Published in final edited form as:

Abdom Radiol (NY). 2019 February ; 44(2): 586–592. doi:10.1007/s00261-018-1765-z.

Detection of Recurrent Pancreatic Cancer: Value of Second-Opinion Interpretations of Cross-Sectional Images by subspecialized radiologists

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Abstract

Purpose—To investigate the value of second-opinion interpretation of cross-sectional images by subspecialized radiologists to diagnose recurrent pancreatic cancer after surgery.

Methods—The IRB approved and issued a waiver of informed consent for this retrospective study. Initial and second-opinion interpretations of 69 consecutive submitted MRI or CT follow up after pancreatic cancer resection between January 1, 2009 and December 31, 2013 were evaluated by one oncologic imaging radiologist, who was blinded to patient's clinical details and histopathologic data. The reviewer was asked to classify each interpretation in reference of the diagnosis of PDAC recurrence. It was also recorded if the radiologic interpretation recommended additional imaging studies to confirm recurrence. The diagnosis of recurrence was determined by pathology when available, otherwise by imaging follow up, clinical or laboratory assessments. Cohen's kappa statistic was used to assess agreement between initial and second-opinion interpretations. The differences between the initial and second-opinion interpretations were examined using McNemar test or Bowker's test of symmetry.

Results—Disagreement on recurrence between the initial report and the second-opinion interpretation was observed in 32% of cases (22/69; $k=0.44$). Second-opinion interpretations had a higher sensitivity and a higher specificity on recurrence compared to the initial interpretations (0.93 vs 0.75 and 0.90 vs 0.68, respectively), and the difference in specificity was significant

($p=0.016$). Additional imaging studies were recommended more frequently in the initial interpretation (22% vs 6%, $p=0.006$).

Conclusions—Our study shows the second-opinion interpretation by subspecialized radiologists improves the detection of pancreatic cancer recurrence after surgical resection.

Keywords

pancreatic ductal adenocarcinoma; second opinion report; recurrence; MRI; CT

Introduction

Pancreatic ductal carcinoma (PDAC) has a high rate of recurrence, occurs in 80–85% of patients after surgical resection (1). There are no consensus recommendations regarding optimal follow up of patients after potentially curative resection. Surveillance methods used to monitor for recurrence include clinical follow up, imaging studies, and tumor marker CA 19–9 measurement (2). Routine imaging surveillance has demonstrated to be useful to detect recurrence, potentially identify patients who will benefit from additional treatment, and has been also associated with prolonged survival after resection (3–6). However, there is wide variation in the utilization of imaging after PDAC resection. Imaging may be utilized for the evaluation of clinical symptoms and for localization of disease suspected by an elevated tumor marker, as well as for routine surveillance (7).

Patients referred to our specialist care cancer center for evaluation after pancreatic cancer resection often arrives with cross-sectional studies obtained in other medical facilities. Frequently there is a request from clinicians to review these studies by internal radiologists, sometimes as a “curbside consult” which is problematic from a workflow standpoint due to these interpretations are time consuming and no professional fee is submitted for reimbursement. Another concern is if no formal report is made part of the medical record, medico-legal hazards exist (8). In an effort to address these issues, formal second opinion interpretation has been increasing as a routine practice by some radiology departments, including our institution.

Several studies have reported that expert second-opinion interpretations of cross sectional images in other malignancies are more accurate and influence patient care. There is increasing evidence that this practice should be considered as a valuable, reimbursable service. Disagreement rates between the initial outside report and second-opinion interpretation by subspecialized radiologists have been reported up to 66% (9–12).

Our study focused on the detection of recurrent pancreatic cancer because of the lack of literature regarding the value of second-opinion interpretations in this setting and the fact that extensive postoperative changes, complications and reactive adenopathy present after surgical resection may be mistaken for recurrence. Familiarity with the spectrum of postoperative imaging findings and patterns of disease recurrence for pancreatic malignancy is essential to distinguish between these entities (13–15).

