Impact of PET-CT scan on management in upper gastrointestinal malignancy

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ABSTRACT

INTRODUCTION: Curative treatments of upper gastrointestinal (UGI) cancers carry significant morbidity and mortality. Therefore, accurate pre-treatment staging is important. PET-CT scan is an expensive modality, and not readily available in New Zealand. The aim of this study was to describe how PET-CT scan influences management in UGI cancer.

METHODS: This retrospective descriptive study included patients with UGI cancer with no evidence of metastatic disease on IV contrast CT scan, and those medically fit for curative treatment. Patients then underwent PET-CT scan. We defined influence or change in management if PET-CT showed metastatic disease or other lesions requiring further investigation.

RESULTS: Seventy-nine patients were identified for the purposes of this study. Fifty-nine (74.7%) had CT scan showing no evidence of metastatic disease. Of these, PET-CT scan influenced management in 14 patients (23.7%) and found distant metastasis in eight patients (13.6%). The remaining 20 of 79 patients (25.3%) had CT scan showing indeterminate lesions. Of these, PET-CT scan influenced management in eight patients (40%), with metastatic disease seen in seven patients (35%).

CONCLUSION: Our study confirms the value of PET-CT scan in pre-operative staging of UGI cancer. It had a greater impact on patients with intermediate lesions on staging CT.

Background

Upper gastrointestinal (UGI) malignancy in the western world differs from other forms of cancer in that it often presents at an advanced stage. Curative treatment, in almost all cases, is only possible if there is no distant metastatic disease (Stage I–III), although there are several palliative management options. Such treatment with curative intent often involves multi-modality therapies with significant morbidity and mortality. Although accurate determination of tumour size, depth of tumour invasion, and involvement of lymph nodes is important in providing prognostic information and tailoring treatment to the individual patient, the detection of metastatic disease is more important to select out those patients who would not benefit from aggressive treatments with curative intent.

Increasingly, accurate pre-treatment staging is possible based on newer imaging and surgical techniques, such as positron emission tomography (PET), laparoscopy, thoracoscopy, laparoscopic ultrasound, and endoscopic ultrasound (EUS).

Traditional imaging methods, including IV contrast computed tomography (CT) scan and/or ultrasound scan (USS), utilise anatomical anomalies for determining staging. PET scan utilises physiological differences between normal tissues and those of neoplastic cells, which may precede detectable structural changes. The glucose analogue 18F-fluorodeoxyglucose (FDG) is commonly used, as it highlights differential in glucose uptake between normal and adjacent abnormally active tissues, including neoplasia. PET scan could therefore detect small or indistinct metastasis, metachronous neoplasms, or primary neoplasms affecting a different organ system, which may not be detected by IV contrast CT or USS. However, it has limited usefulness in assessing tumour size, depth of invasion and loco-regional
nodal involvement. PET scan is commonly combined with a CT scan (PET-CT scan), which allows for representation of lesions anatomically and physiologically.

Due to the costs and logistics of providing radioactive substrates with a short half-life, and the limited availability of PET-CT scanners in New Zealand, we undertook this study to determine the impact of PET-CT scan on the management of upper gastrointestinal cancer in our MidCentral Health District Health Board Regional Cancer Treatment Service (RCTS).

**Objective**

A retrospective study to ascertain how PET-CT scan influenced management of upper gastrointestinal cancer in our MidCentral District Health Board RCTS.

**Methods**

Data was retrieved from the patient database of the MidCentral Health RCTS multi-disciplinary forum for gastro-intestinal and intra-abdominal cancer, to which a vast majority of elective patients with UGI (oesophago-gastric and hepato-biliary/pancreatic) tumours/cancers are referred for imaging, pathology review, and management planning. A significant number of such patients are referred from outside the domicile boundaries of the MidCentral Health District Health Board (Wanganui, Taranaki, Hawkes Bay, and Wairarapa District Health Boards [DHBs]), but whose cancer management falls within the auspices of the MidCentral Health RCTS. Paradoxically however, not all patients with such cancers who live in these other DHBs are referred for management discussion to this forum.

