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PET Recommendation Report 5

PET Imaging in Pancreatic Cancer

S Kanjeekal, J Biagi, and C Walker-Dilks

Report Date: January 19, 2009

PET Recommendation Report 5 is comprised of 2 sections and is available on the CCO Web site (https://www.cancercare.on.ca)
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Section 1: Recommendations
Section 2: Evidentiary Base

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Citation (Vancouver Style): Kanjeekal S, Biagi J, Walker-Dilks C. PET Imaging in pancreatic cancer. Toronto (ON): Cancer Care Ontario; 2009 Jan 19. Program in Evidence-based Care PET Recommendation Report No.: 5.

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Recommendation Report – PET #5: Section 1

PET Imaging in Pancreatic Cancer: Recommendations

S Kanjeekal, J Biagi, and C Walker-Dilks

Report Date: January 19, 2009

QUESTIONS

- What benefit to clinical management does positron emission tomography (PET) or positron emission tomography/computed tomography (PET/CT) contribute to the diagnosis or staging of pancreatic cancer?
- What benefit to clinical management does PET or PET/CT contribute to the assessment of treatment response for pancreatic cancer?
- What benefit to clinical management does PET or PET/CT contribute when recurrence of pancreatic cancer is suspected but not proven?
- What benefit to clinical management does PET or PET/CT contribute to restaging at the time of documented recurrence for pancreatic cancer?
- What is the role of PET when a solitary metastasis is identified at the time of recurrence and a metastectomy is being contemplated?

TARGET POPULATION

Patients with pancreatic cancer.

INTENDED PURPOSE

- This recommendation report is primarily intended to guide the Ontario PET Steering Committee in their decision making concerning indications for the use of PET imaging.
- This recommendation report may also be useful in informing clinical decision making regarding the appropriate role of PET imaging and in guiding priorities for future PET imaging research.

RECOMMENDATIONS AND KEY EVIDENCE

These recommendations are based on an evidentiary foundation consisting of one recent high-quality systematic review from the U.S. Agency for Health Research and Quality (AHRQ) (1) that included primary study literature for the period from 2003 to March 2008.

Diagnosis/Staging

PET is not recommended for primary diagnosis of pancreatic cancer.
Eleven prospective studies were identified that evaluated the role of PET or PET/CT in the diagnosis of a suspicious pancreatic mass. Sensitivity ranged from 69% to 97%, and specificity ranged from 61% to 97% (Giorgi et al [2], Nishiyama et al [3], Rasmussen et al [4], van Kouwen et al [5], Bang et al [6], Heinrich et al [7], Lemke et al [8], Lytras et al [9], Maemura et al [10], Sperti et al [11], Casneuf et al [12]). Meta-analysis of four prospective studies evaluating the diagnostic performance of PET for the purpose of primary diagnosis (Giorgi et al [2], Nishiyama et al [3], Rasumussen et al [4], van Kouwen et al [5]) yielded a pooled positive likelihood ratio (+LR) of 4.28 (95% CI 2.07 to 8.86) and negative likelihood ratio (-LR) of 0.21 (CI 0.12 to 0.40). These LRs had moderate heterogeneity, presenting some difficulties in determining overall accuracy. Meta-analysis of seven prospective studies evaluating the diagnostic performance of PET with the purpose of primary diagnosis and staging (Bang et al [6], Casneuf et al [12], Lemke et al [8], Lytras et al [9], Maemura et al [10], Ruf et al [13], Sperti et al [11]) yielded a +LR of 2.77 (CI 1.62 to 4.73) and –LR of 0.19 (CI 0.10 to 0.34). There was considerable heterogeneity, limiting determination of the overall accuracy of PET. Meta-analysis of three studies on PET/CT (Casneuf et al [12], Heinrich et al [7], Lemke et al [8]) yielded a homogenous +LR of 2.69 (CI 1.84 to 3.94) and –LR of 0.16 (CI 0.10 to 0.26). These pooled LRs suggest that PET and PET/CT offer small benefit in ruling in and ruling out pancreatic cancer when investigating a suspicious pancreatic mass; therefore, they may be useful in establishing a diagnosis when standard investigations are not confirmatory. Five studies compared PET or PET/CT with CT in the diagnosis of a suspicious pancreatic mass. In two that compared PET, PET/CT, and CT (Lemke et al [8], Casneuf et al [12]), PET/CT had the better diagnostic performance.

