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The impact of FDG-PET/CT in the management of patients with vulvar and vaginal cancer

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Abstract

OBJECTIVES—To evaluate the changes in prognostic impression and patient management following PET/CT in patients with vulvar and vaginal carcinoma; and to compare PET/CT findings with those of conventional imaging modalities.

METHODS—We summarized prospectively and retrospectively collected data for 50 consecutive patients from our institution that enrolled in the National Oncologic PET Registry and underwent FDG-PET/CT for a suspected or known primary or recurrent vulvar/vaginal cancer.

RESULTS—54/83 (65%) studies included had a diagnosis of vulvar cancer, and the remaining 29/83 (35%), a diagnosis of vaginal cancer.

Following FDG-PET/CT, the physician's prognostic impression changed in 51% of cases. A change in patient management, defined as a change to/from a non-interventional strategy (observation or additional imaging), to/from an interventional strategy (biopsy or treatment), was documented in 36% of studies. The electronic records demonstrated that 95% of the management strategies recorded in the physician questionnaires were implemented as planned.

MRI and/or CT were performed within one month of the FDG-PET/CT in 20/83 (24%) and 28/83 (34%) cases, respectively. FDG-PET/CT detected nodes suspicious for metastases on 29/83 (35%) studies performed. MRI and CT detected positive nodes on 6 and 11 studies respectively. Distant metastases were identified in 10 cases imaged with FDG-PET and 5 cases that had additional conventional CT imaging. All suspicious lesions seen on CT were positively identified on PET/CT. In 4 cases, an abnormality identified on PET/CT, was not seen on diagnostic CT.

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CONCLUSIONS—FDG-PET/CT may play an important role in the management of vulvar and vaginal carcinoma.

INTRODUCTION

Fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) is being increasingly utilized for the assessment of gynecologic cancers. Its theoretical advantage lies in the ability to depict metabolically active tissue that may be present in the absence of definite structural abnormalities detected with conventional imaging, including CT and magnetic resonance imaging (MRI). Most of the evidence supporting the use of PET/CT in gynecologic cancers is derived from the ovarian and cervical cancer literature. In cervical cancer, PET/CT has been found to be a useful tool for detecting nodal disease, pelvic sidewall invasion and distant metastases beyond the true pelvis [1, 2, 3]. In ovarian cancer, PET/CT appears to be most valuable in detecting recurrence, tumor on the ovarian surface and extension and/or implants on the uterus [4, 5].

Several studies have examined change in patient management following PET imaging, with frequencies ranging from 30% to 40% [6, 7–9]. Some of the largest and most comprehensive data has subsequently come from the National Oncologic PET Registry (NOPR), which was designed to collect imaging, clinical and demographic data on several cancers (both gynecologic and non gynecologic primaries); and which ultimately enabled the Center for Medicare and Medicaid Services to expand PET coverage to include cancers not previously covered [6]. The NOPR data published in 2008 demonstrated that intended patient management changed following PET/CT imaging, in 41.4 % of patients with ovarian cancer, 36.5% with uterine cancer and in 32.7% with cervical cancer [10]. Subsequently, the National Comprehensive Cancer Network (NCCN) amended their recommendation for pretreatment assessment of cervical cancer, to include PET/CT imaging for patients with clinical stage 1B2 or higher [11].

Despite these encouraging reports in other gynecologic tumors, similar data on the role of PET/CT in the management of vulvar and vaginal cancer is sparse. There are a few reports suggesting that these tumors are FDG avid and that PET/CT can be used for staging them, however there is very little published data addressing the diagnostic impact of PET/CT in vulvar and vaginal cancers [12]. Thus, the purpose of this study was to evaluate the changes in prognostic impression and patient management following PET/CT in patients with vulvar and vaginal carcinoma; and to compare the PET/CT findings with those of conventional imaging modalities.

METHODS

The NOPR is a prospective data registry that collected information from a physician requesting a PET scan, and from the interpreting physician's PET report. The NOPR is managed by the American College of Radiology (ACR) through the American College of Radiology Imaging Network (ACRIN) in Philadelphia, PA. All NOPR data was entered by participating PET facilities via a secure Web-based interface. A NOPR Working Group

composed of representatives from the Academy of Molecular Imaging, ACRIN, ACR, and the Center for Statistical Sciences at Brown University directed the research operations [6].