Most referred patients have already undergone IV contrast CT body scan. Such referred patients are nearly always discussed at this multi-disciplinary forum for gastro-intestinal and intra-abdominal cancer, prior to PET-CT scan principally as a means of avoiding unnecessary or inappropriate ordering of PET-CT scans. Although oesophageal, gastro-oesophageal junction (GOJ), and hepato-biliary cancers have a streamlined administrative approval mechanism for PET-CT scan requests, other UGI malignancies (gastric and pancreatic) do not enjoy such a streamlined process. None of the patients recommended to undergo PET-CT scan by this forum were declined funding or the scan itself.

The IV contrast CT scan, typically arterial and delayed portal venous phase CT scan chest and abdomen with oral contrast, was mostly performed and reported in the hospital of the patient’s domicile DBH. PET-CT scan was almost always performed and reported by Pacific Radiology, 98 Churchill Ave, Crofton Downs, Wellington. All images were separately reviewed by our radiologists at the MidCentral Health multi-disciplinary forum for gastro-intestinal and intra-abdominal cancer.

An unquantified, but minority, of patients with upper GI cancer/tumours were referred to another DHB/RCTS without prior discussion here (anecdotal).

**Participants**

We included patients with UGI tumours/cancers who were discussed in the MidCentral Health multi-disciplinary forum for gastro-intestinal and intra-abdominal cancer between June 2004 and June 2014. The following patients were excluded from the study:

- Patients with definite evidence of distant metastatic disease on IV contrast CT scan
- Patients who were not medically fit for curative treatment
- Patients referred with recurrent cancer.

**Baseline characteristics**

Baseline patient characteristics collected included: age, sex, site of malignancy, and histopathology.

**Determining how PET scan influenced management**

To determine how PET-CT scan influenced management, we initially described what the management algorithm would be if PET-CT scan was not available. Medically fit patients with confirmed UGI cancer would undergo IV contrast CT scan +/- staging laparoscopy (the latter at the discretion of the treating surgeon). If there was no evidence of distant metastatic disease, the patient would undergo treatment with curative intent. If IV contrast CT showed indeterminate lesions that were unable to be biopsied, the patient would...
Figure 1: Management of UGI cancer without PET-CT scan.

Figure 2: Management of UGI cancer with addition of PET-CT scan.
be given the benefit of doubt and would undergo treatment with curative intent, with interval CT scan for reassessment. If multi-modality treatment was undertaken, interval imaging typically occurred prior to surgery. If interval CT scan was indicative of distant metastatic disease, treatment intent would change to palliative.

Any deviation from this algorithm because of the PET-CT scan result would be considered a change in management. These included:

- PET-CT scan showing abnormal avid areas indicating distant metastatic disease
- PET-CT scan showing other abnormal avid area(s) aside from the known primary tumour site and not typical for metastatic disease from that primary site, requiring further investigation thus interrupting the intended management pathway.

This is illustrated in Figures 1 and 2. In Figure 2, patients in pathway marked grey would be considered as change in management.

**Ethics**
No ethical committee approval was required as this study was a retrospective data audit.

**Results**
There were 79 patients included for our study. Baseline characteristics are shown in Table 1. Male: female ratio was 2.43:1, mean age 68 years at the time of diagnosis. Oesophageal cancer was the most common pathological site (72.2%), followed by pancreatic and gastric cancer (10.1% each). GOJ cancers, cholangiocarcinoma and gall bladder cancers were a small minority. Adenocarcinoma (69.6%) and squamous cell carcinoma (26.6%) formed the vast majority of histodiagnosis. Histology was not available in two patients, both of whom had pancreatic cancer.

