[18F]-2-Fluoro-2-Deoxy-D-glucose–PET Assessment of Cervical Cancer

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KEYWORDS

• Cervical cancer • PET/CT • PET/MR imaging • Cancer staging • Treatment planning

KEY POINTS

- PET/computed tomography is a highly valuable imaging modality in the assessment of patients with cervical cancer, providing prognostic and staging information.
- The metabolic parameters of the primary tumor (maximum standardized uptake value [SUVmax], metabolic tumor volume, and total lesion glycolysis) have been shown to correlate with patient outcome and survival.
- The presence of lymph node involvement and the SUVmax of the lymph nodes are significant prognostic factors.
- By combining metabolic imaging with the anatomic detail of the primary tumor, PET/MR imaging enhances treatment and care for patients with cervical cancer with a decreased radiation dose.

INTRODUCTION

According to the American Cancer Society, there will be 12,280 new diagnoses and 4210 deaths attributable to cervical cancer in 2017.[1] Worldwide, cervical cancer is the fourth most common cause of cancer, with a disease incidence of approximately 520,000 cases per year with 265,000 deaths.[2] In the Western world, most cancers are now diagnosed in the preclinical stage as a result of active screening with the Papanicolaou test. This screening has reduced the incidence of cervical cancer significantly by more than 50%. Additionally, human papilloma virus (HPV) has been found to be a causal factor, with HPV subtypes 16 and 18 a cause in 99% of cervical tumors.[3] The implementation of the HPV vaccine has decreased the disease incidence as well. Despite these measures, cervical cancer continues to be a major health issue worldwide.

The clinical staging system used worldwide is the International Federation of Gynecology and Obstetrics (FIGO). Where available, modalities such as computed tomography (CT), MR imaging, PET/CT, that provide anatomic and metabolic information are highly useful and impact patient therapy and treatment. The treatment of most stages of cervical cancer is chemoradiation, and imaging helps guide the treatment planning. The goal of this review is to provide evidence of the utility of PET imaging, primarily PET/CT, in the diagnosis, staging, treatment planning, and evaluation of tumor recurrence in patients with cervical cancer.

DETECTION

In the Western world, the use of active screening Papanicolaou testing in women aged 21 to 70 years allows early detection of preinvasive and early

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stage cancers (stage 1) before patients present with symptoms and findings on clinical examination. Symptomatic patients with more advanced tumors may present with postcoital bleeding, intermenstrual and postmenstrual bleeding, foul-smelling discharge, chronic anemia, and mass.[4]

Risk factors for cervical cancer include early age of sexual activity, genital warts, cigarette smoking, greater number of sexual partners, immunosuppression, human immunodeficiency virus positive status, and HPV infection serotypes 16 and 18. With the strong causal relationship between HPV and cervical cancer, patients older than 30 years have HPV testing at the time of a Papanicolaou test.[3]

PATHOLOGY

The World Health Organization histological classification includes squamous (epithelial), glandular (adenocarcinoma), and other epithelial tumors, such as adenosquamous, neuroendocrine, and undifferentiated carcinoma. Most cervical cancer cases are of squamous cell histology, accounting for 70% to 80% of cases. Adenocarcinoma histologies account for 20% to 25%.[5] The nonsquamous pathologies are associated with worse prognoses.[3]

STAGING

Cervical cancer first spreads locally to adjacent structures, such as the vagina, bladder, ureters, and rectum. Then, spread occurs via the pelvic, para-aortic, and supraclavicular lymph nodes in a cephalad fashion. Hematogenous spread occurs to the non-nodal distal sites.[6]

Cervical cancer is most commonly staged using the FIGO and the American Joint Committee on Cancer TNM systems (**Table 1**). FIGO is a clinical staging system that uses a physical examination, including examination under anesthesia, cystoscopy, colposcopy, proctoscopy, hysteroscopy, barium enema examination, intravenous urography (IVU), radiography of the chest and skeleton, and endocervical curettage and biopsy[7] The use of the FIGO system allows for uniform worldwide staging of patients; but the system is limited in that it does not account for information and factors that affect the prognosis and management, such as lymph node status[3]

ANATOMIC IMAGING

CT and MR imaging historically have been performed for anatomic assessment and locoregional involvement before the development of metabolic imaging. CT can assess for regional lymph nodes, distal metastases, and hydronephrosis; it has eliminated the need for lymphoscintigraphy and IVU in areas with access to CT. However, CT is limited in its soft-tissue resolution and assessment of cervical tumor invasion, parametrial invasion, and pelvic sidewall involvement. In this regard, MR imaging is highly valuable in the evaluation of the primary tumor. MR imaging has close to 90% accuracy in the local staging of cervical cancer tumors greater than 1 cm. MR imaging is superior in the evaluation of tumor size, extension, and location. This superiority is very helpful in treatment planning, in separating patients who can undergo surgical resection versus those who receive chemoradiation.[8]

However, the limitation of CT and MR imaging arises in the evaluation of metastatic nodal disease in the preoperative setting. CT and MR imaging are limited in the evaluation of micrometastatic disease in lymph nodes smaller than 1 cm. They also cannot reliably detect reactive nodes versus metastatic nodes greater than 1 cm.

[18F]-2-FLUORO-2-DEOXY-D-GLUCOSE–PET/COMPUTED TOMOGRAPHY

PET is most commonly performed with the radiotracer [18F]-2-fluoro-2-Deoxy-D-glucose (FDG). FDG PET/CT depends on physiologic changes and is based on the degree of uptake and metabolism of glucose, which is abnormal in tumors as compared with surrounding tissues. Historically, PET used to be performed as a standalone procedure. The use of FDG PET alone is an older technique recently replaced with FDG PET/CT given the value of hybrid metabolic and anatomic imaging.

PROTOCOLS

FDG PET/CT can be performed in 2 ways. CT can be performed with a low-dose radiation technique for coregistration and attenuation-correction, or contrast-enhanced (CE) CT can be performed with oral and intravenous contrast administration for diagnosis, attenuation correction, and coregistration.

Patients are asked to fast for 6 hours before the procedure. If diabetic, they are asked to hold their medication or insulin for 6 hours before the study.[8] The intravenous injection of a weight-based amount of FDG (0.22 mCi/kg) is then given. If patients are receiving a CE examination, oral contrast material is given at this time as well. After approximately 60 to 90 minutes to allow for the uptake of radiotracer, the combined PET/CT is obtained. PET acquisition from the proximal thighs to the skull base occurs after patients empty their