Qualifying Statements

- The gold standard as well as the clinical goal is biopsy. When biopsy is inconclusive or not possible and the diagnosis remains in doubt, the above evidence supports the use of PET/CT where a positive result would lead to surgical resection for purposes of both diagnosis and treatment.
- Neuroendocrine tumours of the pancreas are known to be unreliably fluorodeoxyglucose (FDG) avid.

PET is recommended for staging if a patient is a candidate for potentially curative surgical resection as determined by conventional staging.
In four studies (Bang et al [6], Heinrich et al [7], Nishiyama et al [14], Sperti et al [11]), staging and treatment strategy changed after PET or PET/CT scan in 12% to 69% of cases. In one study (Heinrich et al [7]) with 46 patients with pancreatic carcinoma, standard staging followed by PET/CT improved the detection of distant metastases compared with standard staging alone (88% vs 56%, p=0.06 McNemar test). In Nishiyama et al [14], 16 of 42 patients were found to have distant metastases by radiologic evaluation or cytological verification. With the combination of PET and CT, all metastatic sites were detected. Based on the above studies, staging and hence surgical management are impacted in a substantial proportion of patients who are candidates for surgery.

Qualifying Statement

- The clinical importance of change in treatment strategy as an outcome, despite a lack of strong evidence, is noted.

Assessment of Treatment Response

A recommendation cannot be made for or against the use of PET to guide clinical management based on assessment of treatment response due to insufficient evidence.
One study (Bang et al [6]) showed that PET was superior to CT in the detection of treatment response after chemoradiation. Of 102 patients evaluated for a suspicious pancreatic mass, 15 with confirmed pancreatic cancer received chemoradiation. CT did not detect any responders while PET detected 5/15 therapy responders. The response after chemoradiation correlated with longer time to progression (TTP) compared with nonresponders (399 vs 233 days). A second study (Maemura et al [10]) showed that in 23 patients who received chemoradiation, an SUV <7.0 was correlated with improved survival. The above results are based on two small nonrandomized studies and therefore are not strong enough to make a recommendation for using PET in evaluating treatment response outside of a clinical trial.

Qualifying Statement

- A recommendation for PET cannot be made in the setting of incomplete resection due to lack of evidence.

Recurrence/Restaging

PET is not recommended for clinical management of suspected recurrence, nor for restaging at the time of recurrence, due to insufficient evidence and lack of effective therapeutic options.
One study (Ruf et al [15]) compared PET with CT in 31 patients who had suspected recurrence based on symptoms or increased CA 19-9 levels. While PET had higher sensitivity than CT for the detection of recurrence overall (96% versus [vs] 39%), and for nonhepatic intra- and extra-abdominal metastases, CT had a superior sensitivity for the detection of liver metastases (92% vs 42%). However, patient outcomes based on these results were not reported. In a subset of 12 patients in Casneuf et al (12) who were being screened for recurrent pancreatic cancer, the sensitivity, specificity, and accuracy were not different between PET, PET/CT, and CT. In neither study was a reported change in management identified based on scanning modality.

Qualifying Statement

- Pancreatic cancer has high overall mortality, and recurrence is uniformly fatal. At this time, there are insufficient treatment options that improve the outlook in patients who recur after surgical resection that would allow PET to contribute to management. PET imaging in recurrent disease should be restricted to clinical trials.

Solitary Metastasis Identified at Time of Recurrence

A recommendation cannot be made for or against the use of PET for staging if a solitary metastasis is identified at recurrence as there are no trials that identify the utility of PET scanning in this setting.
No studies exist that examine PET in this setting.

Qualifying Statement

None.

Funding

The PEBC is a provincial initiative of Cancer Care Ontario supported by the Ontario Ministry of Health and Long-Term Care through Cancer Care Ontario. All work produced by the PEBC is editorially independent from its funding source.