We summarized prospectively and retrospectively collected data for 50 consecutive patients from our institution who enrolled in the National Oncologic PET Registry and underwent FDG-PET/CT for a suspected or known primary or recurrent vulvar/vaginal cancer. Seventeen patients were referred for more than one FDG-PET/CT scan during the research period. Each scan was assigned an individual study number. In total, 83 imaging studies were included. All FDG-PET/CT scans performed had a pre and post-test intended management questionnaire completed by the referring physician. In each post-test questionnaire, the physician was asked to document their revised patient prognostic impression based on clinical stage and performance status in view of the imaging findings ('worse', 'no change', or 'better'). Subsequent to this, the physician was asked to record any change in intended patient management, and was given four options to classify the change 1. Observation, 2. Additional imaging, 3. Biopsy, or 4. Treatment.

The primary outcome measure evaluated the impact of PET/CT imaging, specifically any change in physician prognostic impression and subsequent change in patient management pre and post-FDG-PET/CT. A change in management was defined as a change to/from a non-interventional strategy (observation or additional imaging), to/from an interventional strategy (biopsy or treatment). This data was collected prospectively through questionnaires completed at the time the imaging studies were performed.

The secondary outcome measure looked at the implementation of the intended management plan following imaging. The questionnaire results were retrospectively correlated with our institution's electronic patient records, to assess whether the continuation or change in management documented by the physician had been executed in accordance with the questionnaire results.

The third outcome measure retrospectively correlated the FDG-PET/CT results with conventional imaging modalities including CT and MRI performed as standard of care. All CT or MRI scans performed within one month of the FDG-PET/CT were reviewed. An experienced radiologist reviewed all imaging and recorded the findings identified by each imaging modality, to evaluate the utility of FDG-PET/CT in addition to conventional CT and MRI imaging.

The study was HIPAA compliant; all patients provided written informed consent for their data to be included in NOPR, and our Institutional Review Board approved the retrospective component of our study with a waiver of informed consent.

RESULTS

54/83 (65%) studies included had a diagnosis of vulvar cancer, and the remaining 29/83 (35%), a diagnosis of vaginal cancer. 89% of all cases were histologically proven squamous cell cancers [Table 1].

Impact of FDG-PET/CT

Following FDG-PET/CT, the physician's prognostic impression changed in 29/54 (54%) cases of vulvar cancer, and 13/29 (45%) of vaginal cancer [Table 2]. A change in patient management, defined as a change to/from a non-interventional strategy (observation or additional imaging), to/from an interventional strategy (biopsy or treatment), was documented in 30/83 (36%) of studies from patients with primary or recurrent vulvar and vaginal cancer [Table 3].

Implementation of intended management following FDG-PET/CT

On review of the electronic clinical records, the physician's management plans recorded following PET/CT imaging could be clearly identified in 78/83 (94%) of cases. In the remaining 5 cases, the patients transferred their care to a different institution, resulting in insufficient clinical data for evaluation of subsequent management. The electronic records demonstrated that 74/78 (95%) of the management strategies recorded in the physician questionnaires were implemented as planned.

FDG-PET/CT in additional to conventional imaging

MRI and/or CT were performed within one month of the FDG-PET/CT in 20/83 (24%) and 28/83 (34%) cases, respectively. 19/20 MRI scans were limited to pelvic imaging for local staging; 1/20 MRIs also included the abdomen, whereas the 23/28 CT scans covered the chest, abdomen and pelvis to evaluate distant disease spread.

FDG-PET/CT detected nodes suspicious for metastases on 29/83 (35%) studies performed. MRI and CT detected positive nodes on 6 and 11 studies respectively [Table 4]. Distant metastases (suspicious lung nodules, adrenal nodule and abdominal wall deposit) were identified in 10 cases imaged with FDG-PET and 5 cases who had additional conventional CT imaging (suspicious lung nodules, abdominal wall deposit). All suspicious lesions seen on CT were positively identified on PET/CT.

A number of abnormalities were identified on both FDG-PET/CT and conventional imaging (MRI and CT), as detailed in Table 5. In 4 cases, an abnormality identified on PET/CT, was not seen on diagnostic CT. One patient was noted to have nodular hypermetabolic adrenal glands suspicious for early metastases on FDG-PET. An adrenal protocol scan was advised, however the patient developed biopsy-proven lung metastases. The patient declined further intervention, abating the requirement for adrenal specific imaging. A second patient was found to have a perianal fistula, not clearly identified on CT but highlighted by abnormal FDG accumulation on PET/CT. The diagnosis was clinically confirmed and no additional imaging was performed. The remaining two findings seen solely on FDG-PET/CT included hypermetabolic thoracic nodes and a focal area of increased FDG uptake in the stomach, both considered reactive/inflammatory in etiology.

