Staging of Pancreatic Ductal Adenocarcinoma
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. CA Cancer J Clin. 2017;67(1):7-30.	Review/Other-Dx	N/A	To estimate the numbers of new cancer cases and deaths that will occur in the United States in the current year and compile the most recent data on cancer incidence, mortality, and survival.	Mortality data were collected by the National Center for Health Statistics. In 2017, 1,688,780 new cancer cases and 600,920 cancer deaths are projected to occur in the United States. For all sites combined, the cancer incidence rate is 20% higher in men than in women, while the cancer death rate is 40% higher. However, sex disparities vary by cancer type. For example, thyroid cancer incidence rates are 3-fold higher in women than in men (21 vs 7 per 100,000 population), despite equivalent death rates (0.5 per 100,000 population), largely reflecting sex differences in the "epidemic of diagnosis." Over the past decade of available data, the overall cancer incidence rate (2004-2013) was stable in women and declined by approximately 2% annually in men, while the cancer death rate (2005-2014) declined by about 1.5% annually in both men and women. From 1991 to 2014, the overall cancer death rate dropped 25%, translating to approximately 2,143,200 fewer cancer deaths than would have been expected if death rates had remained at their peak. Although the cancer death rate was 15% higher in blacks than in whites in 2014, increasing access to care as a result of the Patient Protection and Affordable Care Act may expedite the narrowing racial gap; from 2010 to 2015, the proportion of blacks who were uninsured halved, from 21% to 11%, as it did for Hispanics (31% to 16%). Gains in coverage for traditionally underserved Americans will facilitate the broader application of existing cancer control knowledge across every segment of the population.	4

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2. Howes N, Lerch MM, Greenhalf W, et al. Clinical and genetic characteristics of hereditary pancreatitis in Europe. Clin Gastroenterol Hepatol. 2004;2(3):252-261.	Review/Other-Dx	418 individuals	To determine phenotype-genotype correlations of families	There were 112 families in 14 countries (418 affected individuals): 58 (52%) families carried the R122H, 24 (21%) the N29I, and 5 (4%) the A16V mutation, 2 had rare mutations, and 21 (19%) had no PRSS1 mutation. The median (95% confidence interval [CI]) time to first symptoms for R122H was 10 (8, 12) years of age, 14 (11, 18) years for N29I, and 14.5 (10, 21) years for mutation negative patients (P = 0.032). The cumulative risk (95% CI) at 50 years of age for exocrine failure was 37.2% (28.5%, 45.8%), 47.6% (37.1%, 58.1%) for endocrine failure, and 17.5% (12.2%, 22.7%) for pancreatic resection for pain. Time to resection was significantly reduced for females (P < 0.001) and those with the N29I mutation (P = 0.014). The cumulative risk (95% CI) of pancreatic cancer was 44.0% (8.0%, 80.0%) at 70 years from symptom onset with a standardized incidence ratio of 67% (50%, 82%).	4