The purpose of this study was to investigate the value of second-opinion interpretation of cross-sectional images by subspecialized oncologic radiologists to diagnose recurrent pancreatic cancer after surgical resection.

Materials and methods

The institutional review board of our institution approved and issued a waiver of informed consent for this retrospective study, which was compliant with the Health Insurance Portability and Accountability Act.

Eligibility

A retrospective search of our institutional clinical database was performed to identify patients fulfilling the following inclusion criteria: biopsy proven PDAC, magnetic resonance imaging (MRI) of abdomen or computed tomography (CT) performed and initially interpreted at an outside institution specifically after PDAC resection was performed and second opinion interpretation documented in an official report within 6 months from the performance of the outside scan by subspecialized radiologists at our institution between January 1, 2009 and December 31, 2015. The second-opinion interpretations were performed during the course of normal clinical work by board certified subspecialized radiologists with expertise in oncologic imaging, which actively participate in oncologic tumor boards. As a policy in our institution at the time of image reinterpretation, the subspecialized radiologists also review the initial interpretation to perform the second opinion interpretation. There were a total of 178 second-opinion interpretations issued. Patients already being treated for recurrent pancreatic cancer (n=106) and with biopsy results available between the initial interpretation and second-opinion interpretation (n=2) were excluded because access to this additional information by our radiologists could affect their interpretation. In one case the initial interpretation was incomplete at the time of review and was excluded. The remaining 69 cases formed the basis of our study.

Data analysis and interpretation

The reports from the outside institutions will be referred to as initial interpretations in this article; whereas the reports from our institution will be referred to as second opinion interpretations. The initial and second opinion interpretations were reviewed by a radiologist (initials) with fellowship training in oncologic imaging and 8 years of experience, who was blinded to patient's clinical details and histopathologic data. The analysis was based exclusively on how the CT and MRI studies were interpreted, and the original imaging itself was not reevaluated.

The reviewer was asked first to classify each interpretation into one of three categories in reference of the diagnosis of PDAC recurrence: 1, the radiologic interpretation states no recurrence, 2, the radiologic interpretation states possible recurrence and 3, the radiologic interpretation states recurrence. Interpretations were categorized as PDAC recurrence if included phrases consistent with, compatible with, most likely, suspicious, represents, or is, in reference to the diagnosis. Interpretations in which more than 1 possible diagnosis was suggested or included phrases likely, may represent, possibly, in reference to the PDAC

recurrence were categorized as possible recurrence. Cases in which the interpretation stated either no abnormality, postoperative changes, complications after PDAC surgical resection were classified as no recurrence.

The interpretations were further assessed for agreement in the diagnosis of PDAC recurrence between the two reports. Any disagreement in the categorization of the PDAC recurrence was then classified into major and minor disagreements. Substantive differences in the recurrence status (possible recurrence or recurrence versus no recurrence) were deemed as major disagreement. Where there was only difference in the certainty of recurrence (possible recurrence versus recurrence), these were deemed as minor disagreement.

The final diagnosis of the recurrence status of all the cases was determined with the best standard of reference available, all patient clinical, laboratory, follow up imaging and histopathologic data were reviewed. Pathologic proof was considered the gold standard and was available in 13% of the cases (9/69). If pathologic proof was not available, the diagnosis was made based on imaging follow-up in 67% of the cases (46/69), with an increase in size or new lesions and/or response to treatment considered as evidence of recurrent disease. Finally, if histopathology and follow-up imaging were not available, clinical or laboratory assessments was used in 20% of cases (14/69) with a progressive rise in CA 19-9 considered as evidence of recurrent disease.

The results of the initial and second-opinion interpretation were compared with each other and with the final diagnosis.

The radiologist also classified each interpretation in a binary fashion in terms of whether or not the radiologist who generated the report recommended additional imaging (RAI) to confirm radiologic disease identification. Recommendation for repeating imaging due to insufficient diagnostic quality of the cross-sectional imaging in the second opinion report was recorded.

