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Comparing the Clinical Impact of Pancreatic Cyst Surveillance Programs: A Trial of the ECOG-ACRIN Cancer Research Group (EA2185)

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Abstract

Background: The optimal surveillance strategy for pancreatic cysts, which occur in up to 20% of the adult population, is ill defined. The risk of malignant degeneration of these cysts is low, however the morbidity and mortality associated with pancreatic cancer are high. Two clinical surveillance guidelines are in regular use. Both the Fukuoka and American Gastroenterological Association (AGA) guidelines rely on radiographic and endoscopic imaging. They differ primarily in their recommended frequencies of interval surveillance imaging. While evidence driven clinical guidelines should promote higher quality care, competing guidelines on the same topic may provide discordant recommendations and potential reduction in the quality and/or value of care.

Objectives: The primary objective is to compare the clinical effectiveness of the two surveillance guidelines to identify patients most likely to benefit from pancreatic resection. Secondary objectives include comparison of resource utilization, patient reported outcomes, incidental findings are other clinical outcomes.

Methods: 4606 asymptomatic patients with newly identified pancreatic cysts ≥1cm in diameter will be randomized 1:1 to high intensity (Fukuoka) or low intensity (AGA) surveillance. All participants will be followed prospectively for 5 years.

Conclusion: Differing guidelines confuse providers, patients and policymakers. This large, prospective, randomized trial will compare the clinical effectiveness and resource allocation requirements of two guidelines addressing a common clinical entity.

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Keywords

pancreatic cyst; pancreatic cancer; cost-effectiveness; clinical effectiveness; randomized controlled trial

Introduction

Pancreatic cysts occur in up to 20% of the adult population. (1) Cysts are often identified incidentally in patients undergoing cross sectional imaging for another indication. (2) Because more than 15% of ambulatory visits include MRI or CT scanning, it is predicted that the incidence of cysts will continue to rise. (2) Several types of cyst form in the pancreas. Some are precursor lesions to pancreatic cancer, creating anxiety for patients and providers. Although the risk of malignant progression in any cyst is low (estimated to be approximately 0.5%/y (3)), the morbidity and mortality associated with pancreatic cancer are high.

At present, there are two primary strategies for pancreatic cyst surveillance. The first, commonly called the Fukuoka guidelines were developed based on expert opinion. The alterative guideline was established by the American Gastroenterological Association (AGA) employing a more explicitly evidence-based approach. (4, 5) Both rely on periodic cross-sectional imaging, endoscopic ultrasound (EUS) and cyst fluid sampling to assess cyst type and stratify risk for malignancy. The principle difference between the algorithms is the recommended interval frequency of surveillance imaging.

The clinical effectiveness of either strategy is incompletely known. (6) When patients who undergo cyst resection were studied, reports simulating the impact of each guideline were largely inconclusive. (7, 8) A recent meta-analysis of several retrospective studies found the sensitivity/specificity of Fukuoka for advanced neoplasia and cancer was 0.67 (95% CI 0.64–0.70) and 0.64 (95% CI 0.62–0.66), respectively. In comparison, the sensitivity and specificity of the AGA recommendations were 0.59 (95% CI 0.52–0.65) and 0.77 (95% CI 0.74–0.80). (9) Fukuoka appears to detect more target disease, at the price of more misdiagnosis. Advocates of Fukuoka worry that the AGA strategy will miss opportunities to reduce pancreatic cancer mortality. In contrast, proponents of AGA point to the potential reduction in high morbidity/mortality surgeries for benign disease and substantial costs saving through reduced imaging and endoscopy frequency. The relative acceptability of competing strategies with variable risks of over and under diagnosis requires additional study. (10)

We designed this trial to compare the Fukuoka and AGA guidelines for pancreatic cyst surveillance. The primary goal is to compare the clinical effectiveness of the two guidelines in a prospective, randomized, multicenter study. Secondary goals include the comparison of associated resource utilization and patient reported outcomes of study participants managed under one of the two guidelines for pancreatic cyst surveillance. An important additional study component is the prospective, serial collection of biosamples and radiomics data which will be linked to clinical outcomes. While imaging and endoscopy are mainstays of both guidelines, the discovery and validation of novel biomarker and/or radiomic variations

are active areas of research that may provide complementary predictive or prognostic tools for pancreatic cysts.