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3. Lowenfels AB, Maisonneuve P, DiMagno EP, et al. Hereditary pancreatitis and the risk of pancreatic cancer. International Hereditary Pancreatitis Study Group. J Natl Cancer Inst. 1997;89(6):442-446.	Observational-Dx	246 patients	To assess the frequency of pancreatic cancer and other tumors in patients with hereditary form of pancreatitis.	The mean age (+/- standard deviation [SD]) at onset of symptoms of pancreatitis was 13.9 +/- 12.2 years. Compared with an expected number of 0.150, eight pancreatic adenocarcinomas developed (mean age +/- SD at diagnosis of pancreatic cancer: 56.9 +/- 11.2 years) during 8531 person-years of follow-up, yielding an SIR of 53 (95% confidence interval [CI] = 23-105). The frequency of other tumors was not increased: SIR = 0.7 (95% CI = 0.3-1.6). Eight of 20 reported deaths in the cohort were from pancreatic cancer. Thirty members of the cohort have already been tested for the defective hereditary pancreatitis gene: all 30 carry a mutated copy of the trypsinogen gene. The transmission pattern of hereditary pancreatitis was known for 168 of 238 patients without pancreatic cancer and six of eight with pancreatic cancer. Ninety-nine of the 238 patients without pancreatic cancer and six of the patients with pancreatic cancer inherited the disease through the paternal side of the family. The estimated cumulative risk of pancreatic cancer to age 70 years in patients with hereditary pancreatitis approaches 40%. For patients with a paternal inheritance pattern, the cumulative risk of pancreatic cancer is approximately 75%.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
4. Rebours V, Boutron-Ruault MC, Schnee M, et al. The natural history of hereditary pancreatitis: a national series. Gut. 2009;58(1):97-103.	Observational-Dx	200 patients	To assess genetic, epidemiological, clinical and morphological characteristics of HP in an extensive national survey.	78 families and 200 patients were included (181 alive, 6673 person-years, males 53%, alcoholism 5%, smoking 34%). The prevalence was 0.3/100,000 inhabitants. PRSS1 mutations were detected in 68% (R122H 78%, N29I 12%, others 10%). Penetrance was 93%. Median age at first symptom, diagnosis and date of last news, were 10 (range 1-73), 19 (1-80) and 30 (1-84) years, respectively. HP was responsible for pancreatic pain (83%), acute pancreatitis (69%), pseudocysts (23%), cholestasis (3%), pancreatic calcifications (61%), exocrine pancreatic insufficiency (34%, median age of occurrence 29 years), diabetes mellitus (26%, median age of occurrence 38 years) and pancreatic adenocarcinoma (5%, median age 55 years). No differences in clinical and morphological data according to genetic status were observed. 19 patients died, including 10 directly from HP (8 from pancreatic adenocarcinoma).	4
5. NCCN Clinical Practice Guidelines in Oncology. Pancreatic Adenocarcinoma. Version 2.2017. Available at: http://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf.	Review/Other-Dx	N/A	To provide NCCN practice guidelines on pancreatic carcinoma.	No abstract available.	4
6. Treadwell JR, Mitchell MD, Eatmon K, et al. Imaging Tests for the Diagnosis and Staging of Pancreatic Adenocarcinoma. Comparative Effectiveness Review No. 141. (Prepared by the ECRI Institute-Penn Medicine Evidence-based Practice Center under Contract No. 290-2012-00011-I.) AHRQ Publication No.14-EHC045-EF. Rockville, MD: Agency for Healthcare Research and Quality. September 2014; Available at: https://www.effectivehealthcare.ahrq.gov/ehc/products/513/1973/cancer-pancreas-executive-140923.pdf.	Review/Other-Dx	N/A	To synthesize the available information on the diagnostic accuracy and clinical utility of various imaging tests for the diagnosis and staging of pancreatic adenocarcinoma, as well as screening for pancreatic adenocarcinoma.	Some conclusions are possible at this time, specifically regarding relative test accuracy for different clinical purposes, but many uncertainties remain. Chief among these are the impact of imaging tests on patient management and longterm survival, the influence of patient factors and tumor characteristics on comparative accuracy, and test accuracy when used for screening high risk individuals.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
7. Amin MB, Edge S, Greene F, et al. AJCC Cancer Staging Manual. 8th ed. New York, NY: Springer; 2017.	Review/Other-Dx	N/A	To classify patients with cancer, define prognosis, and determine the best treatment approaches.	No results stated in abstract.	4
8. Overbeek KA, Cahen DL, Canto MI, Bruno MJ. Surveillance for neoplasia in the pancreas. Best Pract Res Clin Gastroenterol. 2016;30(6):971-986.	Review/Other-Dx	N/A	To discuss which individuals are eligible for surveillance, which lesions are aimed to be detected, and which surveillance modalities are being used in current clinical practice.	No results stated in abstract.	4
9. Howlader N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2012, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2012/, based on November 2014 SEER data submission, posted to the SEER web site, April 2015.	Review/Other-Tx	N/A	To present the incidence, mortality, prevalence, and survival statistics of cancer from 1975 through 2012.	N/A	4
10. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics, 2007. CA Cancer J Clin. 2007;57(1):43-66.	Review/Other-Tx	N/A	To estimate the number of new cancer cases and deaths expected in the United States in the current year and compile the most recent data on cancer incidence, mortality, and survival based on incidence data from the National Cancer Institute, Centers for Disease Control and Prevention, and the North American Association of Central Cancer Registries and mortality data from the National Center for Health Statistics.	While the absolute number of cancer deaths decreased for the second consecutive year in the United States (by more than 3,000 from 2003 to 2004) and much progress has been made in reducing mortality rates and improving survival, cancer still accounts for more deaths than heart disease in persons under age 85 years. Further progress can be accelerated by supporting new discoveries and by applying existing cancer control knowledge across all segments of the population.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
11. Koelblinger C, Ba-Ssalamah A, Goetzinger P, et al. Gadobenate dimeglumine-enhanced 3.0-T MR imaging versus multiphasic 64-detector row CT: prospective evaluation in patients suspected of having pancreatic cancer. Radiology. 2011;259(3):757-766.	Observational-Dx	89 patients	To compare the diagnostic performance (detection, local staging) of multiphasic 64-detector row computed tomography (CT) with that of gadobenate dimeglumine-enhanced 3.0-T magnetic resonance (MR) imaging in patients suspected of having pancreatic cancer.	Focal pancreatic masses were present in 63 patients; 43 patients had adenocarcinoma. For reader 1, the sensitivities and specificities in the detection of pancreatic adenocarcinoma were 98% (42 of 43 patients) and 96% (44 of 46 patients), respectively, for CT and 98% (42 of 43 patients) and 96% (44 of 46 patients) for MR imaging. For reader 2, the sensitivities and specificities were 93% (40 of 43 patients) and 96% (44 of 46 patients), respectively, for CT and 95% (41 of 43 patients) and 96% (44 of 46 patients) for MR imaging. Vessel infiltration was determined in 22 patients who underwent surgery, and reader 1 obtained sensitivities and specificities of 90% (nine of 10 vessels) and 98% (119 of 122 vessels), respectively, for CT and 80% (eight of 10 vessels) and 96% (117 of 122 vessels) for MR imaging; for reader 2, those values were 70% (seven of 10 vessels) and 98% (120 of 122 vessels) for CT and 50% (five of 10 vessels) and 98% (120 of 122 vessels) for MR imaging. Both readers correctly assessed resectability in 87% (13 of 15 patients) of cases with CT and 93% (14 of 15 patients) of cases with MR imaging. Nonresectability was assessed correctly with CT in 75% (six of eight patients) of cases by reader 1 and 63% (five of eight patients) of cases by reader 2; nonresectability was correctly assessed with MR imaging in 75% (six of eight patients) of cases by reader 1 and 50% (four of eight patients) of cases by reader 2. None of the differences between modalities and readers were statistically significant ($P > .05$).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
12. Kalser MH, Ellenberg SS. Pancreatic cancer. Adjuvant combined radiation and chemotherapy following curative resection. Arch Surg. 1985;120(8):899-903.	Experimental-Tx	43 patients	To assess the value of this combination regiment in prolonging survival time and disease-free survival time.	Twenty-two patients randomized to no adjuvant treatment and 21 to combined therapy were analyzed. Neither life-threatening toxic reaction nor death due to toxic effect was encountered. The study was terminated prematurely because of an unacceptably low rate of accrual combined with the observation of increasingly large survival differences between the study arms. Median survival for the treatment group (20 months) was significantly longer than that observed for the control group (11 months). Four patients, three in the treated and one in the control group, have survived five years or longer following surgery. The extent of the tumor and initial performance status were significantly and independently related to survival.	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
13. Klinkenbijl JH, Jeekel J, Sahmoud T, et al. Adjuvant radiotherapy and 5-fluorouracil after curative resection of cancer of the pancreas and periampullary region: phase III trial of the EORTC gastrointestinal tract cancer cooperative group. Ann Surg. 1999;230(6):776-782; discussion 782-774.	Experimental-Tx	207 patients	To investigate the survival benefit of adjuvant radiotherapy and 5-fluorouracil versus observation alone after surgery in patients with pancreatic head and periampullary cancers.	Between 1987 and 1995, 218 patients were randomized (108 patients in the observation group, 110 patients in the treatment group). Eleven patients were ineligible (five in the observation group and six in the treatment group). Baseline characteristics were comparable between the two groups. One hundred fourteen patients (55%) had pancreatic cancer (54 in the observation group and 60 in the treatment group). In the treatment arm, 21 patients (20%) received no treatment because of postoperative complications or patient refusal. In the treatment group, only minor toxicity was observed. The median duration of survival was 19.0 months for the observation group and 24.5 months in the treatment group (log-rank, p = 0.208). The 2-year survival estimates were 41% and 51 %, respectively. The results when stratifying for tumor location showed a 2-year survival rate of 26% in the observation group and 34% in the treatment group (log-rank, p = 0.099) in pancreatic head cancer; in periampullary cancer, the 2-year survival rate was 63% in the observation group and 67% in the treatment group (log-rank, p = 0.737). No reduction of locoregional recurrence rates was apparent in the groups.	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
14. Neoptolemos JP, Dunn JA, Stocken DD, et al. Adjuvant chemoradiotherapy and chemotherapy in resectable pancreatic cancer: a randomised controlled trial. Lancet. 2001;358(9293):1576-1585.	Experimental-Tx	353 patients	To assess the roles of chemoradiotherapy and chemotherapy in a randomised study.	541 eligible patients with pancreatic ductal adenocarcinoma were randomised: 285 in the two-by-two factorial design (70 chemoradiotherapy, 74 chemotherapy, 72 both, 69 observation); a further 68 patients were randomly assigned chemoradiotherapy or no chemoradiotherapy and 188 chemotherapy or no chemotherapy. Median follow-up of the 227 (42%) patients still alive was 10 months (range 0-62). Overall results showed no benefit for adjuvant chemoradiotherapy (median survival 15.5 months in 175 patients with chemoradiotherapy vs 16.1 months in 178 patients without; hazard ratio 1.18 [95% CI 0.90-1.55], p=0.24). There was evidence of a survival benefit for adjuvant chemotherapy (median survival 19.7 months in 238 patients with chemotherapy vs 14.0 months in 235 patients without; hazard ratio 0.66 [0.52-0.83], p=0.0005).	1
15. Neoptolemos JP, Stocken DD, Friess H, et al. A randomized trial of chemoradiotherapy and chemotherapy after resection of pancreatic cancer. N Engl J Med. 2004;350(12):1200-1210.	Experimental-Tx	289 patients	To report the final results of the European Study Group for Pancreatic Cancer 1 Trial and update the interim results.	The analysis was based on 237 deaths among the 289 patients (82 percent) and a median follow-up of 47 months (interquartile range, 33 to 62). The estimated five-year survival rate was 10 percent among patients assigned to receive chemoradiotherapy and 20 percent among patients who did not receive chemoradiotherapy (P=0.05). The five-year survival rate was 21 percent among patients who received chemotherapy and 8 percent among patients who did not receive chemotherapy (P=0.009). The benefit of chemotherapy persisted after adjustment for major prognostic factors.	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
16. Yeo CJ, Abrams RA, Grochow LB, et al. Pancreaticoduodenectomy for pancreatic adenocarcinoma: postoperative adjuvant chemoradiation improves survival. A prospective, single-institution experience. Ann Surg. 1997;225(5):621-633; discussion 633-626.	Experimental-Tx	174 patients	To evaluate prospectively survival after pancreaticoduodenectomy for pancreatic adenocarcinoma, comparing two different postoperative adjuvant chemoradiation protocol to those of no adjuvant therapy.	Pancreaticoduodenectomy was performed in 174 patients, with 1 in-hospital death (0.6%). Ninety-nine patients elected standard therapy, 21 elected intensive therapy, and 53 patients declined therapy. The three groups were comparable with respect to race, gender, intraoperative blood loss, tumor differentiation, lymph node status, tumor diameter, and resection margin status. Univariate analyses indicated that tumor diameter < 3 cm, intraoperative blood loss < 700 mL, absence of intraoperative blood transfusions, and use of adjuvant chemoradiation therapy were associated with significantly longer survival ($p < 0.05$). By Cox proportional hazards survival analysis, the most powerful predictors of outcome were tumor diameter, intraoperative blood loss, status of resection margins, and use of postoperative adjuvant therapy. The use of postoperative adjuvant chemoradiation therapy was a predictor of improved survival (median survival, 19.5 months compared to 13.5 months without therapy; $p = 0.003$). The intensive therapy group had no survival advantage when compared to that of the standard therapy group (median survival, 17.5 months vs. 21 months, p = not significant).	1

