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Contribution of FDG-PET/CT to the management of esophageal cancer patients at multidisciplinary tumor board conferences

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ABSTRACT

Background: A multidisciplinary team approach to the management of esophageal cancer patients leads to better clinical decisions.

Purpose: The contribution of CT, endoscopic and laparoscopic ultrasound to clinical staging and treatment selection by multidisciplinary tumor boards (MTB) in patients with esophageal cancer is well documented. However, there is a paucity of data addressing the role that FDG-PET/CT (PET/CT) plays to inform the clinical decision-making process at MTB conferences. The aim of this study was to assess the impact and contribution of PET/CT to clinical management decisions and to the plan of care for esophageal cancer patients at the MTB conferences held at our institution.

Materials and methods: This IRB approved study included all the cases discussed in the esophageal MTB meetings over a year period. The information contributed by PET/CT to MTB decision making was grouped into four categories. *Category I*, no additional information provided for clinical management; *category II*, equivocal and misguiding information; *category III*, complementary information to other imaging modalities, and *category IV*, information that directly changed clinical management. The overall impact on management was assessed retrospectively from prospectively discussed clinical histories, imaging, histopathology, and the official minutes of the MTB conferences.

Results: 79 patients (61 males and 18 females; median age, 61 years, range, 33–86) with esophageal cancer (53 adenocarcinomas and 26 squamous cell carcinomas) were included. The contribution of PET/CT-derived information was as follows: *category I* in 50 patients (63%); *category II* in 3 patients (4%); *category III* in 8 patients (10%), and *category IV* information in 18 patients (23%). Forty-five patients (57%) had systemic disease, and in 5 (11%) of these, metastatic disease was only detected by PET/CT. In addition, PET/CT detected previously unknown recurrence in 4 (9%) of 43 patients. In summary, PET/CT provided clinically useful information to guide management in 26 of 79 esophageal cancer patients (33%) discussed at the MTB.

Conclusion: The study showed that PET/CT provided additional information and changed clinical management in 1 out of 3 (33%) esophageal cancer cases discussed at MTB conferences. These results support the inclusion whenever available, of FDG-PET/CT imaging information to augment and improve the patient management decision process in MTB conferences.

1. Introduction

It is estimated that 18,440 people will be diagnosed with esophageal cancer and 16,170 will die from it in 2020 [1]. This malignancy represents 1% of all new cancer cases in United States and is 4.3 times more common in males than females. Eighty-percent of esophageal cancer cases occur in patients between the ages of 55 and 84 [2].

The overall 5-year survival rate is less than 20%, and it is determined

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by the stage at initial diagnosis. Early esophageal cancer has 5-year survival rates ranging from 57%–78%, with locally advanced disease carrying poor prognosis despite aggressive therapy. Therefore, accurate pre-operative staging is paramount, as it helps guide management and avoids unnecessary surgery. In patients with locoregional advanced disease chemoradiation followed by surgery is the curative treatment of choice. Thus, except for patients at very early stages of the disease, the rest are typically managed using a multidisciplinary tumor board (MTB) approach. Our MTB conferences are held once a week and they are attended by specialists from medical oncology, radiation oncology, thoracic surgery, radiology, gastroenterology, pathology, and clinical nurse specialists.

As with all other cancer types, staging is the basis for esophageal cancer management, and it is a critical component in the initial workup for every esophageal cancer patient. Computed Tomography (CT) has been the first line imaging modality for staging esophageal cancer; however endoscopic ultrasound, laparoscopy with and without ultrasound, FDG-PET and now PET/CT, each with their individual strengths and limitations, contribute to improving pre-operative clinical staging in these patients [3–11]. During the case discussions at our MTB conferences regarding the contributions from various imaging modalities to the management decisions of esophageal cancer patients, it became evident that FDG-PET/CT added important information about the diagnosis, staging and follow-up of these patients.