Methods/Design

Study Overview

Asymptomatic participants (n=4606) with pancreatic cysts at least 1 cm in diameter will be randomized in a 1:1 ratio to either “high” intensity or “low” intensity surveillance. The “high” intensity strategy is modeled on the Fukuoka guidelines, while the “low” intensity is similar to the AGA guidelines with the exception that all participants will be followed for 5 years (the AGA guideline recommends that surveillance can be stopped earlier in select patients). Study duration is 8 years in total, comprising a six-month ramp up period, 2 years to enroll the study cohort, 5 years of prospective follow-up, and a six-month period for data analysis, and manuscript preparation. Once enrolled, we will contact each participant at least annually (via mail, web-based and/or telephone) to arrange collection of serial biospecimens, radiomics data, resource utilization and patient reported outcomes (see Table 1). Study coordinators at each site will be in contact with participants as well as any physician associated with participants’ cyst care to ensure maintenance of randomization and adherence to imaging and endoscopy recommendations. The trial is conducted by the ECOG-ACRIN Cancer Research Group, with support from the National Community Oncology Research Program of the National Cancer Institute.

Study Endpoints and Rationale:

Primary Endpoint

The primary comparison will be between the rates of unfavorable clinical outcomes in the two arms:

- Unfavorable outcomes comprise: (1) any pancreatic cancer without surgery; (2) unresectable pancreatic cancer or cancer >T1a, N0 at surgery; (3) benign disease at surgery
- Favorable outcomes comprise: (1) High grade dysplasia (HGD) and/or resectable, early stage pancreatic cancer (T1a, N0) at surgery; (2) benign disease and no surgery

Delineation of these outcomes represent the result of substantial discussion between various stakeholders (surgery, gastroenterology, radiology) involved in the care of pancreatic cyst patients. Patient input was also solicited. We believe these outcomes best reflect the tension between the desire to identify neoplastic pancreatic lesions at a treatable stage while minimizing the burdens of surveillance (inconvenience, worry and cost) on patients and providers.

Secondary Endpoints

Additional objectives of the study include comparisons of the following endpoints across arms:

1. Clinical:
    a. surgical mortality and major morbidity rates
    b. pancreatic cancer incidence and all-cause mortality
2. Healthcare resource utilization and costs:
    a. institutional (direct costs)
    b. utilization of imaging, invasive testing, surgical and other procedural costs
    c. patient (out of pocket and other indirect) costs
3. Incidental findings
    a. direct and indirect costs
    b. quality of life
4. Patient reported outcomes
    a. patient report of quality of life and situational anxiety
    b. financial distress
    c. adherence by arm assignment

In addition, we will serially collect and bank biospecimens and radiomics data for future study. Biospecimens to be collected include blood, buccals swabs and urine for all participants, as well as pancreatic cyst fluid and surgical resection tissue for participants undergoing EUS-FNA and/or surgery. All specimens will be collected, processed and maintained using existing biorepository protocols. The performance of known and future markers will be assessed as predictors of high-grade dysplasia or cancer.

All radiographic images will be retained for future radiomics analysis and potential association with clinical outcomes. For the study, we suggest standard protocols for acquisition of CT and MRI data, however we do not attempt to enforce these standards as a goal of this study is the assessment of “real world” clinical practices which will vary across sites.

Study Duration

Participants will be recruited over a 2-year period and will be followed for a minimum of 5 years. Of note, the 5-year follow-up for all participants was chosen since most relevant outcomes are predicted to occur in that time frame. However, it is recognized that a small fraction of participants may demonstrate later cyst progression. If available, we intend to seek additional funding to follow the assembled cohort for longer.

Statistical/Analytic Considerations

Primary Endpoint:

The primary endpoint of the trial is the occurrence of one of the “unfavorable” outcomes as defined above. We hypothesize that compared to the high intensity surveillance arm, participants randomized to low intensity surveillance will experience fewer unfavorable outcomes. Time to the first occurrence of an unfavorable outcome will be measured from randomization. Survival analysis methods will be used to estimate and compare distributions of time to an unfavorable outcome between the study arms. In particular Kaplan-Meier estimates will be developed for each arm and a log rank test will be used to compare the two arms.