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17. Ishikawa O, Ohigashi H, Imaoka S, et al. Preoperative indications for extended pancreatectomy for locally advanced pancreas cancer involving the portal vein. Ann Surg. 1992;215(3):231-236.	Observational-Tx	35 patients	To determine the indications for extended pancreatectomy for locally advanced carcinoma of the pancreas, in terms of postoperative prognosis.	An extended pancreatectomy with portal vein or superior mesenteric vein (PV/SMV) resection and regional lymphadenectomy was performed in 35 of 50 consecutive cancers that extended into the retroperitoneal spaces and involved the PV or SMV. Among the many background factors in the 35 resected specimens, the degree of PV/SMV invasion by the cancer was most closely associated with prognosis, despite resection of all involved PV/SMV. This factor generally correlated with the preoperative findings on the portal phase of superior mesenteric arteriograph. In 17 selected patients in whom PV/SMV invasion had been angiographically both semicircular or less and 1.2 cm (1.4 cm on the film) or less in length, the 3-year survival rate was 59%. This survival rate was significantly higher than the 29% 3-year survival rate in all 35 patients (p less than 0.05). Conversely, among the 18 patients in whom invasion was angiographically either beyond semicircular or more than 1.2 cm (1.4 cm on the film) in length, there were no 1.5-year survivors, and this result was even worse than that of 15 nonresectable cases. Based on postoperative survival, the degrees of PV/SMV invasion on preoperative angiography (narrowing pattern and length) are good indicators for aggressive pancreatectomy for locally advanced pancreatic cancer.	2

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18. Katz MH, Marsh R, Herman JM, et al. Borderline resectable pancreatic cancer: need for standardization and methods for optimal clinical trial design. Ann Surg Oncol. 2013;20(8):2787-2795.	Review/Other-Tx	N/A	To review limitations of studies of borderline resectable PDAC reported to date, highlight important controversies related to this disease stage, emphasize the research infrastructure necessary for its future study, and present a recently-approved Intergroup pilot study (Alliance A021101) that will provide a foundation upon which subsequent well-designed clinical trials can be performed.	We identified twenty-three studies published since 2001 which report outcomes of patients with tumors labeled as borderline resectable and who were treated with neoadjuvant therapy prior to planned pancreatectomy. These studies were heterogeneous in terms of the populations studied, the metrics used to characterize therapeutic response, and the indications used to select patients for surgery. Mechanisms used to standardize these and other issues that are incorporated into Alliance A021101 are reviewed.	4
19. Kim HJ, Czischke K, Brennan MF, Conlon KC. Does neoadjuvant chemoradiation downstage locally advanced pancreatic cancer? J Gastrointest Surg. 2002;6(5):763-769.	Observational-Tx	163 patients	To review our experience with preoperative chemoradiation for surgically staged, locally advanced pancreatic cancer to determine whether patients are downstaged with multimodal therapy allowing for curative resection.	Chemoradiation was administered to 87 (53.3%) of 163, and regimens varied from standard 5-fluorouracil/gemcitabine-based therapies to experimental protocols. Only three patients (3/87; 3.4%) had a sufficient clinical response on restaging to warrant reexploration. Of these, two thirds were unresectable on subsequent laparoscopy because of extensive vascular involvement or metastatic disease. Only one patient underwent a potentially curative resection, with a survival of 18 months despite negative margins and no nodal involvement. The overall median survival for all patients with locally advanced disease treated with chemoradiation was 11 months (6.5 months without multimodal therapy; P = 0.004). Although chemoradiation is associated with improved overall survival in locally advanced disease, it rarely leads to surgical "downstaging" allowing for potentially curative pancreatic resections. Novel multimodality approaches are required.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
20. Lu DS, Reber HA, Krasny RM, Kadell BM, Sayre J. Local staging of pancreatic cancer: criteria for unresectability of major vessels as revealed by pancreatic-phase, thin-section helical CT. AJR Am J Roentgenol. 1997;168(6):1439-1443.	Observational-Dx	25 patients	To determine the criteria for unresectability of major peripancreatic vessels in patients with pancreatic carcinoma as revealed by optimally enhanced, pancreatic-phase thin-section helical CT.	At surgery, definitive evaluation was possible for 80 vessels. Forty-eight of 48 vessels graded 0 and three of three vessels graded 1 were resectable. Four of seven vessels graded 2, seven of eight vessels graded 3, and 14 of 14 vessels graded 4 were unresectable. A threshold of between grades 2 and 3, which corresponded to tumor involvement of one-half circumference of the vessel, yielded the lowest number of false-negatives and an acceptable number of false-positives for unresectability. Such a threshold would have yielded a sensitivity of 84%, a specificity of 98%, a positive predictive value of 95%, and a negative predictive value of 93% for unresectability of the vessels studied.	2
21. Mollberg N, Rahbari NN, Koch M, et al. Arterial resection during pancreatectomy for pancreatic cancer: a systematic review and meta-analysis. Ann Surg. 2011;254(6):882-893.	Meta-analysis	26 studies-366 and 2243 patients who underwent pancreatectomy with and without AR	To evaluate the perioperative and long-term outcomes of patients with AR during pancreatectomy for pancreatic cancer.	The literature search identified 26 studies including 366 and 2243 patients who underwent pancreatectomy with and without AR. All studies were retrospective cohort studies and the methodological quality was moderate to low. Meta-analyses revealed AR to be associated with a significantly increased risk for perioperative mortality [Odds ratio (OR) = 5.04; 95% confidence interval (CI), 2.69-9.45; P < 0.0001; I(2) = 24%], poor survival at 1 year (OR = 0.49; 95% CI, 0.31-0.78; P = 0.002; I(2) = 35%) and 3 years (OR = 0.39; 95% CI, 0.17-0.86; P = 0.02; I(2) = 49%) compared with patients without AR. The increased perioperative mortality (OR = 8.87; 95% CI, 3.40-23.13; P < 0.0001; I(2) = 5%) and lower survival rate at 1 year (OR = 0.50; 95% CI, 0.31-0.82; P = 0.006; I(2) = 40%) was confirmed in the comparison to patients undergoing venous resection. Despite substantial perioperative mortality, pancreatectomy with AR was associated with more favorable survival compared with patients who did not undergo resection for locally advanced disease.	M