Other groups have investigated the influence of the MTB on the accuracy of clinical staging and treatment selection for patients with gastro-esophageal cancer using information from CT, endoscopic ultrasound and laparoscopic ultrasound [12–16]. However, to the best of our knowledge, there is a paucity of data specifically addressing the role that FDG-PET/CT plays to inform the clinical decision-making process at MTB conferences [17,18]. Therefore, the aim of this study was to assess the impact and contribution of FDG-PET/CT to the clinical management decisions and to the plan of care prescribed for esophageal cancer patients at the weekly multidisciplinary tumor board conferences held at our institution.

2. Materials and methods

This study was performed as a part of a clinical quality assessment and improvement initiative pertaining to the multidisciplinary esophageal cancer conference. The study was approved by the Institutional Review Board (IRB) to include all the cases discussed in the esophageal MTB meetings over a year period. Informed consent was waived due to the retrospective nature of the study. For a case to be included in the study the FDG-PET/CT exams had to be performed within 3 months prior to the MTB conference, and images had to be available for full interpretation during the conference. On the other hand, follow-up cases that had been discussed for the second or third time were excluded.

The type and quality of information contributed by FDG-PET/CT to MTB decision making was grouped into four categories, as follows: *category I*, no additional information provided for clinical management; *category II*, equivocal and misguiding information for management; *category III*, additional and complementary information to other imaging modalities that reinforced the MTB recommended treatment for the patient, and *category IV*, information that directly changed clinical management recommendations by the MTB.

The overall impact on management was assessed retrospectively from prospectively discussed information that consisted of clinical history, PET/CT images and their corresponding reports, conventional morphologic images and their results (e.g., CT; endoscopic US), histopathology information, and the official minutes of the MTB conferences.

3. Results

A total of 122 patients with biopsy proven esophageal cancer were discussed in the MTB conferences between January 2019 and February 2020. Among these, 43 cases were excluded (7 were follow-up cases; 31 cases did not have PET/CT scans; 4 cases had a PET/CT obtained more than 3 months prior to the MTB meeting, and in one case the PET/CT images were unavailable). Thus, a total of 79 patients (61 males and 18 females; median age, 61 years, range, 33–86) with histologically confirmed esophageal cancer (53 adenocarcinomas and 26 squamous cell carcinomas) were included in the study (Table 1). Thirty-six patients were discussed at the MTB at their initial diagnosis and forty-three for recurrent disease. Fifty-three out of 79 patients (67%) had their PET/CT scans acquired at our institution and 26 (33%) at other hospitals.

The contribution of FDG-PET/CT-derived information to the surgical and clinical management of the study cohort was as follows: *category I* information in 50 patients (63%); *category II* information in 3 patients (4%); *category III* in 8 patients (10%), and *category IV* information in 18 patients (23%) (Table 2). Forty-five patients (57%) had systemic disease, and in 5 (11%) of these, metastatic disease was only detected by PET/CT. In addition, FDG-PET detected previously unknown recurrence in 4 (9%) out of 43 patients in the recurrent disease group.

Thus, FDG-PET/CT provided clinically useful information to guide management in 26 of 79 esophageal cancer patients (33%) discussed at the MTB (Table 2).

Table 3 lists specific clinical examples per category of PET/CT-derived information. Amongst the eighteen *category IV* cases in which PET/CT findings changed management, were the detection of previously unknown mesenteric vessel involvement; previously unexpected organ based and distant FDG-avid nodes metastasis upstaging the disease (Fig. 1); the detection of a highly FDG-avid concurrent lung cancer, which required further investigation and was later confirmed histopathologically; confirmation of vascular structure involvement that precluded surgery (Fig. 2); detection of previously unknown recurrence at surgical and distant sites; ruled out recurrent disease at site of post-surgical inflammation. Examples of *category III* cases that provided complementary information to guide management included: a highly FDG-avid, previously unknown, concurrent prostate cancer that did not affect the course of the patient's esophageal cancer treatment (Fig. 3); PET findings consistent with locally advanced esophageal malignancy concurrent with an anatomo-metabolic pattern of sarcoidosis, which was confirmed after a right paratracheal node biopsy; a reduction in FDG uptake at a site of known esophageal cancer recurrence confirming partial metabolic response to treatment, and exclusion of recurrent disease based on the lack of FDG uptake in an indeterminate CT finding in an area of post-surgical anatomic distortion. The three *category II* cases with equivocal information that misguided management included: malignant pleural disease not identified in FDG-PET/CT that was later confirmed at surgery; an FDG-avid esophageal lesion interpreted as an esophageal primary that was histologically proven to be a Schwannoma, and lastly, a concurrent distal lesion to the esophageal primary with PET/CT pattern of inflammation, but subsequent surgery revealed a second focus of esophageal malignancy. In the 50 patients with PET/CT-derived information classified as *category I,* the anatomo-metabolic imaging findings did not add any new information to what was already known.