Sample Size Considerations:

To arrive at an expected 5-year proportion of participants with an unfavorable outcome we used information from a recent systematic review of pancreatic cyst surveillance to estimate that about 2.7% of participants will undergo surgery each year and 0.25% will be diagnosed with pancreatic cancer. (3) We also assumed that the vast majority of pancreatic cancers will be diagnosed at surgery for participants in the low intensity surveillance arm. Hence we assumed that about 12.25% (i.e., 5*[2.7%−.25%]) of such participants will experience an unfavorable outcome during a five-year period post randomization. The sample size was selected to provide 90% power to detect a 30% relative reduction in the unfavorable outcome proportions at 5 years between the two arms. Computations were performed using the PASS15 software (NCSS, Kaysville, UT) and assumed a log rank test with a two-sided type I error of 5%.

In anticipation of cross-over between arms as well as loss to follow up over 5 years of surveillance, we modeled the impact of various scenarios on sample size requirements. Under the conservative assumption that each arm would suffer 3%/year loss to follow-up and 5%/year crossover, we selected a sample size of 4606 (2303 per arm) participants. We plan to monitor accrual, loss to follow-up and cross-over rates during the trial and will consider adjustments to the sample size in consultation with the trial’s Data and Safety Monitoring Committee and NCI.

The planned sample size is adequate to support all secondary endpoints. Here we provide brief descriptions of the statistical approach to each:

- **i.** Data on health care resource utilization related to cyst surveillance, including management of any incidental findings, will be obtained from hospital and outpatient facilities providing care to study participants. Measures of utilization in categories of interest (such as diagnostic procedures and hospitalizations) will be derived and compared across arms. Aggregate estimates of cost will be developed using standard Medicare prices. We will also collect patient (out-of-pocket and other indirect) costs from patient surveys and compare across arms.
- **ii.** Measures of psychosocial functioning will be assessed longitudinally and compared between the arms. These measures include the Champion Breast

Cancer Fear Scale modified for pancreatic cancer worry (11); Disease Specific Perceived Risk Scale modified for pancreatic cancer (12); Spielberger State Trait Anxiety Inventory (STAI) short form (13) and the PROMIS-10 (14), monitoring processing style (15), and perceived financial toxicity (16). The analysis will rely on longitudinal regression modeling to account for repeated assessments over time.

iii. Rates of major surgical morbidity and/or mortality will be estimated and compared across arms. All-cause mortality will be estimated and compared between the arms using log rank tests.

iv. Pancreatic cancer incidence, pancreatic cancer specific mortality, and all-cause mortality will be estimated and compared between the arms using log rank tests.

Study participants, eligibility criteria, and recruitment procedures

Eligibility Criteria

Study participants will be ≥ 50 years and ≤ 75 years with an ECOG Performance Status 0–1 at baseline. Participants must have received a CT or MRI within 3 months of registration that identifies a new ≥1 cm pancreatic cyst. Patients with a prior diagnosis of a pancreatic cyst, pancreatic malignancy or a history of pancreatic resection are not eligible. Additional exclusion criteria include a history of acute or chronic pancreatitis, a family history of pancreatic adenocarcinoma in 1 or more first degree relatives, imaging findings or clinical signs that would prompt immediate surgical consideration (enhancing mural nodule, solid component in cyst, pancreatic duct >10mm, cyst causing obstructive jaundice), a comorbid illness that precludes pancreatic cyst resection, pregnancy or current participation in an established surveillance program.

Participant Recruitment

Most pancreatic cysts are serendipitously identified when patients undergo cross sectional imaging for unrelated reasons. Once a cyst ≥ 1cm is identified, the great majority of patients are referred to gastroenterologists or surgeons for ongoing surveillance and management. Many centers have created multidisciplinary groups (GI, surgery, radiology) to meet this clinical need. In addition, electronic medical record prompts are easily created to facilitate referral by primary care physicians in response to new radiographic findings. A recruitment strategy that utilizes a subset of ECOG/ACRIN and NCORP members with such clinical systems in place will be complemented by institutions in which such groups can collaborate under an institutional study champion to permit effective accrual.