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22. Nakao A, Kanzaki A, Fujii T, et al. Correlation between radiographic classification and pathological grade of portal vein wall invasion in pancreatic head cancer. Ann Surg. 2012;255(1):103-108.	Observational-Dx	358 patients	To clarify the correlation between radiographic type of portal vein (PV) invasion and pathological grade of PV wall invasion, and their correlation with postoperative prognosis.	Four hundred and sixty-three patients underwent resection, and PV resection was performed in 297. Combined arterial vessel resection was performed in 16 cases. No significant difference in operative mortality was observed between PV preservation (0.6%) and PV-only resection (2.1%), and no operative deaths occurred after 1999. Radiographic classification of PV invasion correlated with incidence of pathological PV wall invasion. In pancreatic head carcinoma, no pathological PV wall invasion was observed in type A (n = 111). Pathological PV invasion was observed in 51% of type B (42/82), 74% of type C (72/97), and 93% of type D (63/68). Long-term survival (>5 years) was observed in types A and B, and grades 0 and 1 subgroups.	3
23. Stitzenberg KB, Watson JC, Roberts A, et al. Survival after pancreatectomy with major arterial resection and reconstruction. Ann Surg Oncol. 2008;15(5):1399-1406.	Observational-Tx	12 patients	To demonstrate that resection of a tumor-involved HA or CA with arterial reconstruction may offer a survival benefit to select patients whose tumors were traditionally regarded as unresectable.	Twelve patients (six men and six women) with adenocarcinoma underwent pancreatectomy with resection of a tumor-involved HA (n = 2) and/or CA (n = 10). Median age at diagnosis was 62 years (range, 53-73 years). All patients completed neoadjuvant chemoradiotherapy with or without full dose chemotherapy before resection. Procedures performed were six extended pancreaticoduodenectomies, two proximal subtotal pancreatectomies, two distal pancreatectomies, and two total pancreatectomies. Ten cases involved celiac resections, and two had isolated HA resections. The 60-day mortality was 17% (2 of 12). Median survival after diagnosis was 20 months (range, 6-41 months). Median survival after resection was 17 months (range, 1-36 months). Survival was not statistically significantly related to age, sex, margin status, or preoperative CA19-9 level. The 3-year survival was 17%. There were no 5-year survivors.	2

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24. Tseng JF, Raut CP, Lee JE, et al. Pancreaticoduodenectomy with vascular resection: margin status and survival duration. J Gastrointest Surg. 2004;8(8):935-949; discussion 949-950.	Observational-Tx	291 patients	To review margin status and survival duration in pancreaticoduodenectomy with vascular resection.	A total of 141 patients underwent VR with PD. Superior mesenteric-portal vein resections included tangential resection with vein patch (n=36), segmental resection with primary anastomosis (n=35), and segmental resection with autologous interposition graft (n=55). Hepatic arterial resections were performed in 10 patients, and resections of the anterior surface of the inferior vena cava were performed in 5 patients. PD was performed for pancreatic adenocarcinoma in 291 patients; standard PD was performed in 181 and VR in 110. Median survival was 23.4 months in the group that required VR and 26.5 months in the group that underwent standard PD (P=0.177). A Cox proportional hazards model was constructed to analyze the effects of potential prognostic factors (VR, tumor size, T stage, N status, margin status) on survival. The need for VR had no impact on survival duration.	2

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25. Winter JM, Cameron JL, Campbell KA, et al. 1423 pancreaticoduodenectomies for pancreatic cancer: A single-institution experience. J Gastrointest Surg. 2006;10(9):1199-1210; discussion 1210-1191.	Observational-Tx	1,175 patients	To update the Johns Hopkins experience with PD for pancreatic cancer.	We examined 1175 PDs for ductal adenocarcinomas in greater detail. Eighteen different histological types of pancreatic cancer were identified; the most common diagnoses included ductal adenocarcinoma, neuroendocrine carcinoma, and IPMN with invasive cancer. Patients with ductal adenocarcinoma were analyzed in detail. The median age was 66 years, with patients in the present decade significantly older (68 years), on average, than patients in the three prior decades (e.g., 60 years in 1970, P = 0.02). The median tumor diameter was 3 cm; 42% of the resections had positive margins and 78% had positive lymph nodes. The perioperative morbidity was 38%. The median postoperative stay declined over time, from 16 days in the 1980s to 8 days in the 2000s (P < 0.001). The perioperative mortality declined from 30% in the 1970s to 1% in the 2000s (P < 0.001). The median survival for all patients with ductal adenocarcinoma was 18 months (1-year survival = 65 %, 2-year survival = 37%, 5-year survival = 18%). In a Cox proportional hazards model, pathological factors having a significant impact on survival included tumor diameter, resection margin status, lymph node status, and histologic grade.	3

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26. Tamm EP, Balachandran A, Bhosale PR, et al. Imaging of pancreatic adenocarcinoma: update on staging/resectability. Radiol Clin North Am. 2012;50(3):407-428.	Review/Other-Dx	N/A	To review recent surgical advances and general treatment approaches that have led to a change in the understanding of resectable disease and staging, the current criteria for staging, current classifications of resectable disease, imaging techniques, imaging, and imaging criteria for staging.	Because of the evolution of treatment strategies staging criteria for pancreatic cancer now emphasize arterial involvement for determining unresectable disease. Preoperative therapy may improve the likelihood of margin negative resections of borderline resectable tumors. Cross-sectional imaging is crucial for correctly staging patients. Magnetic resonance (MR) imaging and computed tomography (CT) are probably comparable, with MR imaging probably offering an advantage for identifying liver metastases. Positron emission tomography/CT and endoscopic ultrasound may be helpful for problem solving. Clear and concise reporting of imaging findings is important. Several national organizations are developing templates to standardize the reporting of imaging findings.	4
27. American College of Radiology. ACR Appropriateness Criteria®: Jaundice. Available at: https://acsearch.acr.org/docs/69497/Narrative/.	Review/Other-Dx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for a specific clinical condition.	No results stated in abstract.	4
28. Lu DS, Vedantham S, Krasny RM, Kadell B, Berger WL, Reber HA. Two-phase helical CT for pancreatic tumors: pancreatic versus hepatic phase enhancement of tumor, pancreas, and vascular structures. Radiology. 1996;199(3):697-701.	Observational-Dx	27 patients	To quantitatively evaluate and validate a two-phase helical computed tomographic (CT) protocol for evaluation of pancreatic tumors.	Mean tumor-pancreas contrast was significantly greater during the pancreatic phase (67 HU +/- 19) than the hepatic phase (39 HU +/- 16) ($P < .001$) This was the result of both greater enhancement of normal pancreas and lower tumor enhancement during the pancreatic phase. Opacification of all vascular structures, including the portal vein, was also greater during the pancreatic phase ($P < .001$).	3
29. Shrikhande SV, Barreto SG, Goel M, Arya S. Multimodality imaging of pancreatic ductal adenocarcinoma: a review of the literature. HPB (Oxford). 2012;14(10):658-668.	Review/Other-Dx	66 articles	To determine the role of current imaging modalities in the diagnosis and determination of resectability of pancreatic and peri-ampullary adenocarcinomas.	Based on 66 articles analysed in the review, MDCT and MRI/MRCP have comparable sensitivity and specificity rates for diagnosis and staging of pancreatic cancers. EUS offers the best sensitivity and specificity rates for lesions <2 cm. Improved staging has been noted when PET-CT scans are added to pre-operative evaluation.	4

