampel J, Sheffield KM, Duncan CB, et al. Preoperative laboratory testing in patients undergoing elective, low-risk ambulatory surgery. Ann Surg. 2012; 256(3):518–528. http://dx.doi.org/10.1097/SLA.0b013e318265bcdb. [PubMed: 22868362]
41. Eeson G, Chang N, McGahan CE, et al. Determination of factors predictive of outcome for patients undergoing a pancreaticoduodenectomy of pancreatic head ductal adenocarcinomas. HPB (Oxford). 2012; 14(5):310–316. http://dx.doi.org/10.1111/j.1477-2574.2012.00448.x. [PubMed: 22487068]
42. Eshuis WJ, van der Gaag NA, Rauws EAJ, et al. Therapeutic delay and survival after surgery for cancer of the pancreatic head with or without preoperative biliary drainage. Ann Surg. 2010; 252(5):840–849. DOI: 10.1097/SLA.0b013e3181fd36a2 [PubMed: 21037440]
43. Institute of Medicine. Crossing the Quality Chasm: A New Health System for the 21st Century. 2001. http://iom.edu/~/media/Files/ReportFiles/2001/Crossing-the-Quality-Chasm/QualityChasm2001reportbrief.pdf
44. Wen SW, Hernandez R, Naylor CD. Pitfalls in nonrandomized outcomes studies. The case of incidental appendectomy with open cholecystectomy. JAMA. 1995; 274(21):1687–1691. [Accessed 30 April 2015] http://www.ncbi.nlm.nih.gov/pubmed/7474273. [PubMed: 7474273]

45. Turner BG, Cizginer S, Agarwal D, Yang J, Pitman MB, Brugge WR. Diagnosis of pancreatic neoplasia with EUS and FNA: a report of accuracy. Gastrointest Endosc. 2010; 71(1):91–98. http://dx.doi.org/10.1016/j.gie.2009.06.017. [PubMed: 19846087]