4. Discussion

The results of this study highlight the contribution of FDG-PET/CT-derived information to clinical decision-making for esophageal cancer patients discussed at our multidisciplinary tumor board conferences (MTB). The study showed that FDG-PET/CT provided additional information and changed clinical management in 26 of 79 (33%) patients with esophageal cancer discussed at the MTB. Moreover, PET/CT detected previously unknown vascular invasion in two patients; organ and distant nodal metastases not apparent on conventional imaging in nine patients, and previously unknown recurrence in four.

A high percentage of patients diagnosed with esophageal cancer present with locoregionally advanced disease and have poor prognosis

Table 1
Flow chart showing patient selection.

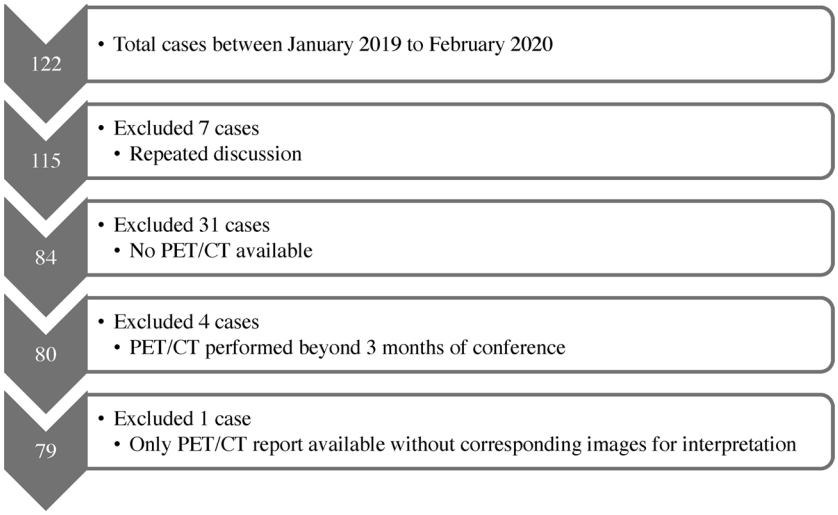

Table 2
Categories of FDG-PET/CT-derived information.

Category	Type of PET/CT-Derived Information	Number of Cases (%)
1	No additional information	50 (63%)
2	Equivocal/misguiding information	3 (4%)
3	Additional and complementary information clarifying indeterminate findings by other imaging modalities	8 (10%)
4	Information that directly changed clinical management recommendations by the MTB	18 (23%)

MTB: Multidisciplinary Tumor Board.

Table 3
Clinical examples per category of PET/CT-derived information.

Category		PET/CT
1	No additional information	
2	Equivocal/misguiding information	- Pleural disease not visualized on PET/CT, and confirmed at surgery - Esophageal lesion positive in PET that turned out to be Schwannoma - Concurrent distal lesion apart from primary interpreted as inflammation in PET/CT, and confirmed as a second focus of malignancy during surgery
3	Additional and complementary information	- Detection of incidental concurrent malignancy not affecting course of treatment of the patient's esophageal cancer - PET metabolic pattern of sarcoidosis concurrent with esophageal cancer - Change of FDG avidity in suspected recurrence confirming treatment response
4	Direct impact on management	- Mesenteric involvement - Unknown recurrence at surgical and distant sites - Distant metastasis - Concurrent malignancy having significant effect on course of esophageal cancer treatment - Additional locoregional and distant avid nodes upstaging the disease - Vascular structure involvement precluding surgery - Ruled out recurrence disease in post-surgical inflammatory focus

despite aggressive therapy. Therefore, to improve surgical outcomes, a systematic collaborative effort by experts is essential for precise staging and to guide informed and individualized aggressive treatment for those with curable disease.