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Recommendation Report – PET #5: Section 2

PET Imaging in Pancreatic Cancer: Evidentiary Base and Consensus Process

S Kanjeekal, J Biagi, and C Walker-Dilks

Report Date: January 19, 2009

QUESTIONS

- What benefit to clinical management does positron emission tomography (PET) or positron emission tomography/computed tomography (PET/CT) contribute to the diagnosis or staging of pancreatic cancer?
- What benefit to clinical management does PET or PET/CT contribute to the assessment of treatment response for pancreatic cancer?
- What benefit to clinical management does PET or PET/CT contribute when recurrence of pancreatic cancer is suspected but not proven?
- What benefit to clinical management does PET or PET/CT contribute to restaging at the time of documented recurrence for pancreatic cancer?
- What is the role of PET when a solitary metastasis is identified at the time of recurrence and a metastectomy is being contemplated?

INTRODUCTION

The Ontario PET Steering Committee made a special request to the Clinical Council of Cancer Care Ontario to co-lead the development of guidance regarding the clinical uses of PET imaging. The Program in Evidence-based Care (PEBC), working together with Pthe PEBC Disease Site Groups (DSGs), synthesized the clinical research and drafted recommendations for 10 disease sites. Recommendations for the use of PET in colorectal cancer, esophageal cancer, head and neck cancer, and melanoma were reviewed at a consensus meeting on 19 September 2008 and recommendations for the use of PET in brain, ovarian, cervical, testicular, small-cell lung, and pancreatic cancer were reviewed at a consensus meeting on 25 November 2008.

METHODS

Overview

In order to develop the recommendations and achieve consensus, a three-step methodology was undertaken.

Step 1 – Systematic review. A systematic review of the published literature was undertaken (see details below). This was conducted by two clinical lead authors,

nominated by the PEBC Gastrointestinal (GI) DSG and a PEBC methodologist. The systematic review served as the evidentiary foundation for a set of draft recommendations developed by this team.

Step 2 – Consensus by the PEBC GI DSG. The draft recommendations were refined during a DSG teleconference. The GI DSG is comprised of medical and radiation oncologists and surgeons and is supported by a PEBC research methodologist.

Step 3 – Provincial PET imaging consensus meeting. The draft recommendations were vetted at a larger provincial PET imaging consensus meeting co-hosted by Cancer Care Ontario and the Provincial PET Steering Committee. The meeting was facilitated and supported by members of the PEBC team. Participants included representatives of the PEBC DSGs, other clinical experts in the areas of nuclear and diagnostic medicine, members of the Cancer Care Ontario clinical leadership team, and representatives from the Ontario PET Steering Committee and the Ontario Health Technology Assessment Committee.

The systematic review and companion recommendations are intended to promote evidence-based decisions in Ontario, Canada. The PEBC is supported by the Ontario Ministry of Health and Long-Term Care through Cancer Care Ontario. All work produced by the PEBC is editorially independent from its funding source.

SYSTEMATIC REVIEW

Literature Search

The PEBC was aware of a technology assessment being produced by the University of Alberta Evidence-based Practice Center for the U.S. Agency for Healthcare Research and Quality (AHRQ) evaluating the use of PET imaging in nine cancers (1) (referred to as the AHRQ review from this point forward). This review updated a previous AHRQ report produced by Duke University in 2004 (2). The Alberta update included individual primary studies dating from 2003 to March 2008 on six of the 10 cancer sites targeted by this project. Because the AHRQ review sufficiently covered the questions and methodologies of interest to this recommendation report, a draft of the AHRQ review was made available to the PEBC and its results were used for the evidentiary base.

Study Selection Criteria

All primary studies in the AHRQ review that addressed the questions of interest in this recommendation report (diagnosis, staging, treatment response, recurrence, and restaging) were included.

The inclusion criteria for primary studies included in the AHRQ review were:

- prospective or retrospective clinical study evaluating the use of FDG PET or FDG PET/CT in primary cancer;
- study not duplicated or superseded by a later study with the same purpose from the same institution;
- study reported numeric data on at least one objective outcome of interest for the key questions of the technology assessment (diagnostic performance, treatment decisions and management strategy, changes in therapy, patient-centred outcomes, and economic outcomes);
- study included ≥ 12 patients with the cancer of interest;
- study used a suitable reference standard (pathological confirmation and clinical follow-up) when appropriate.