Enrollment and randomization procedures

1. Consent will be obtained by the treating physician who, with coordinator assistance, will be responsible for data acquisition and maintenance of randomization

2. Eligible, consenting participants agree to the following

a. Randomization to prospective, high or low intensity pancreatic cyst surveillance

b. Permission for study coordinators to contact all physicians who regularly contribute to cyst management including test requisition. For each participant the study team will identify one responsible, lead physician, however multi-disciplinary care (primary care, gastroenterology, surgery) is common in this setting. It will be important to ensure that all involved providers, as well as the participant, adhere to the same surveillance recommendations.

c. Completion of biopsychosocial questionnaires as described above. Survey data will be collected at baseline, and then annually.

d. Prospective collection of clinical study information (serial imaging, endoscopy, clinical follow-up) into a centralized data repository

e. Consent to provide a blood and other biosamples at study entry as well as access to cyst fluid and/or tissue biopsy material for biorepository storage (optional)

f. Consent to provide every 6 month update information regarding surveillance adherence

High v. Low Intensity Surveillance Strategies

The most salient differences between the two surveillance strategies center on: (1) indications for and recommended intervals of cross sectional imaging and (2) EUS utilization. Table 2 summarizes the components of the surveillance strategies.

The focus of this trial is the comparison of surveillance strategies, not the indication for surgical cyst resection. For this trial, surgery will be recommended for participants randomized to either arm who meet any of the following criteria: (1) obstructive jaundice due to the pancreatic cyst; (2) an enhancing nodule ≥5mm in the cyst wall; or (3) main pancreatic duct dilation ≥10mm.

Adherence to surveillance strategy

Adherence to assigned treatment is a key component of comparing performance of surveillance strategies. It depends on multiple factors, including patient risk perception, provider recommendation, local practice or institutional characteristics. (17)

We will define any surveillance testing occurring in the time period starting 2 months prior to the recommended testing or up to 2 months after the scheduled testing to as adherent. This time range reflects practical aspects of test scheduling for participants. Testing occurring outside of that window or not occurring at all will be considered non-adherent.

Discussion

Pancreatic cysts are common, incidental radiographic findings, especially in older populations. A small fraction of these cysts, either at detection or over time, become malignant. (18) Because pancreatic cancer mortality is very high, a premium is placed on early detection. How best to perform surveillance on the millions of cysts patients at risk for infrequent, but often fatal transformation is controversial. (19) No patient or physician wishes to miss the opportunity to prevent or detect pancreatic cancer early. However, at the population level, despite the inconvenience and high cost of serial imaging, endoscopy and laboratory testing, the yield is low.

The clinical trial described here is, to our knowledge, the largest prospective study of pancreatic cyst surveillance. Most trials in this area are retrospective and focused on patients who ultimately underwent surgery, an intervention required by only a minority of cyst patients. The establishment of relative clinical and cost effectiveness of surveillance for tis common clinical problem is essential. There is great optimism that complementary biomarkers and/or radiomics data will further improve clinical risk stratification. A key strength of the current trial will be linkage of clinical outcomes with prospectively collected, serial biomarker and imaging samples. Because such data will be banked, this trial will provide the study materials required for current and future discovery efforts.

Pancreatic cysts are seen in all adult populations. There is also great variation in who directs cyst-related care. After radiographic detection, care can be obtained from primary care, gastroenterology and/or surgery. Settings can range from individual community physicians to academic referral centers some of which offer multi-disciplinary cyst clinics. This trial is planned to enroll a large, diverse study cohort while capturing a wide range of resource utilization patterns and patient reported outcomes.

The use of clinical guidelines should promote higher quality care. Guidelines on the same topic by different groups often provide discordant recommendations. These variable recommendations confuse providers, patients, and policymakers. Here, we explicitly compare two guidelines already in wide clinical use. Such a comparison of clinical effectiveness or cost effectiveness is very unusual and would improve informed policy making.