Accordingly, a multidisciplinary team approach to the management of esophageal cancer has been shown to lead to better clinical decisions resulting from well-informed and personalized treatment plans that improve clinical outcomes [12–16]. Meguid et al. [13] evaluated the outcomes of 1,747 patients with various gastrointestinal malignancies treated based on recommendations of their multidisciplinary program. They reported a change in diagnosis in 13% and a change in management in 20% of the 406 patients identified with either esophageal or gastric cancer in their cohort. In our experience, one added benefit of the MTB worth emphasizing is that it creates an open forum of experts that weighs in on each case and considers the complete clinical context to include the strengths and limitations of different imaging modalities. EUS, CT and MRI with their superior anatomic information and PET/CT with its anatomo-metabolic global landscape.

The initial staging of esophageal cancers is usually done with endoscopic ultrasound (EUS) in combination with CT of the chest, abdomen and pelvis. EUS is considered the imaging modality of choice to assess T stage (3–5). However, EUS can be unreliable for staging after chemoradiation due to therapy related inflammatory changes or fibrosis [19,20]. Severe stenosis due to tumor can block the passage of the endoscope and depth of penetration of EUS maybe insufficient for finite staging of large tumors. Therefore, computed tomography (CT) of the chest, abdomen, and pelvis serves as a complementary modality to assess the extent of locoregional disease and to look for the presence of systemic disease.

The value FDG-PET imaging is based on its ability to interrogate tumoral biologic behavior as opposed to just lesion size and shape. Hybrid PET/CT imaging takes advantage of the greater anatomical detail provided by CT coupled with the molecular-metabolic phenotype of the PET findings in one whole body pass. In this manner, the fused anatomo-metabolic image overcomes the limitations of either PET or CT images alone.

FDG-PET/CT imaging of esophageal cancer has proven to be superior to other imaging modalities to interrogate the extent of disease. It improves the non-invasive characterization of esophageal lesions; the guidance of biopsy to metabolically active masses minimizing sampling errors; the detection of distant metastatic disease and recurrence; the assessment of the anatomo-metabolic tumoral response to cancer therapy, and finally, tumor FDG uptake is a biomarker of prognosis [7–10, 21–30].

FDG-PET/CT imaging is more accurate than conventional imaging modalities for the detection of non-regional hematogenous and lymphatic metastases from esophageal cancer [27]. In fact, unnecessary