Synthesizing the Evidence

In some cases where sufficient evidence existed, meta-analyses were included with pooled likelihood ratios. The AHRQ review included evidence tables that summarized the characteristics and results of each study according to the outcomes the study addressed. For diagnostic performance, the evidence tables recorded details on the source of the publication and the evidence grade, study design, patient characteristics, PET technical characteristics, criteria for interpretation, and results. In addition to the diagnostic performance of PET, the AHRQ review also sought to evaluate PET in terms of its impact on physician decision-making approaches to diagnosis and management (referred to as diagnostic thinking) and its impact as part of a management strategy to improve patient-centred outcomes (referred to as management strategy). Full text and data extractions of the studies were provided to the clinical lead authors to aid in formulation of the recommendations. Telephone conferences and email correspondence between the clinical leads and the PEBC methodologist took place to clarify details and answer questions.

CONSENSUS

DSG Consensus Process

The clinical lead authors wrote summaries of the key evidence, draft recommendations, and qualifying statements for the questions pertaining to diagnosis/staging, assessment of treatment response, and recurrence/restaging. The ensuing documents were circulated to all members of the GI DSG and discussed during a teleconference. The recommendations that were generated during this process are referred to below as the DRAFT DSG Recommendations. The intent of these recommendations was to guide discussion at the consensus meeting.

Provincial Consensus Process

The consensus meeting on 25 November 2008 was conducted as follows:

- Presentations by each of the clinical lead authors on the DRAFT DSG recommendations and supporting evidence were made to the meeting participants.
- The recommendations were refined by the large group, and in some cases a revised recommendation was proposed, resulting in a FINAL recommendation.
- The participants voted on the FINAL recommendations to indicate their extent of agreement on a scale from 1 to 7 (1 indicating strong agreement, 5 indicating no agreement or disagreement, and 7 indicating strong disagreement).

RESULTS

Literature Search Results

The AHRQ review results for pancreatic cancer included 17 primary studies. Data from the evidence tables are summarized in Appendix 1. In addition to data for diagnostic performance, summaries of results for diagnostic thinking and management strategy are also presented where they apply. The key evidence is described below in an abbreviated fashion.

Key Evidence

Diagnosis/Staging

- Eleven prospective studies were identified that evaluated the role of PET or PET/CT in the diagnosis of a suspicious pancreatic mass. Sensitivity ranged from 69% to 97%, and specificity ranged from 61% to 97% (Giorgi et al [3], Nishiyama et al [4], Rasmussen et al [5], van Kouwen et al [6], Bang et al [7], Heinrich et al [8], Lemke et al [9], Lytras et al [10], Maemura et al [11], Sperti et al [12], Casneuf et al [13]).

- Meta-analysis of four prospective studies evaluating the diagnostic performance of PET with the purpose of primary diagnosis (Giorgi et al [3], Nishiyama et al [4], Rasumussen et al [5], van Kouwen et al [6]) yielded a pooled positive likelihood ratio (+LR) of 4.28 (95% CI 2.07 to 8.86) and negative likelihood ratio (-LR) of 0.21 (CI 0.12 to 0.40). These LRs had moderate heterogeneity, presenting some difficulties in determining overall accuracy.
- Meta-analysis of seven prospective studies evaluating the diagnostic performance of PET, with the purpose of primary diagnosis and staging (Bang et al [7], Casneuf et al [13], Lemke et al [9], Lytras et al [10], Maemura et al [11], Ruf et al [14], Sperti et al [12]) yielded a +LR of 2.77 (CI 1.62 to 4.73) and –LR of 0.19 (CI 0.10 to 0.34). There was considerable heterogeneity, limiting determination of the overall accuracy of PET.
- Meta-analysis of three studies on PET/CT (Casneuf et al [13], Heinrich et al [8], Lemke et al [9]) yielded a homogenous +LR of 2.69 (CI 1.84 to 3.94) and –LR of 0.16 (CI 0.10 to 0.26).
- These pooled LRs suggest that PET and PET/CT offer small benefit in ruling in and ruling out pancreatic cancer when investigating a suspicious pancreatic mass; therefore, they may be useful in establishing a diagnosis when standard investigations are not confirmatory.
- Five studies compared PET or PET/CT with CT in the diagnosis of a suspicious pancreatic mass (Table 1). In two that compared PET, PET/CT, and CT (Lemke et al [9], Casneuf et al [13]), PET/CT had better diagnostic performance.
- In four studies (Bang et al [7], Heinrich et al [8], Nishiyama et al [15], Sperti et al [12]), staging and treatment strategy changed after the PET or PET/CT scan in 12% to 69% of cases.
- In one study (Heinrich et al [8]) with 46 patients with pancreatic carcinoma, standard staging followed by PET/CT improved the detection of distant metastases compared with standard staging alone (88% vs 56%, p=0.06 McNemar test).
- In Nishiyama et al [15], 16 of 42 patients were found to have distant metastases by radiologic evaluation or cytological verification. With the combination of PET and CT, all metastatic sites were detected.
- Based on the above studies, staging and hence surgical management are impacted in a substantial proportion of patients who are candidates for surgery.