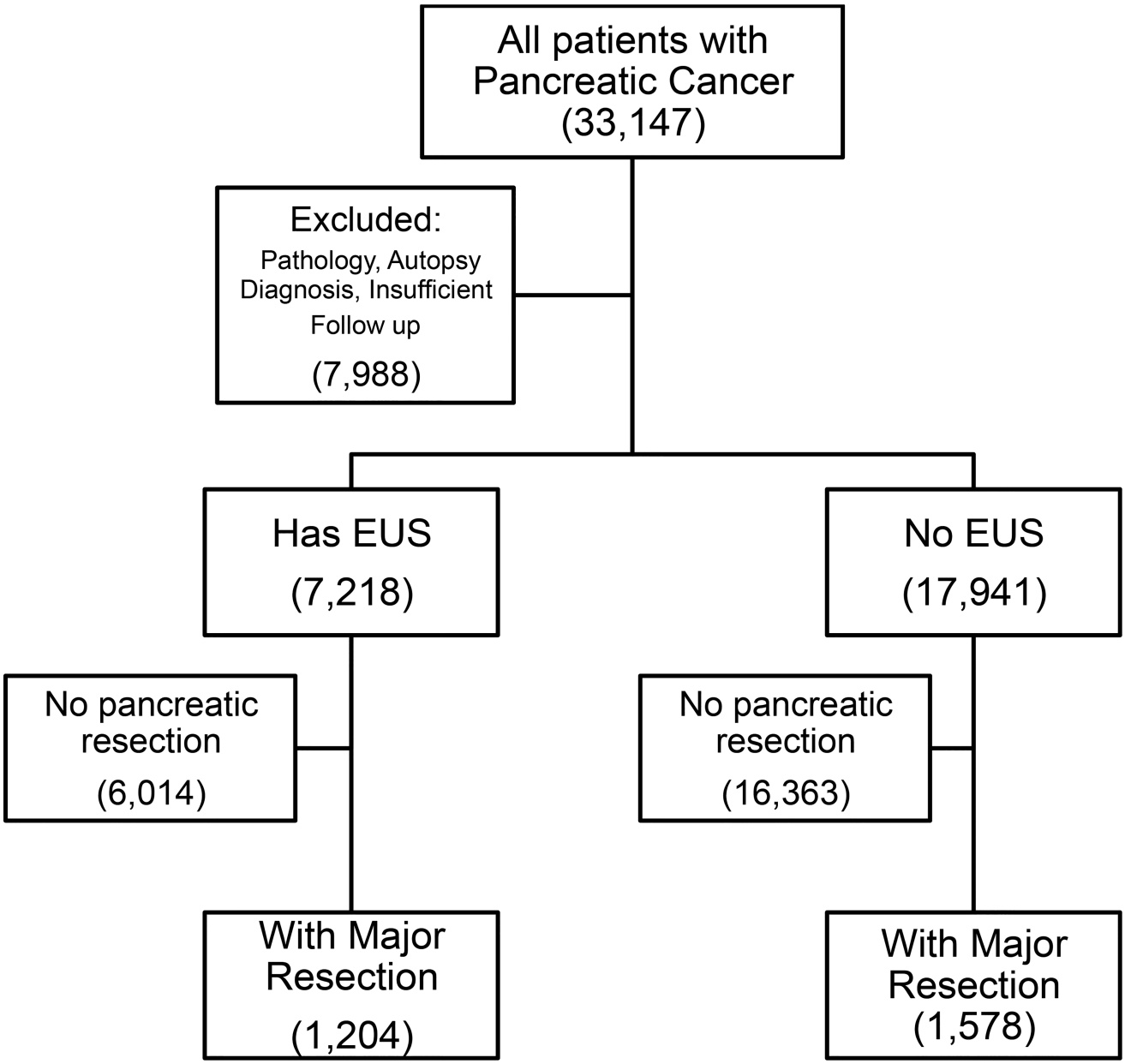

Figure 1.
Patient Cohort Construction

Table 1

Patient demographics

	Total Group	
Clinical Variables	**N = 2,782**	**%**
Age		
66–70	831	30%
71–75	847	30%
76–80	705	25%
81 and older	399	14%
Sex		
Male	1247	45%
Female	1535	55%
Cancer stage		
Local	447	16%
Regional	2002	72%
Other (distant and unstaged)	333	12%
Time from diagnosis to surgery		
Fewer than 30 days	1280	46%
30– 60 days	749	27%
More than 60 days	753	27%
Neoadjuvant chemotherapy	96	3%
Type of Surgery		
Total pancreatectomy	106	4%
Whipple	2115	76%
Distal pancreatectomy	461	17%
Other partial pancreatectomy	100	4%
Charlson Comorbidity Score		
0	985	35%
1	537	19%
2	440	16%
≥ 3	820	30%
Contextual Variables		
Major medical school affiliation	1563	56%
NCI clinical or comprehensive center	616	22%
Number of hospital beds		
<300	483	17%
300– 600	1328	48%
>600	971	35%

Table 2

Comparison of patients who did and did not undergo endoscopic ultrasound (EUS)

	Has EUS		No EUS		P-value
Clinical Variables	**N = 1204**	**%**	**N = 1578**	**%**	
Age					0.1036
66–70	374	31%	475	29%	
71–75	366	30%	481	30%	
76–80	313	26%	392	25%	
81 and older	151	13%	248	16%	
Sex					0.9583
Male	539	45%	708	45%	
Female	665	55%	870	55%	
Cancer stage					0.2448
Local	204	17%	243	15%	
Regional	868	72%	1134	72%	
Other (distant and unstaged)	132	11%	201	13%	
Clinical manifestations of disease					
Jaundice	648	54%	919	58%	0.0199
Cholangitis	140	12%	144	9%	0.0308
Pruritus	95	8%	97	6%	0.0723
First Consulting Service					
Surgery	154	13%	279	18%	0.0004
Gastroenterology	420	35%	421	27%	<0.0001
Internal Medicine	512	43%	671	43%	0.9988
Medical Oncology	33	3%	34	2%	0.3176
Time from Diagnosis to Surgery					
Fewer than 30 days	370	31%	910	58%	<0.0001
30–60 days	365	30%	384	24%	
More than 60 days	469	39%	284	18%	
Neoadjuvant chemotherapy	62	5%	34	2%	<0.0001

HPB (Oxford). Author manuscript; available in PMC 2018 May 01.

	Has EUS		No EUS		P-value
Clinical Variables	**N = 1204**	**%**	**N = 1578**	**%**	
Type of surgery					0.0046
Total pancreatectomy	47	4%	59	4%	
Whipple	951	79%	1164	74%	
Distal pancreatectomy	173	14%	288	18%	
Other partial pancreatectomy	33	3%	67	4%	
Charlson Comorbidity Score					0.7201
0	419	35%	566	36%	
1	225	19%	312	20%	
2	195	16%	245	16%	
≥3	365	30%	455	29%	
Contextual Variables					
SEER Area					<0.0001
Year of diagnosis					<0.0001
Major medical school affiliation	811	67%	752	48%	<0.0001
NCI clinical or comprehensive center	367	30%	249	16%	<0.0001
Number of hospital beds					<0.0001
<300	143	12%	340	22%	
300– 600	539	45%	789	50%	
>600	522	43%	449	28%	
Staging Test Variables					
Any CT scan	1164	97%	1539	98%	0.1157
Any MRI scan	336	28%	367	23%	0.0056
Any PTC	110	9%	190	12%	0.0138
Any ERCP	547	45%	574	36%	<0.0001