Statistical Analysis

Cohen's kappa statistic (K) was used to assess agreement in the diagnosis of recurrence between initial and second-opinion interpretations. The differences between initial and second opinion interpretations were examined using the McNemar's test or Bowker's test of symmetry (more than 2 categories). The sensitivity and the specificity of reported recurrence for initial and second-opinion interpretations were estimated after dichotomizing the reports based on the oncologic radiologist interpretation as negative for recurrence or positive for recurrence (possible recurrence or recurrence). Sensitivities and specificities were compared using McNemar's test. A test with p value < 0.05 was considered significant. All statistical analyses were performed in R version 3.3 (The R Foundation for Statistical Computing).

Results

The second opinion interpretations comprised 54 CT scans and 15 MRI. The studies were submitted from 40 institutions. The median period of time between the initial interpretation and second-opinion interpretation was 10 days. The mean patient age was 66.9 years (range,

46–86 years), 33(48%) male and 36 (52%) female patients. The prevalence of recurrent pancreatic cancer was 41% (n=28/69), 22% were pathologic proven (n=6/28). In the remaining of cases the diagnosis of recurrence was done either with imaging follow up (39%, n=11/28) or based on the clinical or laboratory evidence of recurrent disease (39%, n=11/28).

Disagreement in the assessment of recurrence between the initial interpretation and the second-opinion interpretation was observed in 32% of cases (22/69; $k=0.44$, 95% CI, 0.26–0.62). In 18 cases (82%) were considered as major disagreement and in 4 cases (18%) were considered as minor disagreement. Causes of major disagreement included differences in the assessment of local recurrence versus postsurgical changes in 6 cases. Misinterpretation was other cause of major disagreement including adenopathy in 2 cases in the initial interpretation, liver lesions in 4 cases in the initial interpretation whether in the second opinion interpretation misinterpretation of liver lesion was noted in 1 case and of tumor implant in 1 case. Failure to identify hepatic, pulmonary metastases or peritoneal carcinomatosis on the initial interpretations was noted in 4 cases. Figure 1 and 2 shows representative cases of major disagreement in the status of PDAC recurrence.

Table 1 summarizes the differences between the initial and second opinion interpretations. The second-opinion interpretation detected more cases of recurrence than the initial interpretation, 40% vs 24% (27/69 vs 33/69; $p=0.083$). The second-opinion interpretations by the subspecialized radiologist were more confident in diagnose recurrence with statistically significantly less RAI to confirm radiologic disease identification occurring in 6% of the cases, whereas in the initial interpretations RAI were more often noted, in 22% of the cases (4/69 vs. 15/69; $p=0.006$). RAI by the initial interpretations comprised follow-up CT scans in 5 cases, MRI in 5 cases, PET-CT in 4 cases, endoscopy in 3 cases and in 3 of the initial interpretations recommended more than one additional imaging. For the second interpretation 1 MRI, 1 CT and 1 endoscopy were recommended as additional imaging. In only 1.4% of the cases (n=1/69) the second opinion interpreter recommended repeat imaging due to insufficient diagnostic quality of the scan.

When comparing the initial interpretation recurrence status to the final diagnosis, the initial interpretation was significantly different ($p=0.012$), while the second-opinion interpretation recurrence status was not significantly different from the final diagnosis, with 89% concordance (Table 2).

Table 3 presents the diagnostic performance of the initial and second-opinion interpretations for the detection of recurrence. Second-opinion interpretations had a higher sensitivity and a higher specificity on recurrence compared to the initial interpretations (0.93 vs 0.75 and 0.90 vs 0.68, respectively), and the difference in specificity was significant ($p=0.016$).