All cancer related findings on CT and MRI were visualized on FDG-PET/CT. However, in addition one patient was found to have a rectal fistula seen on CT and MRI, and a second patient was diagnosed with pancreatic cysts and proctocolitis on CT.

37 of the study cases had FDG-PET/CT imaging only. 38 focal abnormalities were identified on 35/37 (95%) of the scans [Table 6]. Specifically, PET/CT identified lung nodules on 3 scans, and a bony lesion on 1 scan, highly suspicious for distant metastases. 2 further studies identified significant incidental findings including a calcified falx cerebri meningioma in one patient, and enlarged subpectoral nodes in a second. Subsequent investigation of the latter revealed histologically proven moderately differentiated invasive ductal breast carcinoma.

One patient had biopsy-proven well-differentiated invasive squamous cell recurrent vulvar cancer (left 2, 3 and 5 o'clock) which was not identified on either FDG-PET/CT or pelvic MRI; however interpretation by the PET/CT was limited by surface contamination.

DISCUSSION

In this study, we found that FDG-PET/CT may play an important role in the management of vulvar and vaginal carcinoma. Using PET/CT for the assessment of suspected or known disease (primary or recurrent), we report a change in prognostic impression and intended patient management, in 51% and 36% of studies performed respectively. We also found that the intended change in management was implemented in the majority of patients.

Several studies have suggested that FDG-PET/CT is useful for detecting nodal and distant metastases in vulvar and vaginal cancer [13, 14]. Cohn et al [15] found that PET-CT had a sensitivity of 80%, specificity of 90%, and a positive predictive value of 80% in identifying vulvar cancer lymph node metastases. It was postulated that given the high specificity of PET/CT, a positive study could be used to locate metastatic nodes and assess response to radiation prior to groin dissection. Furthermore, identification of positive pelvic nodes on PET-CT may allow a patient to avoid extensive surgery, and be treated alternatively with chemoradiation [16].

A high specificity was also reported in a recent study correlating PET-CT with histologically proven vulvar cancer metastatic groin nodes. Kamran et al reported a sensitivity of 50%, a specificity of 100%, a positive predictive value (PPV) of 100%, and a negative predictive value (NPV) of 57.1%. The high PPV supports the notion that FDG-PET could be used prior to surgical staging in patients with Stage III disease; however, the poor sensitivity makes the test unsuitable as a substitute for staging lymphadenectomy [17]. In our study, a patient with primary vulvar carcinoma was found to have a morphologically abnormal para-aortic lymph node on pelvic MRI. This node was also noted to be enlarged on anatomical imaging of the PET/CT, however in contrast to further pelvic adenopathy, did not demonstrated FDG avidity. In view of the widespread nodal disease, the patient did not proceed to biopsy and/or surgery; therefore no histopathological correlation could be made. Given the clinical context, the FDG-PET/CT was thought represent a true positive at a per patient level, however a false negative at lesional/nodal level.

Lin et al studied 23 women, who underwent PET (7 scans) or PET/CT (31 scans) imaging over an 8-year period, and found that PET can have a positive impact on patient management. However, false-positive (FP) lymph node or distant metastatic PET findings were found in 7/17 patients. The group identified one case in which a false-positive PET

resulted in an unnecessary pelvic lymph node dissection at surgery, and therefore may have negatively influenced patient management. On retrospective review of 5/7 false-positive cases, the group state that FP pelvic adenopathy most likely corresponded to urinary FDG excretion; and FP thoracic lymph node enlargement probably represented reactive adenopathy given the typical spread of vulvar cancer. They concluded that PET can have a positive impact, however should be interpreted with caution as false positive lymph node and distant metastasis findings are not uncommon [18].

Very few studies have reported on FDG-PET/CT in the staging of vaginal cancer. Lamoreaux et al demonstrated that FDG-PET detects the primary tumor and abnormal lymph nodes more often than conventional CT [19], however there are no reports looking specifically at combined PET/CT in the evaluation of metastatic disease.

In our study FDG-PET/CT identified nodal disease in 35% of patients imaged. Unfortunately the accuracy of PET/CT in the detection of nodal disease cannot be directly compared to that of conventional imaging, as only a subgroup of patients had additional MRI or whole-body CT scans. Furthermore, FDG-PET/CT identified distant metastases in 10 patients, and significant concomitant disease in 2 patients.