Table 1. Diagnostic performance of studies comparing PET or PET/CT with CT.

Study (n)	Sensitivity			Specificity			Accuracy		
	PET	PET/CT	CT	PET	PET/CT	CT	PET	PET/CT	CT
Bang2006 (102)	97%		80%	78%		44%	95%		76%
Heinrich2005 (59)		89%	93%		69%	21%			
Sperti2007 (64)	92%		58%	97%		82%	95%		72%
Lemki2004 (100)	84%	89%	77%	61%	64%	64%	76%	80%	72%
Casneuf2007 (46)	79%	92%	88%	90%	90%	90%	82%	91%	88%

Abbreviations: PET, positron emission tomography; CT, computed tomography.

Assessment of Treatment Response

- One study (Bang et al [7]) showed that PET was superior to CT in the detection of treatment response after chemoradiation. Of 102 patients evaluated for a suspicious pancreatic mass, 15 with confirmed pancreatic cancer received chemoradiation. CT did not detect any responders, while PET detected 5/15 therapy responders. The response after chemoradiation correlated with longer time to progression compared with nonresponders (399 vs 233 days).
- A second study (Maemura et al [11]) showed that in 23 patients who received chemoradiation, an SUV <7.0 was correlated with improved survival.
- The above results are based on two small nonrandomized studies and therefore are not strong enough to make a recommendation for using PET in evaluating treatment response outside of a clinical trial.

Recurrence/Restaging

- One study (Ruf et al [16]) compared PET with CT in 31 patients who had suspected recurrence based on symptoms or increased CA 19-9 levels. While PET had a higher sensitivity than CT for the detection of recurrence overall (96% vs 39%), and for nonhepatic intra- and extra-abdominal metastases, CT had superior sensitivity for the detection of liver metastases (92% vs 42%). However, patient outcomes based on these results were not reported.
- In a subset of 12 patients in Casneuf et al (13) who were being screened for recurrent pancreatic cancer, the sensitivity, specificity, and accuracy were not different between PET, PET/CT, and CT. In neither study was a reported change in management identified based on scanning modality.

Solitary Metastasis at Time of Recurrence

- No studies exist that examine PET in this setting.

RECOMMENDATIONS

DIAGNOSIS/STAGING

Clinical Question

What benefit to clinical management does PET or PET/CT contribute to the diagnosis or staging of pancreatic cancer?

DRAFT DSG Recommendation

PET is not recommended for primary diagnosis of pancreatic cancer.

Provincial Consensus Meeting Deliberations

There was discussion about the information that PET can provide regarding whether to perform surgery. The suggestion was made that PET is only recommended for the primary diagnosis of pancreatic cancer in patients in whom a biopsy is nondiagnostic or not feasible and the patient is a candidate for surgical resection. This issue had been previously discussed among the GI DSG members and for that reason had included a qualifying statement. The consensus decision was to return to the original recommendation.

FINAL Recommendation Put to Vote

PET is not recommended for primary diagnosis of pancreatic cancer.