Discussion

This study demonstrates the value of second-opinion interpretations of cross-sectional images by subspecialized radiologists for the detection of recurrent PDAC after surgical resection. The specificity of the second-opinion report was significantly superior than the

initial report. Previous studies have shown comparable specificity rates for CT in the detection of pancreatic cancer recurrence following surgery (16,17). CT is an accurate modality in identifying disease recurrence. MRI has very similar potential compared to CT for pancreatic cancer, with higher sensitivity for liver metastases (18). Radiologic recurrence identification is important due to current recommendations do not support initiating treatment in the absence of definitive disease identification (2).

These results further expand the knowledge of the added value of formal second-opinion interpretations in oncologic imaging. Wibmer et al (19) examined the impact of second opinion interpretations in the diagnosis of extracapsular extension of prostate cancer on 71 prostate MRI. The second opinion interpretations issued by subspecialized radiologists found to perform significantly better than did the initial interpretations (AUC, 0.83 vs 0.65). Another study done in a tertiary referral center evaluating the impact of neuroradiologist second opinion interpretation in head and neck cancer found that following the second opinion interpretation, the cancer stage changed in 56.7% of the surgical cases, and these changes were correct 94.1% of the time (20).

A strength of our study was the assessment of the frequencies of RAI in initial and second opinion interpretations. Significantly less recommendations for additional imaging to confirm radiologic recurrent disease were noted in the second-opinion interpretations issued by the subspecialized radiologists than in the initial report (6% vs. 22%). The ACR practice parameter for communication of diagnostic imaging findings states that reports generated by the interpreting physician should suggest additional diagnostic studies to clarify or confirm the impression when appropriate (21). RAI have been reported in different radiologic reports with an incidence ranging from 12 to 31% (22–24). Corrias et al (25) found that initial interpretation for pancreatic cancer staging lead to RAI in 46% and second-opinion interpretation lead to RAI in 7.6% of the cases. In the report by Sistrom et al (22), the authors found that radiologists with increasing levels of experience made fewer RAI.

Concerns over rising imaging services and their costs have been addressed in a recent collaborative national effort to identify and reduce the causes driving overutilization of medical imaging. Radiologists contribute to the overutilization of imaging in several ways, one is through the RAI (26). RAI can also lead to increased patient anxiety, inconvenience for some patients to undergo separate imaging studies, delay in the diagnosis and risk of complications related to additional imaging tests. The lower incidence of RAI in second-opinion interpretations could have an impact in decreasing health costs by reducing the overutilization of medical imaging. Another source of overutilization is duplicated studies. In our study only in 1.4% of the cases the subspecialized radiologist recommended repeating imaging due to insufficient diagnostic quality. Larger studies to evaluate the added value of second opinion report in reducing the number of additional imaging studies and health costs are lacking.

Kalbhen et al. (27) evaluated the value of reinterpretation abdominal CT by radiologists with subspecialty expertise in abdominal imaging in assessing the resectability of PDAC and found a similar rate (32%) of discrepancies between the initial and the reinterpretation reports with comparable kappa value of 0.42 indicating only moderate agreement between

the two reports. They also concluded that the reinterpretation of outside studies is relatively inexpensive when compared with additional imaging. Our study provides further justification of the value of second opinion interpretations by subspecialized radiologist instead of performing additional imaging. The disagreement in the assessment of PDAC recurrence and the differences in RAI observed between the initial and second opinion interpretation may be explained by the oncologic imaging experts being more knowledgeable of the post pancreatic surgical imaging findings, complications and patterns of pancreatic cancer recurrence, allowing for a better assessment.

There are several limitations in our study. First, the retrospective design of our study did not allow us to determine properly the clinical impact in counseling and/or treatment of the second-opinion interpretations. A prospective study would better address this issue. Second, the availability of reviewing the initial interpretation, clinical information, laboratory results and additional imaging studies by the subspecialized radiologists may have biased the results in favor of the second opinion interpretation.

Another limitation is that we only evaluated the cross-sectional imaging studies for which an official second-opinion interpretation was performed. The decision to obtain a second-opinion interpretation was at the discretion of the physician providing care for the patient at our hospital. It is possible that the more difficult cases were submitted for second-opinion interpretations because of discordances between the initial interpretation and the clinician suspicion. These may have resulted in a selection bias. Differences between the initial and second-opinion interpretations may have been lower if all outside studies were included.