**PET-CT influencing management**
Figure 3 shows the influence of PET-CT scan on patient management. Of the 79 patients, 59 (74.7%) had no evidence of distant disease or indeterminate lesions on IV contrast CT scan. Fourteen of this group of 59 patients (23.7%) had PET-CT scans that influenced management, and eight (13.6%) patients had PET-CT showing metastatic disease. The remaining 20 of 79 patients (25.3%) had indeterminate lesions on IV contrast CT scans that were unable to be further characterised. Of this group of 20 patients, eight (40%) had a PET-CT scan result that changed their management, with seven patients (35%) having metastatic disease. Thus, PET-CT scan influenced management in a total of 22 patients out of 79 (27.8%) and showed metastatic disease not seen on CT scan in 18 out of 79 patients (22.8%).

**Analysis of patients where PET-CT scan influenced management**
Table 2 details the patients where PET-CT scan influenced management.
**Figure 3:** How often PET-CT scan influenced patient management.

![PET-CT Influence Diagram](image)

**Table 2:** Detailing the distant metastatic disease seen on PET-CT scan.

<table>
<thead>
<tr>
<th>Location of distant disease on PET-CT scan</th>
<th>Number (%)</th>
<th>Location of indeterminate lesion on IV contrast CT scan</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IV Contrast CT showing no distant disease</strong></td>
<td></td>
<td>NIL</td>
</tr>
<tr>
<td>Liver lesions</td>
<td>4 (6.8)</td>
<td>Retrothyroid nodes</td>
</tr>
<tr>
<td>Skeletal lesions</td>
<td>2 (3.4)</td>
<td>Retrocural and coeliac lymph node</td>
</tr>
<tr>
<td>Distant lymph node</td>
<td>2 (3.4)</td>
<td>Left gastric node</td>
</tr>
<tr>
<td>Stomach lesion</td>
<td>1 (1.7)</td>
<td>Lung</td>
</tr>
<tr>
<td>Adrenal lesion</td>
<td>1 (1.7)</td>
<td>Lung and Liver</td>
</tr>
<tr>
<td>Gluteal lesion</td>
<td>1 (1.7)</td>
<td>Left gastric node and left adrenal</td>
</tr>
<tr>
<td>Bowel lesions</td>
<td>3 (5.1)</td>
<td>Left kidney and Left adrenal</td>
</tr>
<tr>
<td>Total</td>
<td>14 (23.7)</td>
<td>Left gastric node and left adrenal</td>
</tr>
<tr>
<td><strong>IV Contrast CT showing indeterminate lesions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skeletal metastasis (T1)</td>
<td>1 (5)</td>
<td>Retrothyroid nodes</td>
</tr>
<tr>
<td>Retroportal lymph node</td>
<td>1 (5)</td>
<td>Retrocural and coeliac lymph node</td>
</tr>
<tr>
<td>Left Gastric node</td>
<td>1 (5)</td>
<td>Left gastric node</td>
</tr>
<tr>
<td>Lung metastasis</td>
<td>1 (5)</td>
<td>Lung</td>
</tr>
<tr>
<td>Coeliac lymph node involvement</td>
<td>1 (5)</td>
<td>Lung and Liver</td>
</tr>
<tr>
<td>Root of neck</td>
<td>1 (5)</td>
<td>Left gastric node and left adrenal</td>
</tr>
<tr>
<td>Sigmoid lesion</td>
<td>1 (5)</td>
<td>Left kidney and Left adrenal</td>
</tr>
<tr>
<td>Vocal cord metastasis</td>
<td>1 (5)</td>
<td>Left gastric node and left adrenal</td>
</tr>
<tr>
<td>Total</td>
<td>8 (40)</td>
<td></td>
</tr>
</tbody>
</table>
When IV contrast CT scan showed no evidence of distant metastatic disease (59 patients), four (6.8%) had liver lesions. Skeletal lesions and distant lymph node involvement (eg, para-aortic lymphadenopathy) were seen in a four patients (6.8%) each. Stomach (one patient, 1.7%) and adrenal metastasis (one patient, 1.7%) was also seen. There were three patients (5.1%) who had avid lesions in the bowel (one caecal lesion and two sigmoid lesions) needing colonoscopies.