Staging of Pancreatic Ductal Adenocarcinoma
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
30. Dewitt J, Devereaux BM, Lehman GA, Sherman S, Imperiale TF. Comparison of endoscopic ultrasound and computed tomography for the preoperative evaluation of pancreatic cancer: a systematic review. Clin Gastroenterol Hepatol. 2006;4(6):717-725; quiz 664.	Review/Other-Dx	11 studies; 678 patients	To determine whether computed tomography (CT) or endoscopic ultrasound (EUS) is superior for the detection, staging, and resectability of pancreatic cancer.	Eleven studies with 678 patients satisfied inclusion criteria. Nine studies assessed tumor detection, all of which concluded that the sensitivity of EUS was superior to CT. Four of 5 studies that assessed tumor staging accuracy and 5 of 8 that assessed nodal staging accuracy concluded that EUS was superior to CT. Among the 4 studies that assessed resectability, 2 showed no difference between EUS and CT, and 1 favored each modality. Three of 11 studies met all but one of the quality criteria. The most important and frequent study limitations were lack of a consecutive series of patients and biased patient selection for surgery. Quantitative comparisons among studies were precluded by differences in tumor staging classifications, surgical selection, CT and EUS techniques, and reporting of operating characteristics.	4
31. Farma JM, Santillan AA, Melis M, et al. PET/CT fusion scan enhances CT staging in patients with pancreatic neoplasms. Ann Surg Oncol. 2008;15(9):2465-2471.	Observational-Dx	82 patients	To assess the additional value, in relation to computed tomography (CT), of PET/CT imaging for patients with PN.	The sensitivity and specificity of PET/CT in diagnosing pancreatic cancer were 89% and 88%, respectively. Sensitivity of detecting metastatic disease for PET/CT alone, standard CT alone, and the combination of PET/CT and CT were 61%, 57%, and 87%, respectively. Findings on PET/CT influenced the clinical management in seven patients (11%), two with a supraclavicular lymph node (LN), two occult liver lesions, two peritoneal implants, and one peri-esophageal LN.	3
32. Kim JH, Eun HW, Kim KW, et al. Diagnostic performance of MDCT for predicting important prognostic factors in pancreatic cancer. Pancreas. 2013;42(8):1316-1322.	Observational-Dx	111 patients	To investigate diagnostic accuracy of MDCT for determining tumor stage, node metastasis, tumor size, vascular invasion, and perineural invasion prognostic factors.	Statistically, tumor size on specimens (3.4 +/- 1.46 cm) is larger than tumor size on MDCT (3.2 +/- 1.41 cm; P = 0.001). The diagnostic accuracy rates for tumor stage were 82.9% and 77.5%, with moderate agreement (kappa = 0.732). The accuracy rates for node metastasis were 59.5% and 55.0%, with fair agreement (kappa = 0.597). The diagnostic accuracy rates for vascular invasion were 94% and 92%. The areas under the curve for perineural invasion were 0.733 and 0.66 (P = 0.069), with moderate agreement (kappa = 0.77).	2

Staging of Pancreatic Ductal Adenocarcinoma
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
33. Zhang Y, Huang J, Chen M, Jiao LR. Preoperative vascular evaluation with computed tomography and magnetic resonance imaging for pancreatic cancer: a meta-analysis. Pancreatology. 2012;12(3):227-233.	Meta-analysis	8 studies; 296 patients	To compare CT with MRI in preoperative evaluation of vascular invasion in patients with pancreatic cancer.	Eight studies (n = 296) met the inclusion criteria. The pooled sensitivity of CT and MRI in diagnosing VI was 71% (95% CI, 64-78) and 67% (95% CI, 59-74), pooled specificity 92% (95% CI, 89-95) and 94% (95% CI, 91-96), positive likelihood ratio 6.33 (95% CI, 4.51-8.87) and 6.58 (95% CI, 4.62-9.37), negative likelihood ratio 0.34 (95% CI, 0.27-0.43) and 0.38 (95% CI, 0.30-0.47), and AUCs 0.87 and 0.76 (p = 0.63), respectively. There was no significant difference between CT and MRI for preoperative diagnosis of VI. Subgroup analysis of 4 studies (n = 143) showed no significant difference between CT and MRI in preoperative diagnosis of venous or arterial invasion (p = 0.73 and p = 0.81, respectively). When CT was compared with MRA in 3 studies (n = 110), again there was no significant difference for preoperative staging of VI (p = 0.54).	M
34. Chen CH, Yang CC, Yeh YH, Chou DA, Nien CK. Reappraisal of endosonography of ampullary tumors: correlation with transabdominal sonography, CT, and MRI. J Clin Ultrasound. 2009;37(1):18-25.	Observational-Dx	41 patients	To reappraise the accuracy of transabdominal sonography (US), CT, MRI, and endosonography (EUS) in the diagnosis and staging of ampullary tumors.	The detection rates for ampullary tumors were 97.6% for EUS, 81.3% for MRI, 28.6% for CT, and 12.2% for US ($p < 0.001$ for EUS versus CT; $p < 0.001$ for EUS versus US; $p > 0.05$ for EUS versus MRI). The accuracy in T staging for ampullary carcinomas was 72.7% for EUS, 53.8% for MRI, and 26.1% for CT ($p < 0.01$ for EUS versus CT; $p > 0.05$ for EUS versus MRI). The accuracy in N staging for ampullary carcinomas was 66.7% for EUS, 76.9% for MRI, and 43.5% for CT with no statistically significant difference between the 3 modalities. The sensitivity in detecting malignant lymph nodes was 46.7% for EUS, 25.0% for MRI, and 0% for CT ($p < 0.01$ for EUS versus CT; $p > 0.05$ for EUS versus MRI; $p > 0.05$ for MRI versus CT). Transpapillary stenting, advanced tumor extension (>T2), large tumor size (>2 cm), tumor differentiation, and endoscopic appearance of tumor growth did not significantly influence EUS accuracy in T or N staging ($p > 0.05$).	3

Staging of Pancreatic Ductal Adenocarcinoma
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
35. Rivadeneira DE, Pochapin M, Grobmyer SR, et al. Comparison of linear array endoscopic ultrasound and helical computed tomography for the staging of periampullary malignancies. Ann Surg Oncol. 2003;10(8):890-897.	Observational-Dx	48 patients	To compare linear array endoscopic ultrasound (EUS) and helical computed tomography (CT) scan in the preoperative local staging evaluation of patients with periampullary tumors.	Forty-eight patients (28 men and 20 women; mean age, 62 +/- 4.9 years; range, 18-90 years) were identified. Malignancy was histologically confirmed in 44 patients. Parameters evaluated included tumor size, lymph node metastases, and major vascular invasion. EUS was significantly more sensitive (100%), specific (75%), and accurate (98%) than helical CT (68%, 50%, and 67%, respectively) for evaluation of the periampullary mass (P <.05). In addition, EUS detected regional lymph node metastases in more patients than helical CT. Sensitivity, specificity, and accuracy of EUS were 61%, 100%, and 84%, in comparison to 33%, 92%, and 68%, respectively, with CT. Major vascular involvement was noted in 9 of 44 patients. EUS correctly identified vascular involvement in 100% compared with 45% with CT (P <.05).	3
36. Motosugi U, Ichikawa T, Morisaka H, et al. Detection of pancreatic carcinoma and liver metastases with gadoxetic acid-enhanced MR imaging: comparison with contrast-enhanced multi-detector row CT. Radiology. 2011;260(2):446-453.	Observational-Dx	100 patients	To intraindividually compare gadoxetic acid-enhanced magnetic resonance (MR) imaging with contrast material-enhanced multi-detector row computed tomography (CT) in detection of pancreatic carcinoma and liver metastases.	No significant differences were observed between CT and MR images in depiction of pancreatic carcinoma. However, MR imaging had greater sensitivity in depicting liver metastasis than did CT for two of the three readers in the MR imaging-versus-CT analysis (85% vs 69%, P = .046) and for all three readers in the lesion-by-lesion analysis (92%-94% vs 74%-76%, P = .030-.044).	2

Staging of Pancreatic Ductal Adenocarcinoma
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
37. Ikuta Y, Takamori H, Ikeda O, et al. Detection of liver metastases secondary to pancreatic cancer: utility of combined helical computed tomography during arterial portography with biphasic computed tomography-assisted hepatic arteriography. J Gastroenterol. 2010;45(12):1241-1246.	Observational-Dx	192 patients	To define the diagnostic advantage of computed tomography during arterial portography (CTAP) combined with computed tomography-assisted hepatic arteriography (CTHA) for the preoperative detection of liver metastases secondary to pancreatic cancer compared with that of multidetector computed tomography (MDCT).	Liver metastases were identified in 39 patients by means of MDCT. Of the 153 patients who had no evidence of liver metastases on MDCT, 129 patients underwent CTAP + CTHA, and 53 of these 129 patients (41.1%) were diagnosed as having liver metastases that could not be detected by MDCT. These tumors missed by MDCT ranged from 3 to 15 mm in size. On CTAP + CTHA, a solitary nodule in the liver was detected in 11 patients, 2 nodules were detected in 6 patients, 3 lesions were detected in 2 patients, and >==4 lesions were detected in 34 patients. The sensitivity and specificity of CTAP + CTHA versus MDCT were 94.2 versus 48.4% and 82.7 versus 97.9%, respectively.	3