The experience of our multi-disciplinary team with the design of this study highlights the impact of differing clinical, biological and policy assumptions on guideline construction. Nearly two years of discussion and multiple iterations were required to overcome differences in opinion about the most relevant clinical endpoints (for example overall cancer versus specific cancer stage), or important pathophysiology (for example, how often or how quickly does a cyst with high grade dysplasia progress to pancreatic cancer?) Even more vexing were competing concerns about over and under diagnosis of cancer depending on the frequency of surveillance interventions.

It is recognized that over the multi-year duration of this study new discoveries in early detection, pre-operative diagnosis, and disease markers may require modification of the trial as it proceeds. While a potential liability of any longer trial, overall lessons learned: clinical,

biological, analytical, economic, and patient well-being will contribute to improved, individualized risk reduction interventions.

Conclusion

This trial was designed by a multi-disciplinary group devoted to improving the clinical effectiveness and cost effectiveness of pancreatic cyst surveillance strategies. Direct comparison of widely utilized, but competing clinical practice guidelines, while seemingly essential is rarely performed. Beyond important clinical endpoints, this prospective trial will collect biosamples and imaging results that can be exploited for the development of novel biomarker and radiomics tools to augment, and hopefully improve current surveillance techniques.

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References

1. Stark A, Donahue TR, Reber HA, Hines OJ. Pancreatic Cyst Disease: A Review. Jama. 2016;315(17):1882–93. [PubMed: 27139061]
2. Canto MI, Hruban RH. Managing pancreatic cysts: less is more? Gastroenterology. 2015;148(4):688–91. [PubMed: 25724460]
3. Scheiman JM, Hwang JH, Moayyedi P. American gastroenterological association technical review on the diagnosis and management of asymptomatic neoplastic pancreatic cysts. Gastroenterology. 2015;148(4):824–48.e22. [PubMed: 25805376]
4. Tanaka M, Fernández-Del Castillo C, Kamisawa T, Jang JY, Levy P, Ohtsuka T, et al. Revisions of international consensus Fukuoka guidelines for the management of IPMN of the pancreas. Pancreatology. 2017;17(5):738–53. [PubMed: 28735806]
5. Vege SS, Ziring B, Jain R, Moayyedi P. American gastroenterological association institute guideline on the diagnosis and management of asymptomatic neoplastic pancreatic cysts. Gastroenterology. 2015;148(4):819–22; quize12–3. [PubMed: 25805375]
6. Fernández-Del Castillo C, Tanaka M. Management of pancreatic cysts: the evidence is not here yet. Gastroenterology. 2015;148(4):685–7. [PubMed: 25724457]
7. Sighinolfi M, Quan SY, Lee Y, Ibaseta A, Pham K, Dua MM, et al. Fukuoka and AGA Criteria Have Superior Diagnostic Accuracy for Advanced Cystic Neoplasms than Sendai Criteria. Dig Dis Sci. 2017;62(3):626–32. [PubMed: 28116593]
8. Ma GK, Goldberg DS, Thiruvengadam N, Chandrasekhara V, Kochman ML, Ginsberg GG, et al. Comparing American Gastroenterological Association Pancreatic Cyst Management Guidelines with Fukuoka Consensus Guidelines as Predictors of Advanced Neoplasia in Patients with Suspected Pancreatic Cystic Neoplasms. J Am Coll Surg. 2016;223(5):729–37.e1. [PubMed: 27497827]
9. Wu J, Wang Y, Li Z, Miao H. Accuracy of Fukuoka and American Gastroenterological Association Guidelines for Predicting Advanced Neoplasia in Pancreatic Cyst Neoplasm: A Meta-Analysis. Ann Surg Oncol. 2019;26(13):4522–36. [PubMed: 31617119]

