



PET Recommendation Report 4 Version 2

PET Imaging in Esophageal Cancer

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A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Report Date: January 19, 2009

Update: November 30, 2010

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Section 1: Recommendations

Section 2: Evidentiary Base and Consensus Process

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PET Recommendation Report 4 Version 2: Section 1

PET Imaging in Esophageal Cancer: Recommendations

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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 esophageal cancer?
- What benefit to clinical management does PET or PET/CT contribute to the assessment of treatment response for esophageal cancer?
- What benefit to clinical management does PET or PET/CT contribute when recurrence of esophageal 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 esophageal cancer?
- What is the role of PET when a solitary metastasis is identified at the time of recurrence and the metastectomy is being contemplated?

TARGET POPULATION

Patients with esophageal 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 to inform clinical decision making regarding the appropriate role of PET imaging and to guide priorities for future PET imaging research.

RECOMMENDATIONS AND KEY EVIDENCE

These recommendations are based on an evidentiary foundation consisting of one recent high-quality United Kingdom (U.K.) Health Technology Assessment (HTA) systematic review (1) that included systematic review and primary study literature for the period from 2000 to August 2005 and update searches based on those in that original systematic review

and undertaken to retrieve the same level of evidence for the period from August 2005 to May 2010.

Diagnosis/Staging

For the staging workup of patients with esophageal cancer who are potential candidates for curative therapy, PET is recommended to improve the accuracy of M staging.

There is a significant role for PET for its incremental value in detecting distant disease, in addition to CT +/- endoscopic ultrasound (EUS). Especially in the absence of EUS, PET provides an incremental benefit.

HTA review (1): One systematic review containing three primary studies showed the superiority of PET to CT or EUS in detecting distant metastases. Another systematic review of 12 primary studies showed that PET had a sensitivity of 67% and a specificity of 97%, corroborating the first systematic review. One additional primary study showed the incremental benefit of adding PET to CT and EUS, giving a sensitivity of 74% compared with 53% for PET alone and 64% for PET plus CT.

A 2008 systematic review by van Vliet et al, 2008 (2), with two primary studies not included in Facey et al, 2007 (1), and two studies from the update search (Kato et al, 2005 [3] and Katsoulis et al, 2007 [4]) showed higher detection rates for distant metastases with PET than with CT, but the difference was not statistically significant.

When the effect of PET is evaluated, based on whether staging is changed, a correct change occurred in approximately 30% of cases in two studies (one in van Vliet et al [2], and one in Katsoulis et al [4] from the updated search).

There is some evidence that PET/CT is superior to PET alone for nodal staging (Yuan et al, 2006 [5]).

2008-2010 update: Seven primary studies (Chatterton et al, 2009 [6], Cheze-Le Rest et al, 2008 [7], Hsu et al, 2009 [8], Hu et al, 2009 [9], Noble et al, 2009 [10], Okada et al, 2009 [11], and Shimizu et al, 2009 [12]) also showed the significant impact of PET and PET/CT on the clinical management, prognostic stratification of patients with newly diagnosed esophageal cancer, prediction of regional and locoregional lymph nodes, and improvement on the accuracy of pretreatment staging compared to CT and EUS alone.

Qualifying Statement

- The data supporting this recommendation are compelling but sparse. The recommendation is based on patients with a new diagnosis of esophageal cancer.

Assessment of Treatment Response

A recommendation cannot be made for or against the use of PET (post or neoadjuvant therapy) for the purpose of predicting response to neoadjuvant therapy due to insufficient evidence.

There is some evidence that PET, either early in treatment or at the completion of neoadjuvant therapy, can predict complete pathologic response, and therefore, predict the longer-term outcome in terms of survival and event-free survival.

HTA 2007 review (1): One systematic review of four primary studies plus one additional study showed that PET may be superior to CT and comparable to EUS in the assessment of response and of prognosis after neoadjuvant therapy. One additional study showed PET/CT to be more sensitive for the evaluation of response than either CT or endoscopic ultrasound.

2005-2010 update: Thirteen primary studies were identified in the update search. The change in PET parameters before and after neoadjuvant therapy provided a reasonable diagnostic accuracy (68% to 86%) for the prediction of pathological response (Song et al, 2005 [13], Levine et al, 2006 [14], Duong et al, 2006 [15], Kim et al, 2007 [16], Wieder et al, 2007

[17], Smithers et al, 2008 [18], Higuchi et al, 2008 [19], Klaeser et al, 2009 [20], and Shenfine et al, 2009 [21]). Perhaps more importantly, there is evidence that PET response is related to longer-term clinical outcomes, including disease-free survival and overall survival (Duong et al [15], Kim et al [16], Wieder et al [17], Higuchi et al [19], and Shenfine et al [21]). The best cutoff point to use for defining responder versus non-responder remains to be defined. Data derived from the receiver operating characteristic (ROC) curves would suggest a 30% to 50% reduction as a useful parameter (Wieder et al [17], Smithers et al [18],). The prognostic value of PET is further supported by the fact that responders and nonresponders have significantly different SUV change profiles.

The value of PET as an early indicator for future response was evaluated in three studies (Gillham et al, 2006 [22], Westerterp et al, 2006 [23], Wieder et al, 2007 [17b], and Vallbohmer et al, 2009 [24]). While a significant difference existed between pathological responders and nonresponders, further study is required to establish the best criteria and standardized conditions to use if this modality is to be routinely incorporated into clinical practice to guide treatment decisions.

One study evaluated PET as an early tool to predict a response allowing neoadjuvant therapy to be abandoned in favour of early surgery (Lordick et al, 2007 [25]). This study confirmed that responders had better outcomes in terms of survival and disease-free survival.

Qualifying Statement

- Whether the use of PET to assess treatment response would translate into an improved outcome remains to be established, but it is potentially useful in minimizing toxicity related to futile treatment. The optimal parameters to use for defining responders require further validation.

Recurrence/Restaging

A recommendation cannot be made for or against the use of PET for the evaluation of suspected recurrence due to insufficient evidence.

Two studies from the 2005-2010 update (Guo et al, 2007 [26] and Jingu et al, 2010 [27]) showed PET/CT to be accurate in detecting regional and distant recurrence and in predicting the prognosis in patients with postoperative recurrent esophageal cancer. The findings of these studies require corroboration before a recommendation can be made.

Qualifying Statement

None.

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