When IV contrast CT showed indeterminate lesions (20 patients), one (5%) had skeletal metastases (T1 vertebral body). Lung metastases was seen in one patient (5%). Distant lymph node involvement was seen in three (15%) patients (left gastric node, retroportal node, coeliac node), while one patient (5%) had a vocal cord metastasis. One patient (5%) had a sigmoid colon lesion and underwent sigmoidoscopy. The last patient (5%) had a lesion in the root of the neck and underwent palliative treatment. Of these eight patients, only two patients had PET-CT lesions which corresponded to those on IV contrast CT scans.

Table 3: Detailing lesions on PET-CT scan requiring further investigation.

<table>
<thead>
<tr>
<th>Lesions needing further investigation</th>
<th>Final diagnosis</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caecal lesion</td>
<td>Normal colonoscopy</td>
<td>1</td>
</tr>
<tr>
<td>Sigmoid lesion</td>
<td>Low grade tubulovillous adenoma</td>
<td>1</td>
</tr>
<tr>
<td>Sigmoid lesion</td>
<td>Sigmoid adenocarcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Sigmoid lesion</td>
<td>Intramucosal adenocarcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Sigmoid lesion</td>
<td>Hepatic haemangiomia</td>
<td>1</td>
</tr>
<tr>
<td>Sigmoid lesion</td>
<td>Benign lymph node</td>
<td>1</td>
</tr>
<tr>
<td>Sigmoid lesion</td>
<td>Granulomatous lymphadenitis</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>7 (8.9%)</td>
</tr>
</tbody>
</table>

Table 4: Shows how often PET-CT scan influenced management based on location of tumour.

<table>
<thead>
<tr>
<th>Location</th>
<th>Number where PET-CT influenced management (%)</th>
<th>Number where PET-CT showed metastatic disease (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oesophagus</td>
<td>18 (31.6)</td>
<td>12 (21.1)</td>
</tr>
<tr>
<td>GOJ</td>
<td>1 (25)</td>
<td>1 (25)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1 (12.5)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>Stomach</td>
<td>2 (25)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>Cholangiocarcinoma</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Gallbladder</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

When IV contrast CT scan showed no evidence of distant metastatic disease (59 patients), four (6.8%) had liver lesions. Skeletal lesions and distant lymph node involvement (eg, para-aortic lymphadenopathy) were seen in a four patients (6.8%) each. Stomach (one patient, 1.7%) and adrenal metastasis (one patient, 1.7%) was also seen. There were three patients (5.1%) who had avid lesions in the bowel (one caecal lesion and two sigmoid lesions) needing colonoscopies.

When IV contrast CT showed indeterminate lesions (20 patients), one (5%) had skeletal metastases (T1 vertebral body). Lung metastases was seen in one patient (5%). Distant lymph node involvement was seen in three (15%) patients (left gastric node, retroportal node, coeliac node), while one patient (5%) had a vocal cord metastasis. One patient (5%) had a sigmoid colon lesion and underwent sigmoidoscopy. The last patient (5%) had a lesion in the root of the neck and underwent palliative treatment. Of these eight patients, only two patients had PET-CT lesions which corresponded to those on IV contrast CT scans.

Table 3 details patients with other organ lesions highlighted by PET-CT scan that required further investigation/management. It shows that four patients (5.1%) had large bowel lesions that required colonoscopy. Of these, one had a focal avid caecal area but a subsequent normal colonoscopy, one had a large sigmoid tubulovillous adenoma with low-grade dysplasia removed at colonoscopy, one had an intramucosal adenocarcinoma and underwent endoscopic resection with surveillance colonoscopies, and the final patient had a sigmoid adenocarcinoma and underwent an anterior resection prior to oesophagectomy. The remaining three patients had benign lesions. Patient with hepatic haemangiomia had a primary gastric cancer, while the remaining six patients had a primary oesophageal cancer.

