



Prognostic value of PET response

Association of post-treatment positron emission tomography with locoregional control and survival after radiation therapy for squamous cell carcinoma of the vulva



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ABSTRACT

Background/purpose: The aim of this study was to investigate the use of post-treatment F-18 fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) for vulvar cancer and compare metabolic response to clinical outcomes.

Materials/methods: This retrospective study included 21 patients with vulvar squamous cell carcinoma treated with curative-intent radiation between 2007 and 2015. All patients received intensity-modulated radiation treatment (IMRT), a pre-treatment FDG/PET-CT, and a post-treatment FDG-PET/CT performed at a median time of 3 months post-IMRT.

Results: Median follow-up time was 28 months. Post-treatment FDG-PET/CT demonstrated no evidence of disease (NED) in 12 patients and residual or progressive disease (PD) in 9. FDG-PET/CT response significantly correlated with biopsy-proven locoregional failure ($p = 0.02$) and was the only significant factor associated with overall survival (OS) ($p = 0.049$). Patients with NED on FDG-PET had a 2-year locoregional control (LRC) of 89% versus 25% for those with PD ($p < 0.01$). Patients with NED on FDG-PET/CT had a 2-year OS of 100% versus 42% for those with PD ($p = 0.02$). FDG-PET/CT evaluation had a sensitivity of 100% and a specificity of 71% for detecting pathologically proven residual disease in patients receiving neoadjuvant or definitive radiation.

Conclusion: In this single-institution study of women with vulvar cancer, post-treatment response on FDG-PET/CT was associated with LRC and OS.

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Carcinoma of the vulva is a relatively rare gynecologic malignancy in the United States, accounting for approximately 6000 new cases in 2016 [1]. The majority of women who initially present with vulvar cancer are post-menopausal with a median age of 68 years; however, recent trends suggest a rising incidence among younger women [2,3]. This may be due to known risk factors that include human papilloma virus (HPV) infection, lichen sclerosus, a history of tobacco use, immunodeficiency syndromes, and a prior history of cervical cancer [4]. Radiation therapy (RT) has emerged

to play a major role in the curative treatment of vulvar cancer in not only the adjuvant setting but also the neoadjuvant and definitive settings [5,6]. Despite the emergence of both treatment consensus and contouring guidelines [7–9], approximately 25–30% of patients with vulvar cancer will develop a local recurrence at five years. The role of F-18 fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) in the assessment of therapy response and recurrence for vulvar cancer is still unknown given very limited data; however, it is starting to play a larger role for other gynecologic malignancies such as cervical and ovarian cancers where prior studies have shown the utility of FDG-PET/CT as a prognostic indicator [10–14]. The most recent guidelines for post treatment surveillance of vulvar cancer patients have been primarily adapted from other, more common, gynecologic malignancies [15]. Current NCCN guidelines [9] recommend interval

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history and physical examinations every three to six months for two years after completion of therapy. Imaging and laboratory assessments for surveillance are currently recommended only if indicated based on symptoms or examination findings suspicious for recurrence. The purpose of this study was to evaluate the use of post-treatment FDG-PET/CT for restaging of patients with vulvar cancer and to address whether metabolic response to therapy is predictive of clinical outcomes.

Methods and materials

Study population

The records of twenty-one patients with vulvar cancer treated with curative intent radiation therapy at Washington University in St. Louis School of Medicine from January of 2007 through January of 2015 were reviewed. All patients underwent a complete staging workup according to the International Federation of Gynecology and Obstetrics (FIGO) and American Joint Committee on Cancer (AJCC) 7th edition criteria for cancer staging, including a full history and physical examination, routine laboratory evaluation, and metastatic evaluation. All patients received both a pre- and post-treatment whole-body FDG-PET/CT. No patient had metastatic disease at the time of diagnosis. The data source for this study was the Washington University in St. Louis Radiation Oncology Department's IRB-approved, retrospective registry of treatment data (IRB Approval # 20131149). The data were de-identified by an "honest broker" before research use.

Surgical resection

Surgical resection was performed in ten patients while eleven underwent biopsy alone. A radical vulvectomy was performed on six patients while four received modified radical vulvectomy, hemi-vulvectomy, or wide local excision. All patients receiving surgery to the primary tumor also underwent a bilateral inguinal lymph node dissection.