	1 – Strongly Agree		4 – Neither Agree nor Disagree			7 – Strongly Disagree		N/A
	1	2	3	4	5	6	7	
Total	10	10			1			

Votes = 21

Issues raised on voting questionnaires:

-For surgical patients with negative biopsy, PET may have utility.

-Prefer second wording as discussed, PET for surgical candidate where biopsy negative or nondiagnostic.

Qualifying Statements

- The gold standard as well as the clinical goal is biopsy. When biopsy is inconclusive or not possible and the diagnosis remains in doubt, the above evidence supports the use of PET/CT where a positive result would lead to surgical resection for purposes of both diagnosis and treatment.
- Neuroendocrine tumours of the pancreas are known to be unreliably FDG avid.

DRAFT DSG Recommendation

PET or PET/CT is recommended for staging if a patient is a candidate for curative surgical resection as determined by conventional staging.

Provincial Consensus Meeting Deliberations

The extent of agreement with this recommendation was strong and suggestions were minor.

FINAL Recommendation Put to Vote

PET is recommended for staging if a patient is a candidate for potentially curative surgical resection as determined by conventional staging.

	1 – Strongly Agree		4 – Neither Agree nor Disagree			7 – Strongly Disagree		N/A
	1	2	3	4	5	6	7	
Total	11	10			1			

Votes = 21

Qualifying Statement

The clinical importance of change in treatment strategy as an outcome, despite a lack of strong evidence, is noted.

ASSESSMENT OF TREATMENT RESPONSE

Clinical Question

What benefit to clinical management does PET or PET/CT contribute to the assessment of treatment response for pancreatic cancer?

DRAFT DSG Recommendation

PET is not recommended to guide clinical management based on the assessment of treatment response outside a clinical trial.

Provincial Consensus Meeting Deliberations

No major issues were raised during discussions about this recommendation. The group determined that the wording should be consistent with other recommendations that indicate a lack of evidence.

FINAL Recommendation Put to Vote:

A recommendation cannot be made for or against the use of PET to guide clinical management based on assessment of treatment response due to insufficient evidence.

	1 – Strongly Agree		4 – Neither Agree nor Disagree			7 – Strongly Disagree		N/A
	1	2	3	4	5	6	7	
Total	10	7	3	1				

Votes = 21

Issues raised on voting questionnaire:

-Too weak! Should not be recommending.

Qualifying Statement

- A recommendation for PET cannot be made in the setting of incomplete resection due to lack of evidence.

RECURRENCE/RESTAGING

Clinical Question

What benefit to clinical management does PET or PET/CT contribute when recurrence of pancreatic cancer is suspected but not proven? What benefit to clinical management does PET or PET/CT contribute to restaging at the time of documented recurrence for pancreatic cancer?

DRAFT DSG Recommendation

A recommendation cannot be made for or against the use of PET or PET/CT for the clinical management of suspected recurrence, nor for restaging at the time of recurrence, due to insufficient evidence.

Provincial Consensus Meeting Deliberations

During discussions, mention was made that, in addition to absence of data, the poor prognosis and lack of salvage treatment were also arguments against the use of PET. The comment was made that in this case clinical management is lagging behind technology. The decision was made to amend the recommendation to note this fact.

FINAL Recommendation Put to Vote

PET is not recommended for clinical management of suspected recurrence or for restaging at the time of recurrence, due to insufficient evidence and a lack of effective therapeutic options.

	1 – Strongly Agree			5 – Neither Agree nor Disagree				9 – Strongly Disagree		N/A
	1	2	3	4	5	6	7	8	9	
Total	13	7	1							

Votes = 21

Issues raised on voting questionnaire:

-Agree with 1 exception – isolated local recurrence post-Whipple being considered for radiation.

Qualifying Statement

- Pancreatic cancer has high overall mortality, and recurrence is uniformly fatal. At this time, there are insufficient treatment options that improve the outlook in patients who recur after surgical resection that would allow PET to contribute to management. PET imaging in recurrent disease should be restricted to clinical trials.