Abnormal PET-CT scan influencing management according to primary cancer site

Table 4 shows that management was changed in 31.6% of patients with oesophageal cancer, 23% with GOJ cancer, 12.5% with pancreatic cancer, 25% with gastric cancer, and in none of the patients with cholangiocarcinoma or gallbladder cancer.
Discussion

Upper GI cancer in the western world often presents at an advanced stage that precludes treatment with curative intent. The prevalence of hepatic metastasis at initial diagnosis is 50% for oesophageal cancer, and 12% for gastric cancer. Furthermore, curative intent treatment is frequently multi-modal and carries significant morbidity and mortality. Therefore, it is important to undergo comprehensive pre-treatment staging particularly to exclude distant metastatic disease, where the management will almost always be palliative.

IV contrast CT scan has accuracy in predicting tumour respectability of 60%. It has shown to be very useful in detecting hepatic, pulmonary and adrenal metastasis, but less so in assessing local disease and lymph node involvement in upper GI cancer. It is particularly less effective in distal third of oesophagus due to motion artefact from surrounding heart, diaphragm and lungs. It is also limited in assessing the depth of tumour invasion.

Compared to structural changes seen in most imaging modalities like IV contrast CT scan, MRI scan or EUS, PET-CT scan using FDG utilises physiological variance seen with neoplasms where there is increased glucose uptake compared to normal tissues. There have been limited studies published on the impact of PET-CT scan in the management of upper GI cancer. Indeed, not all centres utilise routine PET-CT scan as part of the staging of UGI cancer.

Our baseline participants are comparable to a UK study by Blencowe et al. In our study, PET-CT scan influenced management in 27.8% of patients. Blencowe et al, in a dataset combining oesophageal and gastric cancers, found that PET-CT scan influenced management in 38% of patients, but their database did not include pancreatic, biliary and gall bladder carcinomas.

In our study of 79 patients, 75% had an IV contrast CT scan that did not show any evidence of distant metastatic disease or other abnormal areas of concern. Despite this, PET-CT scan showed lesions in over 23% that needed further investigation, with 14% showing metastatic disease, which is comparable to Blencowe et al (18%).

Of the 25% of patients in our study with indeterminate lesions, 40% had change in management due to PET-CT scan, with 35% of patients showing metastatic disease. This suggests that PET-CT scan is more crucial in the presence of intermediate lesions on IV Contrast CT scan. Of the eight patients with intermediate lesions on IV contrast CT scan, six had PET-CT showing distant disease which did not correspond to the lesions seen on the IV contrast CT scan.

In our series, oesophageal cancer formed the largest histopathologic diagnostic group (57 out of 79, 72%), of which over 60% were in the lower oesophagus. PET-CT scan influenced management in these patients in 31.6%, with metastatic disease in 21%. This is comparable to previous studies suggesting 14–25%.

PET-CT influenced gastric cancer patients in 25%, with 12.5% showing distant disease not seen on IV contrast CT scan. Use of PET-CT in gastric cancer remains controversial with limited evidence on its usefulness. A study by Hur et al compared 142 patients with PET-CT scan and their surgical diagnosis to predict curability of the disease. A further study by Mukai et al, with 62 gastric cancer patients, investigated tumour size and nodal involvement. However, these studies did not comment on the proportions of positive PET-CT with a negative IV contrast CT scan. Similar influence of PET-CT was seen on pancreatic cancer, where one patient (12.5%) had metastatic disease with IV contrast CT showing no evidence of distant disease. Our database only included four GOJ cancers, one gallbladder cancer, and one cholangiocarcinoma, so no conclusions can be drawn regarding the impact of PET CT scan for these diagnoses.