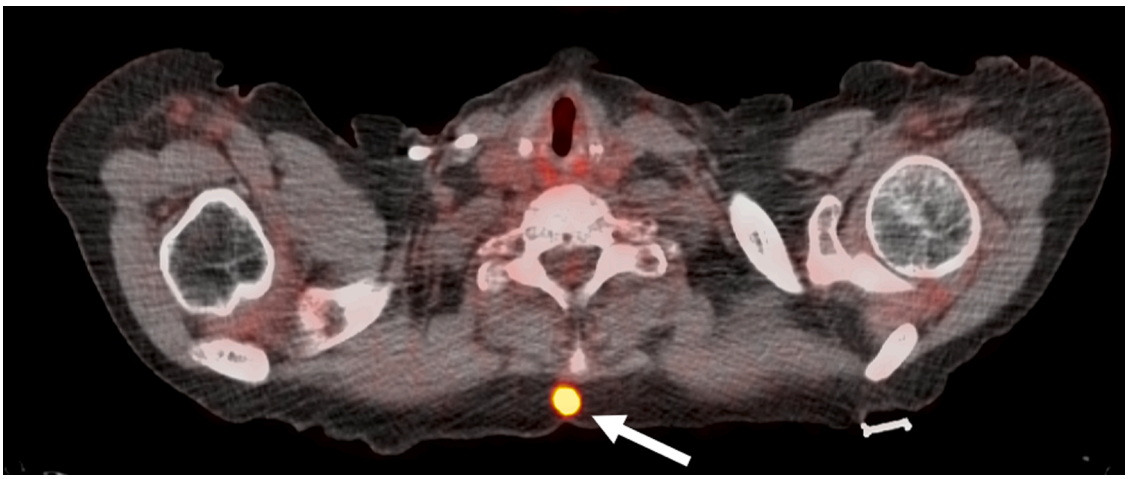

Fig. 1. Axial fused PET/CT image of 56-year-old male showing an FDG avid nodule in the posterior chest wall subcutaneous tissue consistent with metastatic disease (arrow).

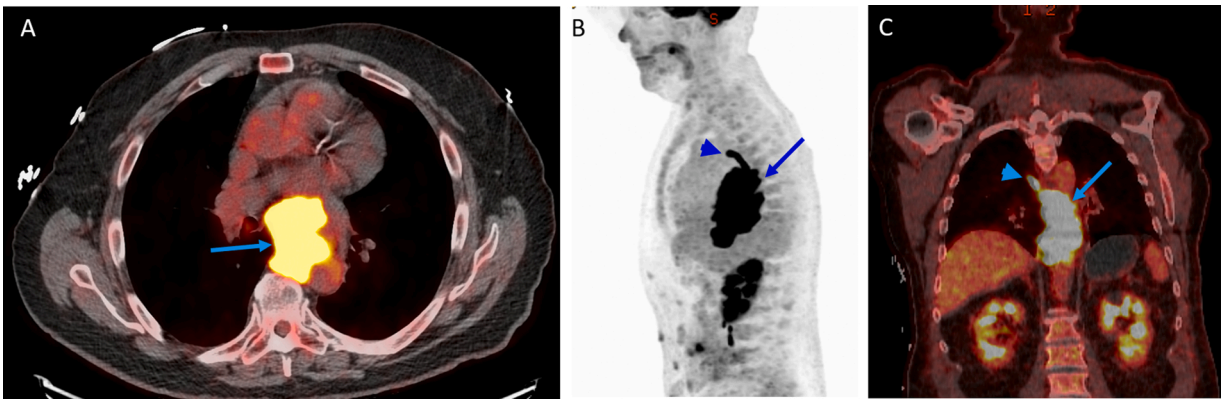

Fig. 2. A) Axial fused PET/CT image of 73-year-old male showing a highly FDG avid mass in the mid esophagus consistent with known malignancy (arrow). B) Sagittal FDG-PET and C) coronal fused PET/CT images showing esophageal malignancy (arrows) extending into the azygous vein (arrow head).