Table 3

Multivariable logistic regression for receipt of endoscopic ultrasound (EUS)

Explanatory Variables	Adjusted Odds Ratio for Undergoing Eus (95% CI)	P-value
Disease characteristics		
Jaundice	0.55 (0.45 – 0.69)	<0.0001
Pruritus	1.25 (0.90 – 1.74)	0.1758
Cholangitis	1.14 (0.868– 1.50)	0.3627
Type of Surgery		
Whipple	1.00 (Ref)	
Total pancreatectomy	1.14 (0.74 – 1.76)	0.5611
Distal pancreatectomy	0.57 (0.44 – 0.74)	<0.0001
Other partial pancreatectomy	0.50 (0.31 – 0.81)	0.0044
First consulting service		
Surgery	0.71 (0.56 – 0.89)	0.0037
Gastroenterology	1.41 (1.17 – 1.70)	0.0002
Race		0.5147
Caucasian	1.00 (Ref)	
African American	1.17 (0.82 – 1.67)	0.3902
Other	0.86 (0.60 – 1.23)	0.4188
Date of diagnosis		
2000	1.00 (Ref)	
2001	1.53 (1.04 – 2.24)	0.0305
2002	1.72 (1.19 – 2.50)	0.0042
2003	1.84 (1.28 – 2.66)	0.0011
2004	2.41 (1.69 – 3.43)	<0.0001
2005	2.57 (1.81 – 3.67)	<0.0001
2006	2.65 (1.86 – 3.76)	<0.0001
2007	2.85 (2.00 – 4.07)	<0.0001
Income		
≤25000	1.00 (Ref)	
25001 – 35000	1.40 (1.12 – 1.75)	0.0035
35001 – 45000	1.16 (0.90 – 1.50)	0.2542
≥45001	1.46 (1.15 – 1.86)	0.0018
SEER area	See Supplement B	<0.0001
Surgery at NCI designated center	1.74 (1.41 – 2.16)	<0.0001
Academic affiliation	1.61 (1.32 – 1.96)	<0.0001
Neoadjuvant chemotherapy	1.54 (0.98 – 2.41)	0.0614
Size of hospital		
<300	1.00 (Ref)	

Explanatory Variables	Adjusted Odds Ratio for Undergoing Eus (95% CI)	P-value
300–600	1.20 (0.94 – 1.56)	0.1451
>600	1.48 (1.11 – 1.97)	0.0069
Staging Tests		
Any MRI	1.13 (0.93 – 1.37)	0.2253
Any PTC	0.80 (0.59 – 1.07)	0.1271
Any ERCP	1.29 (1.05– 1.86)	0.0147

Table 4

Multivariable Linear Regression for Number of Staging Procedures Per 100 Patients and Time to Surgery

Explanatory Variables[A]	**Beta Estimate of Number of Tests per 100 Patients**	**P-value**
Has EUS	40tests	<0.0001
Hospital size (largest vs. smallest)	32 tests	<0.0001
Income (highest vs. lowest)	−18 tests	<0.0001
Charlson (highest vs. lowest)	24 tests	<0.0001
Jaundice	63 tests	<0.0001
Cholangitis	137 tests	<0.0001
Surgery consult first	−29 tests	<0.0001
NCI	32 tests	<0.0001
Explanatory Variables[B]	**Beta Estimate (Days)**	**P-value**
Has EUS	17.8 days	<0.0001
Has ERCP	11.2 days	<0.0001
Has MRI	15.1 days	<0.0001
Jaundice	−18.3 days	<0.0001
Cholangitis	15.9 days	<0.0001
Surgery consult first	−20.5 days	<0.0001
GI consult first	−15.1 days	<0.0001
Medicine consult first	−17.4 days	<0.0001
NCI	8.1 days	<0.0001

[A] SEER area, Diagnosis Year, Income, Age, Sex Charlson, Marital Status, Race, Stage, Academic Institution, Coagulopathy, Pruritus, Patient Residence, Has PTC, Medicine first consult, GI first consult, Oncology first consult, Type of surgery, and Education were removed from the model as they were removed on stepwise selection.

[B] SEER area, Diagnosis Year, Income, Age, Sex Charlson, Marital Status, Race, Stage, Academic Institution, Coagulopathy, Pruritus, Patient Residence, Has PTC, Oncology consult first, Type of surgery, and Education were removed from the model as they were removed on stepwise selection.