Of our patients with PET-CT scan suspicious of distant metastatic disease, two patients deserve special mention. One patient had a focal avid area in the vocal cord, while another had a right gluteal avid lesion (the latter was subsequently shown to be metastatic adenocarcinoma on percutaneous core biopsy). These lesions would have been out of the conventional IV contrast CT ‘scanning zone’. This illustrates the rare distant metastatic sites that PET-CT scan can detect.

There were four patients (5.1%) where IV contrast CT scan showed no definite distant
metastatic disease, but PET-CT showed large bowel lesions needing colonoscopies. Even though two of these patients had a benign process, we included them as a change in management because scheduling of the colonoscopy interrupted the conventional management pathway for the upper GI cancer. Furthermore, two of the patients had an asymptomatic sigmoid adenocarcinoma, which would have been undetected without the PET-CT scan, until it presented clinically.

There were three other patients that had other lesions requiring further investigations. One patient had a PET-CT scan suspicious of a hepatic metastasis. He underwent an MRI scan and a laparoscopy, with a final diagnosis of hepatic haemangioma. One patient had a PET-CT scan suggesting an adrenal lesion. Subsequent MRI scan showed an abnormal lymph node corresponding to the lesion on PET-CT scan. This was resected during the oesophagectomy with the final histology not showing any evidence of malignancy. The final patient had a PET-CT scan showing an avid retroportal lymph node. Subsequent laparoscopic lymph node excision showed granulomatous lymphadenitis. The presence of granulomatous changes causing a false positive PET-CT scan has been previously described. Our false positives included five patients with benign processes out of the 22 patients (22.8%), with PET-CT suggesting distant disease. This is slightly higher compared to previous studies suggesting false positive rates of 10–18%,.

There were two patients in our series who had IV contrast CT and PET-CT scan that showed no evidence of distant metastatic disease. These patients underwent a staging laparoscopy which showed biopsy confirmed hepatic metastasis. Thus, we had a false negative rate for distant metastatic disease of 4.4%. Previous studies have shown variable sensitivities with PET-CT to be ranging between 72–100%.

Our study has several limitations. Our patient numbers are small, as with most studies on this subject. Statistical analysis was not possible as this is a descriptive study. Our definition of ‘influencing management’ was different to that of other studies, and our ‘without PET-CT scan’ management plan may differ from that of other centres. We included synchronous tumours and benign processes (false positives) in ‘influencing management’ group as they have resulted in investigations and treatments delaying curative surgery of the UGI cancer. Even though it may have not changed management of the UGI cancer, it has influenced the management of the patient. We have, however, also provided the proportions of patients with PET-CT showing distant disease, which would be more clinically relevant to some clinicians. Oesophageal cancer formed the majority of our patients followed by gastric and pancreatic cancer. Therefore our results would be best applied to these patients and extrapolation to other malignancies should be made with caution.

Use of PET-CT in gastric and pancreatic cancer remains controversial due to limited evidence, as was the case in our study due to small numbers. An unquantifiable number of patients with obstructive gastric cancers were not referred for PET-CT scan and underwent acute surgical resections. Therefore, our database is potentially an underestimate of the true incidence of gastric cancer in our treatment area.

**Conclusion**

PET-CT scan influences management in over one-quarter (27.8%) of patients with UGI cancer and shows distant disease not seen on IV contrast CT scan in 22.8%. PET-CT has a larger effect when IV contrast CT scan shows indeterminate lesions (from 27.8% to 40%). Our study confirms the value of PET-CT scan in the treatment staging of oesophageal cancer. There is some evidence of its usefulness in gastric and pancreatic cancer, but more numbers are required to shed light on this. We cannot comment on the usefulness of PET-CT scan in gallbladder cancer and cholangiocarcinoma as our study database had very few patients with this diagnosis.
REFERENCES:


