PET Recommendation Report 17

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

PET Imaging in Anal Canal Cancer

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PET Imaging in Anal Canal Cancer

Section 1: Recommendations and Key Evidence

OBJECTIVES

To provide a synthesis and summary of evidence surrounding the clinical utility of positron emission tomography (PET) imaging in patients with anal canal cancer.

TARGET POPULATION

Adult patients diagnosed with anal canal cancer.

INTENDED USERS

This recommendation report is intended to guide the Ontario PET Steering Committee in their decision making with respect to the development of indications. This recommendation report may also be useful to inform clinicians who are involved in the management of patients with anal canal cancer.

RECOMMENDATIONS, KEY EVIDENCE, AND INTERPRETATION OF EVIDENCE

Recommendation 1
PET or positron emission tomography/computed tomography (PET/CT) may provide added benefit to the initial staging of patients with T2-4 squamous carcinoma of the anal canal with or without evidence of nodal involvement on anatomical imaging. However, no strong evidence is currently available to justify its use as part of routine investigation, and access should be restricted to the registry-type setting.
Qualifying Statements for Recommendation 1
• PET or PET/CT is sensitive in identifying but not characterizing already known primary tumours. It is not clear whether PET or PET/CT should be used to increase or decrease the gross tumour or clinical target volumes of the primary tumour compared with those defined by standard magnetic resonance imaging (MRI) of the pelvis. • PET or PET/CT is able to identify nodes not seen on conventional imaging; however, specificity is modest and there would be the risk of overtreatment if the radiation field is expanded to include non-enlarged but PET-positive nodes.
Key Evidence for Recommendation 1
• Eight studies assessed the sensitivity of PET or PET/CT for the detection of primary tumour in situ [1-8]. The pooled sensitivity on a per-patient based analysis was 99% (95% confidence interval [CI], 97% to 100%). In comparison, the pooled sensitivity of CT from three studies [1,2,6] was 67% (95% CI, 50% to 82%). • For the detection of inguinal lymph nodes, PET/CT had an overall sensitivity of 93% (95% CI, 76% to 99%) and specificity of 76% (95% CI, 61% to 87%) [6,7]. • Across four studies, PET/CT identified distant metastatic sites not seen on conventional imaging in 2.4% to 4.7% of cases [1,4,7,9]. • Eleven studies evaluated the impact of PET or PET/CT on patient management. Information from PET or PET/CT upstaged 5.1% to 37.5% of patients [1-4,6-12] and downstaged 8.2% to 26.7% of patients [1,3,6,8,9,11]. Patients staged T2-4 were more likely to have a change in the overall staging [3,8]. Treatment plans were modified in 12.5% to 59.3% of patients [2-4,6-8,11,12], which consisted mainly of radiotherapy dose or field changes. In one particular study [12], PET/CT led to changes in gross tumour volume (GTV) and clinical target volume (CTV) contours in 55.6% and 37.0% of

cases, respectively, with the majority of cases (80%) in patients staged T3-4. Moreover, PET/CT-delineated GTV and CTV that were used for treatment purposes were significantly greater than those drawn on CT (p=0.00006). Likewise, Mai et al [11] reported that 15.4% (6/39) of patients with CT-enlarged inguinal lymph nodes had a reduction in irradiation dose due to PET-negative findings; none of these patients developed recurrence or distant metastases.

Interpretation of Evidence for Recommendation 1

Despite the lack of comparison with pelvic MRI, which is considered the current standard in the diagnostic work-up of anal canal cancer, PET or PET/CT showed high sensitivity in visualizing the primary tumour and identifying involved lymph nodes as compared with CT. While there were uncertainties surrounding the interpretation of the index tests (PET or PET/CT, conventional imaging) and reference standard (post-surgical or post-biopsy histology, clinical or radiologic follow-up) across the studies, the Working Group believe that obtaining biopsy from all patients may not be feasible or practical and thus this was considered an acceptable study limitation.

Recommendation 2

There is insufficient evidence to recommend the use of PET or PET/CT in the assessment of treatment response.

Qualifying Statements for Recommendation 2

- Given that anal cancers tend to respond slowly after completion of chemoradiotherapy treatment, PET or PET/CT shortly after therapy should be avoided to minimize the number of false-positive findings.
- An appropriate timing of assessment remains controversial, and the optimal time point at which residual uptake of fluorodeoxyglucose (FDG) in a primary tumour should trigger salvage surgery is unknown.
- Complete response on PET or PET/CT is a good prognostic factor for overall and progression-free survival (PFS).

Key Evidence for Recommendation 2

- Mistrangelo et al [6] reported that at one month after the end of treatment, PET/CT detected persistent disease with a sensitivity of 66.6% (2/3), a specificity of 92.5% (37/40), a positive predictive value (PPV) of 40% (2/5), and a negative predictive value (NPV) of 97.4% (37/38). At three months after the end of treatment, the sensitivity, specificity, PPV, and NPV were 100% (2/2), 97.4% (37/38), 66.6% (2/3), and 100% (37/37), respectively.
- Consistent across all studies, a partial response (PR) or no response (NR) on PET or PET/CT was predictive of significantly worse two-year PFS (complete response [CR]: 68% to 95% versus PR: 22% to 40%; p<0.0001 or NR: 0%, p<0.0001) [2,13,15], two-year disease-free survival (CR: 77.5% versus PR: 14%; p<0.0001) [16], two-year cause-specific survival (CR: 94% versus PR: 39%; p=0.0008) [13], and overall survival at two (CR: 95.7% versus PR: 49.9%; p<0.0001) [16] and five years (CR: 88% versus PR: 69%; p=0.03 or NR: 0%; p<0.0001) [15].

Interpretation of Evidence for Recommendation 2

Owing to the small number of studies evaluating the role of PET or PET/CT in the assessment of response after chemoradiotherapy and the inconsistent timing of assessment, the evidence is currently insufficient to support the use of PET or PET/CT in this setting.

Recommendation 3

There is insufficient evidence to recommend the use of PET or PET/CT for evaluation of

suspected or proven recurrence.
Qualifying Statements for Recommendation 3
• PET or PET/CT can be useful in the follow-up when persistence or recurrence of disease is suspected; however, it is unknown whether PET or PET/CT has a positive impact on overall survival.
Key Evidence for Recommendation 3
• Vercellino et al [5] reported that the sensitivity, specificity, PPV, NPV, and accuracy of PET/CT on a per-site basis in detecting persistent or recurrent disease were 86.4% (19/22), 96.8% (149/154), 79.2% (19/24), 98.0% (149/152), and 95.5% (168/176), respectively. When analyzed by examination, the sensitivity was 93.3% (14/15), specificity was 81.0% (17/21), PPV was 77.8% (14/18), NPV was 94.4% (17/18), and accuracy was 86.1% (31/36). • Overall, management was altered in 16.7% to 25.0% of cases, which includes one case where PET/CT prompted unnecessary cytology as this patient was found to be disease free 11 months later [5,8].
Interpretation of Evidence for Recommendation 3
Owing to small sample size as well as the lack of data on the frequency and timing of routine follow-up, the evidence is currently insufficient to support the use of PET or PET/CT in this setting.

IMPLEMENTATION CONSIDERATIONS

The incorporation of PET or PET/CT into the current initial staging assessment would be feasible provided that there is capacity to support the new indication.

FUTURE RESEARCH

Future directions may include investigation into the role of PET/CT in assessing response to treatment at an appropriate time interval and its usefulness in routine follow-up. This may also help in exploring an option of more aggressive treatment approaches for partial responders.