Solitary Metastasis Identified at Time of Recurrence

Clinical Question

What is the role of PET when a solitary metastasis is identified at the time of recurrence and a metastectomy is being contemplated?

DRAFT DSG Recommendation

A recommendation cannot be made for or against the use of PET for staging if a solitary metastasis is identified at recurrence as there are no trials that identify the utility of PET scanning in this setting.

Provincial Consensus Meeting Deliberations

No major issues were raised during discussion of this recommendation.

FINAL Recommendation Put to Vote

A recommendation cannot be made for or against the use of PET for staging if a solitary metastasis is identified at recurrence as there are no trials that identify the utility of PET scanning in this setting.

	1 – Strongly Agree			5 – Neither Agree nor Disagree			9 – Strongly Disagree		N/A
	1	2	3	4	5	6	7	8	9	
Total	6	11	2	2						

Votes = 21

Issues raised on voting questionnaire:

-Future isolated recurrence being considered for radical radiation (on study).

-Don't like the clinical trials phrase – also discussion reflects low likelihood of potential benefits.

-Poor wording.

Qualifying Statement

None.

FUTURE RESEARCH

Areas for future research were not discussed in the process of drafting these recommendations.

ACKNOWLEDGEMENTS

The GI DSG would like to thank Dr. Sindu Kanjeekal and Dr. Jim Biagi for taking the lead in drafting this systematic review.

For a complete list of the Gastrointestinal DSG members, please visit the CCO Web site at http://www.cancercare.on.ca/

Funding

The PEBC is a provincial initiative of Cancer Care Ontario supported by the Ontario Ministry of Health and Long-Term Care through Cancer Care Ontario. All work produced by the PEBC is editorially independent from its funding source.

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Appendix 1. PET for pancreatic cancer: summary of the evidence from 2003 to March 2008.

PANCREATIC Diagnostic performance						
Citation (ref #)	Study design	PET imaging	Reference std	Sens	Spec	Evidence grade
Primary diagnosis						
Giorgi2004 (3)	Prospective	PET	Hist/bx or clin fup	69%	100%	C
Mansour2006 (17)	Retrospective	PET	Hist/bx or clin fup	57%	85%	C
Nishiyama2005 (4)	Prospective	PET	Hist/bx or clin fup	89%	65%	B
Rasmussen2004 (5)	Prospective	PET	Hist/bx	75%	88%	B
Van Kouwen2005 (6)	Prospective	PET	Hist/bx or clin fup	91%	87%	B
Staging						
Nishiyama2005 (15)	Prospective	PET	Hist/bx or clin fup	81%	88%	C
Wakabayashi2008 (18)	Retrospective	PET	Hist/bx	Paraaort LN met 57% Hepat met 52% Bone met 50%	Paraaort LN met Not calc Hepat met Not calc Bone met Not calc	D
Primary diagnosis and staging						
Bang2006 (7)	Prospective	PET	Hist/bx or clin fup	97%	78%	B
Borbath2005 (19)	Retrospective	PET	Hist/bx or clin fup	87%	54%	C
Heinrich2005 (8)	Prospective	PET/CT	Hist/bx or clin fup	89%	69%	B
Lemke2004 (9)	Prospective	PET & PET/CT	Hist/bx or clin fup	PET 84% PET/CT 89%	PET 61% PET/CT 64%	C
Lytras2005 (10)	Prospective	PET	Hist/bx or clin fup	73%	61%	C
Maemura2006 (11)	Prospective	PET	Hist/bx or clin fup	87%	67%	B
Ruf2006 (14)	Prospective	PET	Hist/bx or clin fup	93%	41%	B
Sperti2007 (12)	Prospective	PET	Hist/bx or clin fup	92%	97%	B
Casneuf2007 (13)	Prospective	PET & PET/CT	Hist/bx or clin fup	PET 79% PET/CT 88%	PET 90% PET/CT 90%	B
Recurrence						
Ruf2005 (16)	Prospective	PET	Hist/bx or clin fup	95%	100%	B

Abbreviations: bx, biopsy; calc, calculated; clin, clinical; CT, computed tomography; fup, follow up; hepat, hepatic; hist, history; LN, lymph node; met, metastasis; paraaort, paraaortic; PET, positron emission tomography; Sens, sensitivity; Spec, specificity; std, standard.

