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Clinical Investigation: Gynecologic Cancer

Metabolic Response on Post-therapy FDG-PET Predicts Patterns of Failure After Radiotherapy for Cervical Cancer

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Summary

This study reports the patterns of failure for patients with cervical cancer treated with definitive radiotherapy and evaluated with a 3 month post-therapy FDG-PET. Of those who had a recurrence, 24% had isolated local failures and 76% had some component of distant failure. Patients with a partial metabolic response (PMR) within the cervix had an increased rate of isolated pelvic failures although there was a 35% false positive rate.

Purpose: To determine the patterns of failure in patients with cervical cancer treated with definitive radiotherapy and evaluated for metabolic response with early posttherapy ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET).

Methods and Materials: The records of 238 patients with cervical cancer were reviewed. All patients were treated with a combination of external radiotherapy and intracavitary brachytherapy. Two hundred and nineteen patients (92%) received concurrent chemotherapy. All patients underwent pretreatment FDG-PET, and posttherapy FDG-PET was performed within 8−16 weeks of the completion of radiotherapy. Posttherapy FDG-PET results were categorized as complete metabolic response (CMR), partial metabolic response (PMR), and progressive disease (PD). Failure patterns were categorized as none, isolated local failure (central pelvis ± pelvic lymph nodes), distant failure, or combined local plus distant failure.

Results: Of the 91 patients (38%) who had a recurrence, 22 had isolated local failures, and 69 had distant failures (49 distant failures and 20 combined local plus distant failures). Of the 173 patients with a CMR, 40 (23%) experienced treatment failure. All 25 patients with PD experienced treatment failure, which was distant in 24 patients (96%). Among the 40 patients with PMR, no failure has been observed for 14 patients (35%). Of the 26 failures within the PMR group, 15 (58%) were limited to the pelvis. Differences in the patterns of failure between the three groups (CMR, PMR, PD) were statistically significant (chi-square test; $p < 0.0001$).

Conclusions: The majority of failures after definitive radiotherapy for cervical cancer include distant failures, even in the setting of concurrent chemotherapy. PMR within the cervix or lymph nodes is more commonly associated with isolated local recurrence.

Keywords: Metabolic response, Cervical cancer, FDG-PET

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Introduction

Despite significant advances in screening and prevention strategies for cervical cancer, treatment of this disease continues to present a clinical challenge in the United States and throughout the world. Worldwide, more than 470,000 cases are diagnosed each year. In the United States in 2009, there were 11,270 new diagnoses and 4,070 cancer deaths (1). Almost half of patients with newly diagnosed cervical cancer present with advanced disease (2). Locally advanced cervical cancer is treated with a combination of pelvic radiotherapy and concurrent cisplatin chemotherapy. This treatment strategy is associated with a 5-year overall survival rate of 70% and a 5-year local failure rate of 18%–30% depending on the study (3, 4). The vast majority of treatment failures occur within the first 2 years of completing chemoradiation therapy (5). A number of pretreatment and treatment-related factors have been associated with clinical outcome, including both pretreatment stage and lymph node status (6).

We have reported that metabolic response determined by positron emission tomography (PET) using ^{18}F-fluorodeoxyglucose (FDG) performed within 8–16 weeks after the completion of therapy can be used to predict clinical outcome (7). In our initial study, metabolic response on the posttherapy FDG-PET was evaluated qualitatively and divided into three groups: (*1*) complete metabolic response (CMR)—absence of abnormal FDG uptake at sites of abnormal FDG uptake noted on the pretreatment FDG-PET study; (*2*) partial metabolic response (PMR)—any persistent abnormal FDG uptake at these sites; and (*3*) progressive disease (PD)—any new sites of abnormal FDG uptake that were not present on the pretreatment PET. The 3-year cause-specific survivals were 100% for those patients with a CMR, 51% for those patients with a PMR, and 17% for patients with PD ($p < 0.0001$). The corresponding 3-year progression-free survivals were 78%, 35%, and 0%, respectively ($p < 0.0001$). Although patients with PMR had decreased cause-specific and progression-free survival, it was unclear whether this was due to local failure, the development of distant metastatic disease, or both. The purpose of this study was to determine the patterns of failure for patients undergoing chemoradiation therapy and evaluated by early posttherapy FDG-PET.

Methods and Materials

Patients

Patients were treated at Washington University for cervical cancer with curative intent between March 1998 and April 2009. Approval was obtained from the institutional review board (Washington University Human Research Protection Office) for this retrospective outcomes analysis.

There were 238 patients who fulfilled the selection criteria for this study (treatment with curative intent, completion of all planned radiotherapy, and posttherapy FDG-PET 8–16 weeks of the completion of therapy). Patient characteristics are presented in Table 1.

All patients were treated with a combination of external radiotherapy and intracavitary brachytherapy for a mean total dose to point A >80 Gy, and 219 patients (92%) received weekly concurrent chemotherapy (40 mg/m^2 cisplatin).

Table 1 Patient characteristics

Age (years)	Mean 51	Range 24–86
Histology		
Squamous		210
Adenocarcinoma		18
Adenosquamous		5
Clear cell		4
Small cell		1
FIGO stage		
I		
IA2		1
IB1		35
IB2		43
II		
IIA		4
IIB		92
III		
IIIA		4
IIIB		55
IV		
IVA		4

Abbreviation: FIGO = Fédération Internationale de Gynécologie Obstétrique.

PET imaging

The average time from completion of treatment to the posttherapy FDG-PET study was 12.1 weeks (SD 2.4; range, 8–16 weeks). Before November 2002, PET was performed using a conventional PET scanner and interpreted as previously described (8). Thereafter, all FDG-PET studies were performed with a hybrid PET/computed tomography (CT) scanner using methods described by Wright *et al.* (9). PET studies were deferred if the blood glucose concentration exceeded 200 mg/dL. PET/CT images were interpreted in a standard clinical fashion, both separately and in a fused mode. Metabolic response was determined qualitatively using the following definitions: CMR was defined as absence of abnormal FDG uptake at sites of abnormal FDG uptake noted on the pretreatment FDG-PET study. PMR was defined as any persistent abnormal FDG uptake at these sites. PD was defined as any new sites of abnormal FDG uptake that were not present on the pretreatment PET (7).

Clinical follow-up

Duration of follow-up ranged from 5 to 133 months (mean, 43 months). At the time of last follow-up, 137 patients had no evidence of disease, 26 patients were alive with disease, 61 patients had died of disease, and 14 patients had died from causes other than cervical cancer. Clinical follow-up of patients was performed 6 weeks after the completion of therapy and periodically as follows: monthly for 3 months, every 3 months until 12 months, every 4 months for the second year, and every 6 months during years 3 to 5. Follow-up imaging studies beyond 16 weeks postcompletion of therapy consisted of CT and/or FDG-PET/CT as clinically indicated. Failure was defined as biopsy-proven recurrence or documentation of progression of disease on serial imaging studies (7). Failure patterns were determined by follow-up imaging studies and divided into four groups: none, isolated local failure (central pelvis ± pelvic lymph nodes), distant failure (which includes para-aortic and supraclavicular lymph