Radiotherapy

All patients in the study received external beam intensity modulated radiation therapy (IMRT) with or without high-dose-rate (HDR) brachytherapy. Radiation treatment volumes, techniques, and doses were determined according to our institutional guidelines. All patients received a treatment planning CT simulation for IMRT. Radiation intent was definitive in 11 (52%) patients, adjuvant in 7 (33%), and neoadjuvant prior to surgical resection in 3 (14%). All patients received IMRT to the vulva, pelvic lymph nodes, and inguinal lymph nodes. The median external beam radiation dose was 5120 cGy (range, 5040–7000). In general, IMRT plans were created to limit the small bowel V40 to <30%, the rectum V40 to <60%, the bladder V45 to <50%, and the maximum spinal cord dose to 45 Gy. HDR iridium-192 interstitial brachytherapy was performed in seven patients after completion of external beam radiation therapy (EBRT) using the method described by Dyk et al. [16] Brachytherapy was performed on patients with large locally invasive tumors at initial diagnosis or patients with residual tumor after IMRT. If indicated, HDR brachytherapy was performed three weeks after completion of IMRT. The median total HDR dose was 1200 cGy (range, 1000–2000) delivered in eight fractions given twice a day. The median combined IMRT and HDR dose was 7000 cGy (range, 5040–7520) in patients treated with definitive radiation. The median IMRT dose was 5040 cGy (range, 5040–6000) in patients receiving adjuvant radiation.

Chemotherapy

The decision on use of chemotherapy was made by the treating gynecologic oncologist based on patient-specific criteria, but was typically reserved for locally advanced disease. Concurrent weekly cisplatin (40 mg/m²) was delivered to ten (48%) patients. Concurrent chemotherapy was delivered in 8 of 14 patients treated with definitive or neoadjuvant radiation, and 2 of 7 patients treated with adjuvant radiation.

Follow-up and response assessment

Patients, on average, were seen at six weeks, three months, six months, and 12 months post completion of RT. Post-treatment whole body FDG-PET/CT was performed at a median of 3 months (range, 0.2–7) after completion of EBRT. Locoregional control (LRC) was defined as time until biopsy proven recurrence in the vulva or regional lymph nodes, with censoring at last follow-up or death. Overall survival (OS) was defined as time until death, with censoring at last follow-up in patients still alive. Follow-up times used in the LRC and OS analysis were defined starting from the date of diagnosis. Complete clinical response (cCR) was defined as no evidence of disease noted on physical exam after completion of RT. Complete pathological response (pCR) was defined as a biopsy or surgery of the vulva showing no carcinoma within one year of completion of RT.

FDG-PET/CT technique

FDG-PET/CT was performed prior to start of any therapy and was typically also performed 2–3 months post completion of EBRT for patients treated with adjuvant RT and prior to consolidative surgery or interstitial brachytherapy for patients treated with neoadjuvant or definitive RT. All patients underwent FDG-PET/CT with a hybrid PET/CT scanner (Biograph Duo, LSO-40, or mCT, Siemens Medical Solutions, Malvern, PA). The CT portion of the study was performed without administration of intravenous contrast. CT images were obtained from the base of skull through the proximal thighs. FDG-PET images were obtained over the same anatomic extent beginning 50–76 min (median, 59.5) post administration of 11.3–17.7 mCi FDG, depending on the patient's weight. Urinary tract activity was minimized by placement of a Foley catheter before the injection of FDG and by administration of furosemide and intravenous fluids after FDG injection in most patients. Fourteen patients had a urinary catheter (typically 14-French) at the time of the pre-treatment PET. Sixteen patients had a urinary catheter at the time of the post-treatment PET. The reason for not receiving a urinary catheter was patient refusal in the majority of cases.

The FDG-PET/CT images were interpreted in standard clinical fashion, both separately and in a fused mode. Previous diagnostic images were available for review and comparison at the interpretation of the post-treatment FDG-PET/CT scans. These included the pretreatment diagnostic FDG-PET/CT scan, as well as any previous diagnostic CT studies. The FDG-PET/CT images were reviewed for abnormal FDG uptake at the primary tumor site, regional lymph node sites, and distant sites. A complete metabolic response or no evidence of disease (NED) was defined as the absence of abnormal FDG uptake on post-treatment FDG-PET/CT compared to sites of abnormal FDG uptake noted on pretreatment FDG-PET/CT as described by a board-certified radiologist/nuclear medicine physician in an imaging report. Residual or progressive disease was defined as persistent abnormal FDG uptake, new sites of abnormal FDG uptake, or increased intensity or size of abnormal FDG uptake within the irradiated area including the vulva, inguinal nodes or pelvic nodes compared to baseline pre-treatment FDG-PET/CT as

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