Meta-analysis: Studies evaluating dx performance with purpose of primary diagnosis and staging
Imaging: PET
Design: Prospective
Reference standard: Histology/biopsy or clinical follow-up
7 studies: Bang et al (7), Casneuf et al (13), Lemke et al (9), Lytras et al (10), Maemura et al (11), Ruf et al (14), Sperti et al (12)
Pooled +LR = 2.77 (95% CI 1.62 to 4.73)
Pooled –LR = 0. 19 (95% CI 0.10 to 0.34)

Imaging: PET/CT
Design: Prospective
Reference standard: Histology/biopsy or clinical follow-up
3 studies: Casneuf et al (13), Heinrich et al (8), Lemke et al (9)
Pooled +LR = 2.69 (95% CI 1.84 to 3.94)
Pooled –LR = 0.16 (95% CI 0.10 to 0.26)

Meta-analysis: Studies evaluating dx performance with purpose of primary diagnosis
Imaging: PET
Design: Prospective
Reference standard: Any reference standard
4 studies: Giorgi et al (3), Nishiyama et al (4), Rasmussen et al (5), van Kouwen et al (6)
Pooled +LR = 4.28 (95% CI 2.07 to 8.86)
Pooled –LR = 0.21 (95% CI 0.12 to 0.40)

Imaging: PET
Design: Prospective
Reference standard: Histology/biopsy or clinical follow-up
3 studies: Giorgi et al (3), Nishiyama et al (4), van Kouwen et al (6)
Pooled +LR = 4.11 (95% CI 1.74 to 9.70)
Pooled –LR = 0.20 (95% CI 0.09 to 0.44)

PANCREATIC Diagnostic thinking					
Citation (ref #)	Study design	PET imaging	Purpose of PET	Management decision	Evidence grade
Bang2006 (7)	Prospective	PET	Primary diagnosis & staging	Rx strategy & staging changed for 25/93 pts (27%): -Upstaged 20 pts -Downstaged 5 pts. Rx modality changed in 20/25 pts (80%): -Upstaged & deemed unresectable 17/20 -Downstaged and deemed resectable 3/20 -Previously unidentified distant mets found in the 17 pts deemed unresectable.	B
Heinrich2005 (8)	Prospective	PET/CT	Diagnosis & staging	Rx strategy changed for 6/37 pts (16%) judged to have resectable cancer: -Distant mets detected by PET/CT only in 5 pts -Simultaneous cancer found & led to change in surgery in 2 pts (1 curative, 1 palliative). Detected benign lesions in 17 pts of which 10 were not identified by CT.	B
Nishiyama2005 (15)	Prospective	PET	Staging	Rx strategy changed for 5/42 pts (12%): -From curative to palliative (3 pts) -From palliative to curative (2 pts)	B
Ruf2006 (14)	Prospective	PET	Primary diagnosis & staging	Interpretation of PET improved through fusion of PET/MRI in 8/32 pts (25%). Image fusion changed treatment in only 1 pt (surgery expanded to curative).	B
Sperti2007 (12)	Prospective	PET	Primary diagnosis & staging	Rx strategy changed for 44/64 pts (69%): -Positive PET results affected Rx in 10 pts. -Negative PET results affected management in 34 pts.	B

Abbreviations: CT, computed tomography; mets, metastases; MRI, magnetic resonance imaging; PET, positron emission tomography; pts, patients; Rx, treatment.

PANCREATIC Management strategy					
Citation (ref #)	Study design	PET imaging	Purpose of PET	Patient centred outcomes and prognosis	Evidence grade
Bang2006 (7)	Prospective	PET	Primary diagnosis and staging	Comparison groups: 1) PET assessment of response to chemorad'n (15 pts) 2) Dynamic CT fup to chemorad'n (same 15 pts). -Discrepancy between groups 9/15 (60%) -Therapy responders: PET 5/15 vs CT 0/15. -Time to progression in PET responders 399 d vs nonresponders 233 d	B

Abbreviations: CT, computed tomography; fup, follow up; PET, positron emission tomography; pts, patients.