10. Welch HG, Black WC. Overdiagnosis in cancer. J Natl Cancer Inst. 2010;102(9):605–13. [PubMed: 20413742]
11. Ziner KW, Sledge GW, Bell CJ, Johns S, Miller KD, Champion VL. Predicting fear of breast cancer recurrence and self-efficacy in survivors by age at diagnosis. Oncol Nurs Forum. 2012;39(3):287–95. [PubMed: 22543387]
12. Dwarte T, McKay S, Johns A, Tucker K, Spigelman AD, Williams D, et al. Genetic counselling and personalised risk assessment in the Australian pancreatic cancer screening program. Hered Cancer Clin Pract. 2019;17:30. [PubMed: 31666883]
13. Marteau TM, Bekker H. The development of a six-item short-form of the state scale of the Spielberger State-Trait Anxiety Inventory (STAI). Br J Clin Psychol. 1992;31(3):301–6. [PubMed: 1393159]
14. Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005–2008. J Clin Epidemiol. 2010;63(11):1179–94. [PubMed: 20685078]
15. Miller SM. Monitoring processing style: to see or not to see. Eur J Pain. 2015;19(4):449–50. [PubMed: 25808064]
16. de Souza JA, Yap BJ, Wroblewski K, Blinder V, Araújo FS, Hlubocky FJ, et al. Measuring financial toxicity as a clinically relevant patient-reported outcome: The validation of the COmprehensive Score for financial Toxicity (COST). Cancer. 2017;123(3):476–84. [PubMed: 27716900]
17. Hoffman RM, Lobo T, Van Den Eeden SK, Davis KM, Luta G, Leimpeter AD, et al. Selecting Active Surveillance: Decision Making Factors for Men with a Low-Risk Prostate Cancer. Med Decis Making. 2019;39(8):962–74. [PubMed: 31631745]
18. Gardner TB, Glass LM, Smith KD, Ripple GH, Barth RJ, Klibansky DA, et al. Pancreatic cyst prevalence and the risk of mucin-producing adenocarcinoma in US adults. Am J Gastroenterol. 2013;108(10):1546–50. [PubMed: 24091499]
19. Harris RP. Incidental findings in the pancreas (and elsewhere): putting our patients (and ourselves) in a difficult situation. Ann Intern Med. 2015;162(11):787–9. [PubMed: 25807075]

TABLE 1:

Schedule to perform surveillance imaging (radiographic and endoscopic), collect biosamples, resource utilization data and patient reported assessments

	Baseline (T0)	Imaging Events (interval frequency based on clinical events)	Endoscopy Events (interval frequency based on clinical events)	Surgery (if clinically indicated)	5 Year Follow-up[6]
High Intensity Surveillance[1]		X	X		X
Low Intensity Surveillance[1]		X	X		X
Blood sample (biomarker baseline, serial collection)[2]	X				
Cyst fluid collection[3]			X	X	
Healthcare utilization and system cost assessment[4]		X			
PRO Assessment (see below)[5]	X				

1. See text for surveillance strategy requirements.

2. Venipuncture for biomarker collection will be performed at baseline and if/when new clinical event occurs (clear cyst progression prompting EUS/FNA, change in imaging frequency, surgery, cancer diagnosis).

3. With any EUS-FNA (assuming cyst fluid available after standard clinical evaluation) and at surgical resection.

4. Every 6 months starting after baseline

5. Baseline is completed within 14 days of registration, and then every 12 (±1) months.

6. Patients will be followed 5 years from the date of registration.

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TABLE 2:

Description of imaging and endoscopic features of low and high intensity surveillance arms

Low Intensity Surveillance		High Intensity Surveillance	
1	All participants undergo MRI or CT at study entry and again in 1 year.	**1**	All participants undergo MRI or CT at study entry.
2	Following the 1 year imaging test, patients with no abnormalities repeat MRI or CT every 2 years.	**2**	Participants with baseline 1–2 cm cyst undergo MRI or CT every 6 months for 1 year, then every 12 months for 2 years, and then every 24 months thereafter.
3	Participants with negative imaging repeat MRI or CT in 2 years.	**3**	Participants with baseline2–3 cm cyst undergo EUS within 6 months, and if EUS is negative, patients repeat MRI or CT in 1 year. If second EUS is negative, patients undergo alternate MRI or CT and EUS every 12 months.
4	articipants with positive MRI and CT imaging features at 1 or 2 years undergo EUS	**4**	Participants with baseline cyst > 3 cm undergo EUS within 6 months, and if EUS is negative, patients alternate MRI or CT with EUS every 3–6 months.
5	If EUS negative, participants revert to MRI or CT in 1 year.		