Staging of Pancreatic Ductal Adenocarcinoma
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
38. Allen VB, Gurusamy KS, Takwoingi Y, Kalia A, Davidson BR. Diagnostic accuracy of laparoscopy following computed tomography (CT) scanning for assessing the resectability with curative intent in pancreatic and periampullary cancer. Cochrane Database Syst Rev. 2013;11:CD009323.	Meta-analysis	15 studies; 1015 patients	To determine the diagnostic accuracy of diagnostic laparoscopy performed as an add-on test to CT scanning in the assessment of curative resectability in pancreatic and periampullary cancer.	Fifteen studies with a total of 1015 patients were included in the meta-analysis. Only one study including 52 patients had a low risk of bias and low applicability concern in the patient selection domain. The median pre-test probability of unresectable disease after CT scanning across studies was 40.3% (that is 40 out of 100 patients who had resectable cancer after CT scan were found to have unresectable disease on laparotomy). The summary sensitivity of diagnostic laparoscopy was 68.7% (95% CI 54.3% to 80.2%). Assuming a pre-test probability of 40.3%, the post-test probability of unresectable disease for patients with a negative test result was 0.17 (95% CI 0.12 to 0.24). This indicates that if a patient is said to have resectable disease after diagnostic laparoscopy and CT scan, there is a 17% probability that their cancer will be unresectable compared to a 40% probability for those receiving CT alone.A subgroup analysis of patients with pancreatic cancer gave a summary sensitivity of 67.9% (95% CI 41.1% to 86.5%). The post-test probability of unresectable disease after being considered resectable on both CT and diagnostic laparoscopy was 18% compared to 40% for those receiving CT alone.	M
39. Hariharan D, Constantinides V, Kocher HM, Tekkis PP. The role of laparoscopy and laparoscopic ultrasound in the preoperative staging of patients with resectable colorectal liver metastases: a meta-analysis. Am J Surg. 2012;204(1):84-92.	Meta-analysis	12 studies; 1047 patients	To clarify the role of SL/LUS in patients with potentially resectable CRLM by performing a review and meta-analysis on all available recent literature, with particular emphasis on sensitivity analyses such as that for high-quality studies (STAndards for the Reporting of Diagnostic accuracy [STARD] [scores, > 14] and large [> 100 patients] studies).	Twelve studies satisfied the inclusion criteria. A total of 1,047 patients underwent SL/LUS. The true yield of SL/LUS for CRLM was 19% (95% confidence interval [CI], 16%-22%), with a diagnostic odds ratio of 132 (95% CI, 56-310) and an overall sensitivity of 59% (95% CI, 53%-65%). Subgroup analysis for detection of other liver and peritoneal lesions showed a sensitivity of 59% (95% CI, 49%-67%) and 75% (95% CI, 63%-85%) respectively. There was major between-study heterogeneity for all analyses, with no obvious cause revealed by meta-regression.	M

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
40. Tapper E, Kalb B, Martin DR, Kooby D, Adsay NV, Sarmiento JM. Staging laparoscopy for proximal pancreatic cancer in a magnetic resonance imaging-driven practice: what's it worth? HPB (Oxford). 2011;13(10):732-737.	Review/Other-Dx	124 patients	To perform a retrospective, indirect cost-effectiveness analysis of SL after MRI for pancreatic head lesions.	The average costs of hospitalization for patients undergoing pancreaticoduodenectomy, open palliative bypass and endoscopic palliation were: US$26, 122.43, US$21, 957.18 and US$11, 304.00, respectively. The calculated cost of SL without laparotomy was US$2966.25 or US$1538.61 prior to laparotomy. The calculated cost of treating unresectable disease by outpatient laparoscopy followed by endoscopy was US$5943.17. Routine SL would increase our costs by US$76, 967.46 (3.6%).	4
41. Nawaz H, Fan CY, Kloke J, et al. Performance characteristics of endoscopic ultrasound in the staging of pancreatic cancer: a meta-analysis. JOP. 2013;14(5):484-497.	Meta-analysis	29 studies; 1,330 patients	To assess accuracy and performance characteristics of EUS in determining nodal staging, vascular invasion, and prediction of resectability of pancreatic cancer. A secondary aim was to perform head to head comparison of performance characteristics between EUS and CT for nodal staging, vascular invasion and resectability.	Forty-nine studies were considered of which 29 met inclusion criteria with a total of 1,330 patients. Pooled summary estimates for EUS-nodal staging were 69% for sensitivity and 81% for specificity. For vascular invasion, sensitivity was 85% and specificity was 91%. The sensitivity and specificity for resectability was 90% and 86%, respectively. CT scan showed lower sensitivity than EUS for nodal staging (24% vs. 58%) and vascular invasion (58% vs. 86%); however, the specificities for nodal staging (88% vs. 85%) and vascular invasion (95% vs. 93%) were comparable in studies where both imaging techniques were performed. The sensitivity and specificity of CT in determining resectability (90% and 69%) was similar to that of EUS (87% and 89%).	M

Staging of Pancreatic Ductal Adenocarcinoma
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
42. Shin HJ, Lahoti S, Sneige N. Endoscopic ultrasound-guided fine-needle aspiration in 179 cases: the M. D. Anderson Cancer Center experience. Cancer. 2002;96(3):174-180.	Observational-Dx	179 EUS-FNAs in 166 consecutive patients	To evaluate the diagnostic accuracy of EUS-FNA and to evaluate factors influencing diagnostic accuracy, using our initial experience with EUS-FNA in a consecutive series of 179 cases obtained from 166 patients.	The review FNA diagnoses were as follows: NND (49 cases), atypia (17 cases), suspicious for malignancy (12 cases), benign tumor/cyst excluding NEN (10 cases), NEN (6 cases), carcinoma (85 cases). Follow-up methods included resection (49 cases), surgical biopsy (21 cases), repeat FNA or brushing cytology (28 cases), and clinical follow-up only (81 cases). Of the 49 NND cases, 23 (47%) had positive follow-up results (i.e., false-negative diagnosis) that were confirmed by tissue diagnosis (resection/surgical biopsy in 11 cases [48%] and repeat FNA/brushing in 12 cases [52%]). These included pancreatic/ampullary adenocarcinoma in 20 cases, esophageal squamous carcinoma in 1 case, and NEN in 2 cases. Follow-up also revealed carcinoma in all 12 suspicious cases and 13 pancreatic adenocarcinomas and 1 microcystic adenoma in 14 of the 17 atypical cases. Overall, repeat computed tomography (CT)-guided FNA samples yielded a definite diagnosis in four atypical and seven NND cases, whereas EUS-FNA results provided a definite diagnosis in three cases in which CT-guided FNA failed and in two cases in which ampullary biopsy failed. No false-positive cases were identified. The false-negative rate due to inadequate sampling was 13.2%. Sensitivity (including cases with inadequate cellularity and nondiagnostic aspirates) was 81.7% and specificity was 100%. None of the factors evaluated (lesion characteristics, aspiration site, and tumor type) significantly influenced diagnostic results.	3

