Quantitative Assessment of Gynecologic Malignancies

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KEYWORDS

• FDG • PET/CT • Standardized uptake value • Metabolic tumor volume • Total lesion glycolysis
• Gynecologic malignancies

KEY POINTS

- PET imaging for oncology has advanced rapidly in last couple of decades.
- The ability to image pathophysiologic processes much before there are discernible anatomic abnormalities makes it an ideal modality for imaging.
- The most important radiotracer used for the imaging is ^{18}F-fluorodeoxyglucose.

INTRODUCTION

PET imaging for oncology has advanced rapidly in last couple of decades. The ability to image pathophysiologic processes much before there are discernible anatomic abnormalities makes it an ideal modality for imaging. The most important radiotracer used for the imaging is ^{18}F-fluorodeoxyglucose (FDG). Evaluation of gynecologic malignancies with PET/computed tomography (CT) is an ongoing process and much of the significant work has been done with cervical, ovarian, and endometrial malignancies. FDG PET/CT scanning has been found to be superior to conventional imaging modalities in staging, restaging, and response assessment in many cases, with the additional advantage of quantifying tumor burden. However, the major limitation is the possibility of false-negative results, in some cases owing to high bladder activity secondary to predominant renal excretion of FDG. To overcome this limitation, some institutes follow the imaging protocol with a bladder catheter in situ. In this protocol, there remains the possibility of urinary activity interference. Besides this, the additional risk of urinary tract infection is also there. So, in our institute, postdiuretic images of the pelvis are taken separately after 3 to 4 times of voiding.

In this review, we discuss the role of PET as quantitative imaging in the assessment of gynecologic malignancies. Our discussion is limited to carcinomas of the cervix, endometrium, and ovary, because there is little literature regarding other gynecologic malignancies.

CERVICAL CANCER

Cervical cancer is the third most common malignancy affecting females, and is one of the leading causes of cancer-related death worldwide.[1] Major risk factors include human papilloma virus infection, an increased number of sexual partners, smoking, and early age of first coitus, with human papilloma virus infection exposure being most common. Clinically, patients complain of postcoital bleeding with menorrhagia and metrorrhagia

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being the most common signs. Cervical cancer is staged in accordance with International Federation of Gynecology and Obstetrics (FIGO) staging. Early stage disease (stages I and IIA) are treated with surgery, whereas advanced stages undergo radiation therapy or concurrent chemoradiotherapy. The most important prognostic factors include tumor size, parametrial invasion, and lymph nodal involvement, with lymph node metastases being the single most important prognostic factor.[2] Lymphatic spread of disease is more common than hematogenous spread, with common iliac and paraaortic lymph nodes being the most common draining stations. Hematogenous spread accounts for just 5% of the cases, and is most commonly to lungs, liver, and bone marrow.[3]

PET/Computed Tomography with ^{18}F-fluorodeoxyglucose in the Evaluation of Primary Lesions

Imaging modalities that play a crucial role in diagnosis and management planning include ultrasound (US), CT, MR imaging, and PET/CT scanning. For localization of the initial lesion in the cervix, MR imaging has been found to be superior owing to better soft tissue resolution among all the modalities. US examination, wither transrectal or transvaginal, can be of benefit in detecting parametrial and urinary bladder invasion, as well as in evaluation of hydronephrosis.[4,5] Various studies over the last few years have shown that FDG PET/CT scanning can have a deep impact ranging from pretreatment planning to response assessment to chemotherapeutic regimens.

MR imaging has been considered as the reference standard for evaluation of primary lesions in the cervix (T staging) because of better soft tissue contrast resolution, which can be superior in identification of parametrial extension and other adjacent soft tissue structures with greater accuracy.[6] PET/CT scanning usually has a role to play in the assessment of involved lymph nodes in cases of cervical cancer. The pattern of lymph node involvement includes pelvic, paraaortic, and then supraclavicular lymph node spread. FDG PET/CT scanning provides a noninvasive imaging modality for the assessment of lymph nodes in such cases and helps to prevent an unnecessary procedure of lymphadenectomy. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy to detect metastasis at the nodal level are 51.1%, 99.8%, 85.2%, 98.9%, and 98.7%, respectively, and 50%, 90.9%, 66.7%, 83.3% and 80.0%, respectively, at the patient level.[7] In another study by Leblanc and colleagues,[8] PET/CT scanning had a sensitivity, specificity, PPV, and NPV of 33.3%, 94.2%, 53.8%, and 87.5%, respectively, to detect microscopic lymph node metastasis in 125 locally advanced stage IB to IVA patients with cervical cancer who had a negative result on CT scanning and MR imaging. Similarly, in one of the other studies in 65 stage IB to IVA patients who had normal studies on morphologic imaging for paraaortic lymphadenopathy, the sensitivity, specificity, PPV, and NPV of PET/CT scans were 36%, 96%, 71%, and 83%, respectively.[9] PET/CT scanning has been shown to be more accurate than CT scanning and MR imaging for lymph nodal assessment; the accuracy for CT scanning and MR imaging is about 43% and 86%, respectively.[10–12] The low accuracy of CT scanning and MR imaging in detecting metastatic lymph nodes can be attributed to the fact that normal sized lymph nodes can contain micrometastatic disease and enlarged lymph nodes can be inflammatory in nature. However, the pooled sensitivity and specificity of PET/CT scanning for detecting metastatic lymph nodes at the patient level are 82% and 95%, respectively, and at the regional or nodal level 54% and 97%, respectively. Similarly, the pooled sensitivity and specificity for CT scanning at the patient level are 50% and 92%, respectively, and at the nodal level 52% and 92%, respectively, whereas those of MR imaging at the patient level are 56% and 91%, respectively, and at the nodal level 38% and 97%, respectively.[13] Left supraclavicular lymph node involvement has been found in about 5% of the patients with cervical cancer.[14] However, the frequency of left supraclavicular lymph node involvement ranges from 4% to 35% in patients with biopsy-proven paraaortic lymph node metastases.[15,16] The PPV of detecting abnormal supraclavicular lymph node metastases in patients with cervical cancer on FDG PET/CT scanning has been reported to be as high as 100%.[17] Using the metabolic semiquantitative functional imaging parameter, namely, the maximum standardized uptake value (SUV_{max}), FDG PET had a sensitivity, specificity, PPV, NPV, and accuracy of 74.4%, 78.6%, 95.5%, 33.3%, and 75%, respectively, to detect metastasis in supraclavicular lymph nodes with an SUV_{max} of greater than 3.[18] Apart from the SUV_{max}, a metabolic tumor volume (MTV) of less than 60 cm^3 in primary cervical lesions has been associated with better overall survival (OS) and progression-free survival (PFS) as compared with an MTV of greater than 60 cm^3.[19]

It has been observed that the serum squamous cell carcinoma antigen (SCC-Ag) had a statistically significant association with lymph node metastasis ($P = .0373$).[20] However, there was no correlation observed between the SUV_{max} of the