There are a number of limitations to our study. First, the definition of a change in patient management is subjective. We chose to use the implementation or cancellation of intervention as the threshold for change, however this does not take into account changes in medical management, which although not recorded are of importance in oncological care. The second major limitation of our study is the lack of comparative imaging tests in all cases. For ideal comparison, all patients would have undergone FDG-PET/CT and whole-body conventional CT imaging +-MRI, using histopathology data as the reference standard. The sensitivity, specificity, PPV and NPV of PET-CT could then be evaluated in the assessment of the primary tumor, nodal disease and distant metastases. However, CT and MRI were not required as part of NOPR, and therefore were only obtained at the discretion of the referring physician. The available evidence suggests that FDG-PET/CT may play an important role in the staging of both vulvar and vaginal cancer; however further studies are required to define this role.

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HIGHLIGHTS

- The role of FDG-PET/CT in the management of vulvar and vaginal cancer is sparse.
- Using FDG-PET/CT for the assessment of suspected or known disease (primary or recurrent).
- We report a change in prognostic impression & intended patient management, in 51% & 36% of studies performed respectively.
- FDG-PET/CT may play an important role in the management of vulvar and vaginal carcinoma.

Table 1

Vaginal and vulvar histopathology

Histopathology	Number
Squamous cell carcinoma vagina	22
Adenocarcinoma vagina	6
Serous vagina	1
Squamous cell carcinoma vulva	52
Adenocarcinoma vulva	2

Table 2

Change in physician’s prognostic impression

Table 3

Change in patient intended management plan post FDG-PET/CT

Pre-PET Plan	Post-PET Plan				
	Non-Treatment		Treatment		
	Image	Observe	Biopsy	Continue same treatment	Add/stop treatment modality *
Image	5	17	2	0	16 (Surgery initiated 11/16)
Observe	0	1	1	0	0
Biopsy	0	2	2	0	3
Treatment	0	9 (Surgery cancelled 4/9)	0	13 (Planned surgery continued 10/13)	12 (Surgery initiated 4/12; Supportive care 3/12)

* Treatment modalities include radiotherapy, chemotherapy, surgery or supportive care.

Table 4

Detection of nodes suspicious for metastases by modality

Nodal Group	FDG-PET/CT	MRI	CT
Inguinal	14/83 (17%)	3/20 (15%)	4/28 (14%)
Iliac	12/83 (14%)	2/20 (10%)	4/28 (14%)
Pelvic	2/83 (2%)	0/20 (0%)	1/28 (4%)
Para-aortic	0 [*] /83 (1%)	1/20 (5%)	1/28 (4%)
Thoracic	1/83 (1%)	0/20 (0%)	1/28 (4%)

^{*} Suspicious enlarged left para-aortic node on anatomical FDG-PET/CT imaging, however not FDG avid

Table 5

Pathology identified on FDG-PET/CT and conventional imaging (MRI or CT)

Number of patients	Abnormality	Identified on CT or MRI
PROBABLY BENIGN		
2	Pulmonary nodules	CT
3	Interstitial lung disease	CT
2	Benign hepatic lesion	CT
1	Benign renal lesion	CT
1	Hydronephrosis	MRI
2	Thyroid nodules	CT
2	Fracture or focal bony abnormality	CT and MRI
2	Likely inflammatory/stable pelvic nodule	CT
SUSPICIOUS FOR MALIGNANCY		
1	Primary mass/tumor	CT and MRI
4	Hypermetabolic lung nodules	CT
2	Abdominal soft tissue nodule	CT

Table 6

Pathology identified solely on FDG-PET/CT

Number of Patients	Abnormality on FDG-PET/CT	Additional conventional imaging? (including anatomical location of FDG- PET/CT abnormality)	Additional imaging modality
PROBABLY BENIGN			
11	Thyroid disease	0/11	n/a
4	Interstitial lung disease	0/4	n/a
1	Benign liver lesion	0/1	n/a
2	Benign renal lesion	0/2	n/a
5	Fracture or focal bony abnormality	0/5	n/a
1	FDG avidity stomach	1/1	CT
1	Perianal fistula	1/1	CT
4	Likely inflammatory/stable nodule	1/4	CT
SUSPICIOUS FOR MALIGNANCY			
1	Primary mass/tumor	0/1	n/a
1	Nodal recurrence	0/4	
1	Adrenal nodule	1/1	CT
3	Suspicious lung nodule	0/3	n/a
1	Suspicious osseous abnormality	0/1	n/a
1	Subpectoral lymph node enlargement suspicious for underlying breast carcinoma	0/1	n/a
1	Calcified meningioma falx cerebri	0/1	n/a