Staging of Pancreatic Ductal Adenocarcinoma
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
43. Barber TW, Kalff V, Cherk MH, Yap KS, Evans P, Kelly MJ. 18 F-FDG PET/CT influences management in patients with known or suspected pancreatic cancer. Intern Med J. 2011;41(11):776-783.	Observational-Dx	22 PET/CT scans in 21 patients	To assess and validate the incremental information of positron emission tomography/computed tomography (PET/CT) over conventional staging investigations (CSI) and to assess the management impact of PET/CT in patients with known or suspected pancreatic cancer.	PET/CT and CSI were discordant in 14/22 (64%: 95% CI; 43-84%) scans. Of the 14 discordant scans, PET/CT assessment was correct in eight, conventional imaging in four and there was insufficient information in two. Overall, PET/CT management impact was classified as high (n= 6), medium (n= 3), low (n= 9) or none (n= 4). Significant changes in management (high or medium impact) were induced by PET/CT in 9/22 scans (41%: 95% CI; 20-62%) predominantly by correctly modifying the disease extent.	3
44. Crippa S, Salgarello M, Laiti S, et al. The role of (18)fluoro-deoxyglucose positron emission tomography/computed tomography in resectable pancreatic cancer. Dig Liver Dis. 2014;46(8):744-749.	Observational-Dx	72 patients	To retrospectively assess the value of (18)fluoro-deoxyglucose positron emission tomography/computed tomography in addition to conventional imaging as a staging modality in pancreatic cancer.	Overall, 21% of patients had a maximum standardized uptake value </= 3, and 60% of those had undergone neoadjuvant treatment (P=0.0001). Furthermore, 11% of patients were spared unwarranted surgery since positron emission tomography/computed tomography detected metastatic disease. All liver metastases were subsequently identified with contrast-enhanced ultrasound. Sensitivity and specificity of positron emission tomography/computed tomography for distant metastases were 78% and 100%. The median CA19.9 concentration was 48.8 U/mL for the entire cohort and 292 U/mL for metastatic patients (P=0.112).	3

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
45. Einersen P, Epelboym I, Winner MD, Leung D, Chabot JA, Allendorf JD. Positron emission tomography (PET) has limited utility in the staging of pancreatic adenocarcinoma. J Gastrointest Surg. 2014;18(8):1441-1444.	Observational-Dx	123 patients	To assess the utility of PET in identifying metastatic disease and evaluate the prognostic potential of standard uptake value (SUV).	For 123 patients evaluated 2005-2011, PET and CT/MRI were concordant in 108 (88 %) cases; however, PET identified occult metastatic lesions in seven (5.6 %). False-positive PETs delayed surgery for three (8.3 %) patients. In a cohort free of metastatic disease in 78.9 % of cases, the sensitivity and specificity of PET for metastases were 89.3 and 85.1 %, respectively, compared with 62.5 and 93.5 % for CT and 61.5 and 100.0 % for MRI. Positive predictive value and negative predictive value of PET were 64.1 and 96.4 %, respectively, compared with 75.0 and 88.9 % for CT and 100.0 and 91.9 % for MRI. Average difference in maximum SUV of resectable and unresectable lesions was not statistically significant (5.65 vs. 6.5, $p = 0.224$) nor was maximum SUV a statistically significant predictor of survival ($p = 0.18$).	3
46. Kim MJ, Lee KH, Lee KT, et al. The value of positron emission tomography/computed tomography for evaluating metastatic disease in patients with pancreatic cancer. Pancreas. 2012;41(6):897-903.	Observational-Dx	125 patients	To reassess the clinical impact of PET/CT for the detection of distant metastasis of pancreatic cancer.	After the conventional staging workup, we determined that 76 patients (60.8%) had resectable lesions, whereas 48 patients had unresectable lesions. One patient underwent explorative laparotomy due to equivocal resectability. Positron emission tomography/computed tomography diagnosed distant metastasis in only 2 (2.6%) of the 76 patients with resectable lesions, and these patients did not undergo unnecessary surgical treatment. Complete resection was not performed in 8 of the 74 operative patients because they had distant metastasis detected during the operative procedure. Positron emission tomography/computed tomography diagnosed distant metastasis in 32 of the 44 patients with metastatic lesions that were histologically shown to have sensitivity of 72.7%.	3

Staging of Pancreatic Ductal Adenocarcinoma
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
47. Pappas SG, Christians KK, Tolat PP, et al. Staging chest computed tomography and positron emission tomography in patients with pancreatic adenocarcinoma: utility or futility? HPB (Oxford). 2014;16(1):70-74.	Observational-Dx	247 patients	To determine if routine staging chest computed tomography (CT) or positron emission tomography (PET) scanning alters the clinical management of patients with newly diagnosed pancreatic adenocarcinoma.	Pancreatic adenocarcinoma was present in 247 consecutive patients. Abdominal CT demonstrated metastases in 108 (44%) and localized disease in 139 (56%) patients. Chest CT and PET were not performed in 15 (11%) of these 139 patients. In the remaining 124 patients, CT imaging suggested resectable disease in 46, borderline resectable disease in 52 and locally advanced disease in 26 patients. Chest CT demonstrated an unsuspected lymphoma in one patient with borderline resectable disease and PET identified extrapancreatic disease in two patients with locally advanced disease. Chest CT and PET added no information in 121 (98%) of the 124 patients.	4
48. Yao J, Gan G, Farlow D, et al. Impact of F18-fluorodeoxyglycose positron emission tomography/computed tomography on the management of resectable pancreatic tumours. ANZ J Surg. 2012;82(3):140-144.	Observational-Dx	36 patients with 37 potentially resectable pancreatic tumours	To investigate the impact of this technique on the management of patients with resectable pancreatic tumours.	Pancreatic adenocarcinoma was diagnosed in 30 patients, neuroendocrine tumours in 3, mass-forming pancreatitis in 3 and serous cystadenoma in 1. The median standard uptake (max) value was 5.0 (range 2.2-12.0). Sensitivity and specificity of detecting extrapancreatic metastatic disease were 73% and 100%, respectively. Three occult liver metastases were detected at laparotomy following negative PET/CT. PET/CT findings influenced the management of 8 (22%) patients - 3 with liver metastases, 3 with bone metastases, 1 with lymph node metastases and 1 by identifying the benign appearance of the pancreatic tumour.	3

Staging of Pancreatic Ductal Adenocarcinoma
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
49. Wang Z, Chen JQ, Liu JL, Qin XG, Huang Y. FDG-PET in diagnosis, staging and prognosis of pancreatic carcinoma: a meta-analysis. World J Gastroenterol. 2013;19(29):4808-4817.	Meta-analysis	39 studies	To investigate the potential role of positron emission tomography (PET) in the diagnosis, staging and prognosis predicting of pancreatic carcinoma (PC).	A total of 39 studies were included. The pooled sensitivity of PET in diagnosing PC (30 studies, 1582 patients), evaluating N stating (4 studies, 101 patients) and liver metastasis (7 studies, 316 patients) were 0.91 (95%CI: 0.88-0.93), 0.64 (95%CI: 0.50-0.76), and 0.67 (95%CI: 0.52-0.79), respectively; and the corresponding specificity was 0.81 (95%CI: 0.75-0.85), 0.81 (95%CI: 0.25-0.85), and 0.96 (95%CI: 0.89-0.98), respectively. In prognosis analysis (6 studies, 198 patients), significant difference of overall survival was observed between high and low standardized uptake value groups (HR = 2.39, 95%CI: 1.57-3.63). Subgroup analysis showed that PET/CT was more sensitive than PET alone in evaluating liver metastasis of PC, 0.82 (95%CI: 0.48-0.98) and 0.67 (95%CI: 0.52-0.79), respectively.	M
50. Cassinotto C, Cortade J, Belleannee G, et al. An evaluation of the accuracy of CT when determining resectability of pancreatic head adenocarcinoma after neoadjuvant treatment. Eur J Radiol. 2013;82(4):589-593.	Observational-Dx	80 patients	To evaluate the accuracy of MDCT for determination of resectability R0 after neoadjuvant therapy in patients with pancreatic head adenocarcinoma locally advanced.	41/42 patients in control group and 31/38 patients in neoadjuvant group finally had curative resection. While resection R0 is similar in both groups (83% and 81%), CT accuracy in determining resectability R0 was significantly decreased in neoadjuvant group (58% versus 83%; p=0.039). CT scan specificity was significantly lower after neoadjuvant therapy (52% versus 88% in control group) due to an overestimation of vascular invasion: 12/31 patients with complete resection in neoadjuvant group were evaluated at high risk of incomplete resection on CT scan. Tumor size tends to be underestimated in control group (-2mm) and overestimated in neoadjuvant group (+10mm). T-staging accuracy was decreased in neoadjuvant group (39% versus 78% in control group; p=0.002).	2