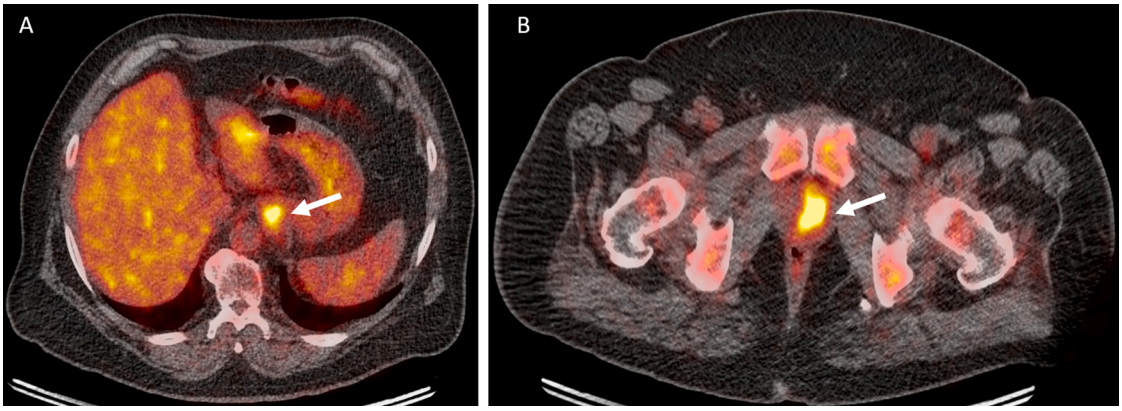

Fig. 3. A) Axial fused PET/CT image of 61-year-old male with an FDG avid mass at the gastro-esophageal junction (arrow) consistent with known malignancy. B) Axial fused PET/CT image of same patient showing FDG avid focus in the prostate gland (arrow), which was confirmed histologically to be prostate cancer.

surgery can be avoided after PET/CT mainly because of detection of occult distant metastases [28,29,31]. Our results showed just that. FDG-PET/CT detected distant metastases in 5 patients who were initially considered to have resectable disease by conventional staging, changing their management from curative to palliative. Another advantage of PET/CT imaging that we observed, was the identification of distant metastases in lymph nodes that were not pathologically enlarged, and the detection of previously unknown vascular invasion.

Our results are comparable to those of other investigators in the United Kingdom that investigated the value of PET information to guide MTB decisions. Blencow and colleagues [17] studied newly diagnosed esophageal cancer patients selected for radical treatment without CT evidence of systemic metastases. They analyzed the influence of PET/CT on multidisciplinary team decision making by confirming whether the

PET/CT findings were congruent with CT findings of M0 disease or whether the PET/CT showed unsuspected M1 disease. The investigators found that PET/CT imaging results confirmed CT findings in 61.8% of patients. On the other hand, PET/CT results changed multidisciplinary team decisions in 38.2% of their cohort by detecting unknown systemic metastases and by disproving CT findings that were suspicions of systemic disease. Moreover, PET/CT prevented 19.7% of patients from curative treatment due to the detection of metastatic disease otherwise missed by CT [17].

Similarly, Berrisford and co-investigators [18] reported that in 6 of 50 (12%) patients discussed in their MTB conferences, unnecessary surgery was avoided due to stage IV disease being detected by PET/CT and missed by other staging modalities.

The anatomic distortion following esophageal cancer treatment makes it difficult to differentiate scar tissue from viable tumor recurrence using anatomical imaging alone. These modalities often encounter indeterminate findings when attempting to characterize the presence of esophageal cancer recurrence in the post-treatment phase. Our results showed that FDG-PET/CT imaging has advantages in this setting. PET clarified CT findings that were indeterminate or suspicious for local and distant recurrent disease, providing additional information in 9% of the cases with recurrent disease, allowing for prompt decision making at the MTB.

PET/CT improved the accuracy of staging and restaging compared with CT and EUS alone, but one important benefit worth emphasizing, was that the well-rounded assessment of the whole clinical picture by the expert MTB members, was without a doubt, the main driver of superior, more efficient and effective clinical decision making for all patients being discussed.

The main limitation of this study is its small number of patients; however, its main strength is that the MTB decision process was always based on clinical information coupled with results of all imaging modalities for the entire cohort. Another important limitation is that histological confirmation was not obtained in a few cases in which PET/CT showed metastatic or recurrent disease that was undetected by other imaging modalities. However, in these cases the PET/CT pattern of the findings was indisputably malignant, and therefore, assumed accurate, and clinical follow up confirmed that the change in MTB recommendations was in fact correct.

5. Conclusion

This study showed that FDG-PET/CT contributes important clinical value by providing additional information and changing clinical management in one out of three esophageal cancer cases (33%) discussed at multidisciplinary tumor board conferences. These results support the inclusion whenever available, of FDG-PET/CT imaging information to help augment and improve the patient management decision process in multidisciplinary tumor board conferences.

Declaration of Competing Interest

The uploaded manuscript entitled “Contribution of FDG-PET/CT to the Management of Esophageal Cancer Patients at Multidisciplinary Tumor Board Conferences” has been read and approved by all authors, who attest not to have any conflict of interests or financial disclosures to make.

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