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PET Recommendation Report 9

PET Imaging in Small Cell Lung Cancer

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Report Date: January 19, 2009

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Section 1: Recommendations
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Recommendation Report – PET #9: Section 1

PET Imaging in Small Cell Lung 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 small cell lung cancer (SCLC)?
- What benefit to clinical management does PET or PET/CT contribute to the assessment of treatment response for SCLC?
- What benefit to clinical management does PET or PET/CT contribute when recurrence of SCLC 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 SCLC?
- 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 SCLC.

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 recommended for staging in patients with SCLC who are potential candidates for the addition of thoracic radiotherapy to chemotherapy.
Six studies were based on PET alone (Bradley et al [2], Brink et al [3], Kut et al [4], Pandit et al [5], Vinjamuri et al [6], Blum et al [7]). Two studies were based on PET/CT (Fischer et al [8], Fischer et al [9]). Overall higher sensitivity and specificity is achieved with PET/CT versus PET versus conventional imaging (Fischer et al [8]). In terms of diagnostic accuracy, the diagnostic performance of PET compared with CT for extrathoracic lymph node metastases was 100% versus (vs) 70% sensitivity and 98% vs 94% specificity; for distant metastases 98% vs 83% sensitivity and 92% vs 79% specificity; and for brain mets (compared with MRI) was 46% vs 100% sensitivity and 97% vs 100% specificity (Brink et al [3]). For the differentiation of extensive disease (ED) from limited disease (LD), PET/CT had sensitivity and specificity of 93% and 100%, PET had sens and specificity of 93% and 83%, and standard staging had sensitivity and specificity of 79% and 100% (Fischer et al [8]). SCLC has a high metabolic rate and invariably the primary site is fluorodeoxyglucose (FDG) avid (Bradley et al [2], Brink et al [3], Kut et al [4], Niho et al [10], Blum et al [7]). The rate of upstaging from limited to extensive disease varies from 0% to 33%. The sample size of the reported studies varies from four to 63 patients with limited disease. Only two studies specifically evaluated the role of PET in LD SCLC (Bradley et al [2], Niho et al [10]). In these two studies, upstaging ranged from 8.3% to 9.5%, with the most common sites for detected metastases being in the bone, liver, and lymph nodes (bilateral supraclavicular, cervical, and axillary). The remaining seven studies had a mixture of LD and ED SCLC, with varying percentages of upstaging LD to ED SCLC from 0% to 33% (Brink et al [3], Fischer et al [8], Kut et al [4], Pandit et al [5], Vinjamuri et al [6], Blum et al [7], Kamel et al [11]). Some downstaging of ED SCLC occurred but primarily in cases where conventional imaging found suspected adrenal metastases (Brink et al [3], Vinjamuri et al [6]) or contralateral lung nodule (Vinjamuri et al [6], Kamel et al [11]) as the only site for ED SCLC, and PET downstaged some of these patients. The impact of PET imaging is seen in cases where the unsuspected lymph nodes metastases (FDG-avid disease) is found and causes a change in the thoracic radiation treatment volume. The thoracic radiation treatment volumes were altered from 19% to 34% (Bradley et al [2], Vinjamuri et al [6], Blum et al [7], Niho et al [10], Kamel et al [11]).

Qualifying Statement

- PET or PET/CT performs better for staging the primary tumour in SCLC than for areas outside the chest, including the extrathoracic lymph nodes and distant metastases. There is greater discordance between PET and conventional imaging results in the evaluation of the mediastinal nodes, extrathoracic nodes, and distant sites.

Assessment of Treatment Response

A recommendation cannot be made for or against the use of PET for the assessment of treatment response in SCLC due to insufficient evidence.
Only one study addressed the issue of change in therapy or continuation of therapy based on response (Kamel et al [11]). In this study, restaging with PET after therapy was available in 20 patients. PET correctly identified the five patients with CR, 11 of 12 patients with residual disease, and three patients with progressive disease. CR was verified by clinical and radiological follow-up. Discordance was found between PET and CT in three patients where no FDG uptake was seen in abnormally enlarged nodes and further chemotherapy was deemed unnecessary due to a metabolic CR. In one patient, PET detected residual disease that CT had missed, and further chemotherapy was given. Two studies evaluated the concordance of response evaluation of PET with conventional imaging (Fischer et al [9], Kut et al [4]). In the study by Fischer et al (9), PET/CT was performed after one cycle of chemotherapy in 12 patients (early response assessment). Major disagreement between PET/CT and CT was seen in one patient, and minor disagreement was seen in six patients. The one-year survival rate for patients responding on PET/CT was 64%. One nonresponder on PET/CT and CT died after eight months. PET/CT was also performed after six cycles of chemotherapy (final response assessment) in 19 patients. Overall, disagreement between CT and PET/ CT was found in eight patients (42%) and major disagreement in two patients (11%). One-year survival was 65% for responders and 50% for nonresponders. No changes in therapy were made based on early or final response assessment. In the study by Kut et al (4), nine of 21 patients had a response assessment. Based on both PET and conventional imaging, there were seven partial responses (PR), one complete response (CR), and 1 stable disease (SD). PET failed to identify liver progression as PET indicated SD but CT showed new liver lesions. In two cases, PET showed CR while CT showed persistent lymphadenopathy. The prognostic value of PET response was evaluated in two studies (Pandit2003 [5], Blum2004 [7]). In the study by Pandit et al (5), the two-year survival in nine of 10 PET-negative patients was 67%, and in four of 27 PET-positive patients it was 23% (p=0.0108). In the study by Blum et al (7), the median time to progression in PET CR was 13.7 vs 9.7 months in no CR. The role for PCI only in complete responders was not addressed in any of these studies but was raised for discussion by Kamel et al (11). None of the studies addressed the issue of whether change in therapy affected patient outcomes.

Qualifying Statements

- Response evaluation may be used for various reasons:
  a) to determine if a change in therapy is needed in non-responders or those with progressive disease
  b) to determine if additional consolidation therapy is needed
  c) to determine prognosis
  d) to determine the role for PCI
- Issues in SCLC that need to be addressed before changing therapy include:
  1) what effective salvage or second line treatment is available?
  2) do we know that additional consolidation therapy is needed beyond four to six cycles?
  3) what is the optimal time to do response assessment?
  4) do we only give prophylactic cranial irradiation (PCI) to CR and exclude PR?

Recurrence/Restaging

A recommendation cannot be made for or against the use of PET for evaluation of recurrence or restaging due to insufficient evidence.
None of the studies address these questions but rather address the concordance of PET vs conventional imaging in evaluating response.

Qualifying Statement

- Detecting early recurrence is useful if there is effective salvage therapy, but in SCLC second-line chemotherapy has a low response rate.

Solitary Metastasis Identified at Time of Recurrence

A recommendation cannot be made for or against the use of PET when metastectomy or stereotactic body radiation therapy is being contemplated for solitary metastases due to insufficient evidence.
None of the studies address this question. In the uncommon setting where there is persistent localized disease after treatment with CT radiation therapy (RT), surgical resection may be a possibility or with newer RT techniques, stereotactic body radiation therapy may be possible, and in this unusual scenario, there may be a role for PET/CT, but currently there are no data to support this.

Qualifying Statement

None.

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