Furthermore, the gold standard of reference was not uniform because pathologic proof was not always obtained. However, in our center, as in most centers, resection for recurrent disease is not the standard of care and biopsy confirmation of recurrence is not often done if there is a clinical and/or laboratory suspicion of recurrence. Finally, due to the lack of consensus recommendations regarding imaging follow up of patients after PDAC resection, the indications for cross sectional imaging are wide and may have been development of symptoms, rise in Ca 19–9 that could have created another selection bias.

In conclusion, our study demonstrates that second opinion interpretation radiologic studies by subspecialized oncologic radiologists improves the detection of pancreatic cancer recurrence after surgical resection and decreases requests for additional imaging. Second opinion interpretations by subspecialized oncologic radiologists impact patient care.

Abbreviations

CT	Computed tomography
MRI	Magnetic resonance imaging
PDAC	Pancreatic ductal adenocarcinoma
RAI	Recommended additional imaging

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Figure 1.

(A) Axial venous phase CT on a liver window and (B) sagittal venous phase CT on soft tissue window from a CT in a 46 year old male with recurrent pancreatic cancer. Initial interpretation did not describe any liver lesions and stated “soft tissue associated with surgical clips possibly representing residual tissue of the uncinate process”. Second-opinion interpretation stated, “soft tissue mass between the superior mesenteric artery, superior mesenteric vein and left renal vein (arrowheads) consistent with tumor recurrence. Solitary segment 6/7 liver lesion (arrow) suspicious for metastasis. (C) Axial venous phase CT on a liver window 6 months later demonstrates the liver lesion has increased in size (arrow), consistent with metastasis. The soft tissue in the surgical bed (arrowheads) also increased in size consistent with tumor recurrence. Patient underwent liver biopsy which confirmed hepatic metastasis.

Figure 2.

(A) Axial T1 post gadolinium images from a MRI in a 57 year old woman after PDAC resection. Initial report impression stated “multiple enhancing mass lesions (arrows) noted in the liver. Findings are consistent with metastatic disease”. Second-opinion report stated “multiple arterially enhancing lesions throughout the hepatic parenchyma consistent with vascular shunts”. Follow up MR 4 months later showed stable arterial enhancing lesions (arrows) in the axial T1 post gadolinium (B) images, without corresponding T1 (C) or T2

(D) abnormality, consistent with vascular shunts. Liver biopsy was performed and was negative for malignancy.

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Table 1:

Differences between the initial and second-opinion interpretations.

Initial interpretation	Second-opinion interpretation			p Value
Parameter	No	Yes	Possible	
Recurrence				0.083
No	28 (41%)	6 (9%)	1 (1%)	
Yes	6 (9%)	17(25%)	0 (0%)	
Possible	5 (7%)	4 (6%)	2 (3%)	
Recommendation of additional imaging				0.006
No	53 (77%)	1 (1%)		
Yes	12 (17%)	3 (4%)		

Table 2:

Differences between the recurrence status in the initial and second-opinion interpretations status compared to gold standard.

Recurrence	Gold standard reference		p Value
	No	Yes	
Initial interpretation			0.012
No	28 (41%)	7 (10%)	
Possible	7 (10%)	16 (23%)	
Yes	6 (9%)	5 (7%)	
Second-opinion interpretation			0.362
No	37 (54%)	2 (3%)	
Possible	1 (1%)	2 (3%)	
Yes	3(4%)	24 (35%)	

Table 3:

Diagnostic performance of the initial and second opinion interpretations

	Sensitivity (95% CI), N	Specificity (95%CI), N
Initial interpretation	0.75 (0.551,0.893), 21/28	0.683 (0.519,0.819), 28/41
Second opinion interpretation	0.929 (0.765,0.991), 26/28	0.902 (0.769,0.973), 37/41
P Value	0.131	0.016