Staging of Pancreatic Ductal Adenocarcinoma
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
51. Donahue TR, Isacoff WH, Hines OJ, et al. Downstaging chemotherapy and alteration in the classic computed tomography/magnetic resonance imaging signs of vascular involvement in patients with pancreaticobiliary malignant tumors: influence on patient selection for surgery. Arch Surg. 2011;146(7):836-843.	Observational-Dx	41 patients	To determine whether computed tomography (CT)/magnetic resonance imaging (MRI) signs of vascular involvement are accurate after downstaging chemotherapy (DCTx) and to highlight factors associated with survival in patients who have undergone resection.	We operated on 41 patients (1992-2009) with locally advanced periampullary malignant tumors after a median of 8.5 months of DCTx. Before DCTx, most patients (38 [93%]) were unresectable because of evidence of vascular contact on CT/MRI scan or operative exploration. Criteria for exploration after DCTx were CT/MRI evidence of tumor shrinkage and/or change in signs of vascular involvement, cancer antigen 19-9 decrease, and good functional status. None had progressive disease. At operation, we resected tumors in 34 of 41 patients (83%), and 6 had persistent vascular involvement. Surprisingly, CT/MRI scan was only 71% sensitive and 58% specific to detect vascular involvement after DCTx. "Involvement" on imaging was often from tumor fibrosis rather than viable cancer. Radiographic decrease in tumor size also did not predict resectability (P = .10). Patients with tumors that were resected had a median 87% decrease in cancer antigen 19-9 (P = .04) during DCTx. The median follow-up (all survivors) was 31 months, and disease-specific survival was 52 months for patients with resected tumors.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
52. Ferrone CR, Marchegiani G, Hong TS, et al. Radiological and surgical implications of neoadjuvant treatment with FOLFIRINOX for locally advanced and borderline resectable pancreatic cancer. Ann Surg. 2015;261(1):12-17.	Observational-Tx	188 patients	To evaluate the accuracy of imaging in determining the resectability of PDAC and to determine the surgical and clinicopathologic outcomes of pancreatic resections after neoadjuvant FOLFIRINOX therapy.	Of 188 patients undergoing resection for PDAC, 40 LA/borderline received FOLFIRINOX and 87 received no neoadjuvant therapy. FOLFIRINOX resulted in a significant decrease in tumor size, yet 19 patients were still classified as LA and 9 as borderline. Despite post-FOLFIRINOX imaging suggesting continued unresectability, 92% had an R0 resection. When compared with no neoadjuvant therapy, FOLFIRINOX resulted in significantly longer operative times (393 vs 300 minutes) and blood loss (600 vs 400 mL), but significantly lower operative morbidity (36% vs 63%) and no postoperative pancreatic fistulas. Length of stay (6 vs 7 days), readmissions (20% vs 30%), and mortality were equivalent (1% vs 0%). On final pathology, the FOLFIRINOX group had a significant decrease in lymph node positivity (35% vs 79%) and perineural invasion (72% vs 95%). Median follow-up was 11 months with a significant increase in overall survival with FOLFIRINOX.	2

Staging of Pancreatic Ductal Adenocarcinoma
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
53. Brook OR, Brook A, Vollmer CM, Kent TS, Sanchez N, Pedrosa I. Structured reporting of multiphasic CT for pancreatic cancer: potential effect on staging and surgical planning. Radiology. 2015;274(2):464-472.	Observational-Dx	48 structured and 72 nonstructured multiphasic CT reports	To compare structured versus nonstructured reporting of multiphasic computed tomography (CT) for staging of pancreatic cancer and the effects of both types of reporting on subjective assessment of resectability.	Forty-eight (40%) structured and 72 (60%) nonstructured multiphasic CT reports were reviewed. Nonstructured reports contained a mean +/- standard deviation of 7.3 key features +/- 2.1 (range, 1-11) and structured reports contained 10.6 +/- 0.9 (range, 9-12) features (P < .001). Information for surgical planning was deemed easily accessible in 94%, 60%, and 98% of structured and 47%, 54%, and 32% of nonstructured reports by the three surgeons, respectively (P < .001, .79, < .001). Surgeons had sufficient information for surgical planning in 96%, 69%, and 98% of structured and 31%, 43%, and 25% of nonstructured reports (P < .001, .009, and < .001). When surgeons reviewed reports in combination with multiphasic CT images, they were more likely to convert an answer of "unsure" regarding resectability to a definitive answer (ie, resectable or unresectable) when the reports were structured than when they were nonstructured.	2
54. Marcal LP, Fox PS, Evans DB, et al. Analysis of free-form radiology dictations for completeness and clarity for pancreatic cancer staging. Abdom Imaging. 2015;40(7):2391-2397.	Observational-Dx	295 free-form computed tomography (CT) reports	To assess the completeness and clarity of current free-form radiology reports for pancreatic cancer staging by evaluating them against the elements of the RSNA CT oncology primary pancreas mass dictation template.	Primary lesion location, size, and effect on bile duct (BD) were provided in 93.9% (277/295), 69.8% (206/295), and 67.5% (199/295) of reports, respectively. Standard terms to describe vascular involvement were used in 47.5% (140/295) of reports. In 20.3% (60/295), the resectability status could not be defined based on the report alone. In 36.9% (109/295) of reports, review of CT images was necessary to understand vascular involvement. Radiologists expert in pancreatic oncology had a higher proportion of reports using standardized terminology and reports in which vascular involvement was understood without revisiting the images.	3

Staging of Pancreatic Ductal Adenocarcinoma
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
55. Al-Hawary MM, Francis IR, Chari ST, et al. Pancreatic ductal adenocarcinoma radiology reporting template: consensus statement of the Society of Abdominal Radiology and the American Pancreatic Association. Radiology. 2014;270(1):248-260.	Review/Other-Dx	N/A	To address the integration of the appropriate descriptive terms defining the stage based on the disease extent, suggest a lexicon to be used in the reporting of the imaging findings to avoid confusion in terminology, and provide a structured template to improve the completeness of radiology reporting in cases of PDA.	Adoption of this standardized imaging reporting template should improve the decision-making process for the management of patients with pancreatic ductal adenocarcinoma by providing a complete, pertinent, and accurate reporting of disease staging to optimize treatment recommendations that can be offered to the patient. Standardization can also help to facilitate research and clinical trial design by using appropriate and consistent staging by means of resectability status, thus allowing for comparison of results among different institutions.	4
56. Gottlieb RA. CT onco primary pancreas mass template. 2012; Available at: http://www.radreport.org/txt/0000018.	Review/Other-Dx	N/A	N/A	N/A	4
57. American College of Radiology. ACR Appropriateness Criteria® Radiation Dose Assessment Introduction. Available at: http://www.acr.org/~/media/ACR/Documents/AppCriteria/RadiationDoseAssessmentIntro.pdf.	Review/Other-Dx	N/A	Guidance document on exposure of patients to ionizing radiation.	N/A	4

Evidence Table Key

Study Quality Category Definitions

- *Category 1*: The study is well-designed and accounts for common biases.
- *Category 2*: The study is moderately well-designed and accounts for most common biases.
- *Category 3*: There are important study design limitations.
- *Category 4*: The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  c) the study is an expert opinion or consensus document.
- M = Meta-analysis

Dx = Diagnostic

Tx = Treatment