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Integrated PET/CT for the evaluation of para-aortic nodal metastasis in locally advanced cervical cancer patients with negative conventional CT findings

Y. Yildirim [a,*], S. Sehirali [a], M.E. Avci [a], C. Yılmaz [b], K. Ertopcu [a], S. Tinar [a], Y. Duman [c], S. Sayhan [d]

[a] Department of Gynecologic Oncology, Aegean Obstetrics and Gynecology Training and Research Hospital, Izmir, Turkey
[b] Department of Radiology, Izmir Training and Research Hospital, Izmir, Turkey
[c] Anatolia Nucleer Medicine and Radiology Center, Izmir, Turkey
[d] Department of Pathology, Aegean Obstetrics and Gynecology Training and Research Hospital, Izmir, Turkey

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Abstract

Objective. The aim of this study was to evaluate the usefulness of integrated 2-[18F] fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (PET/CT) for the detection of para-aortic nodal status and to test whether PET/CT change management strategy in locally advanced cervical cancer (LACC) patients with negative conventional CT findings.

Materials and methods. Sixteen locally advanced (FIGO stage IIB–IVA) cervical squamous cancer patients with negative conventional CT findings were eligible to enter this prospective study. All patients underwent firstly PET/CT scans then extraperitoneal surgical exploration for para-aortic lymphadenectomy. Based on histopathologic confirmation, the accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the PET/CT for para-aortic lymph node metastasis were estimated.

Results. The median age was 48.7 (range 42–67). The accuracy, sensitivity, specificity, PPV and NPV of the PET/CT were 75%, 50%, 83.3%, 50% and 83.3%, respectively. The treatment was modified in four of sixteen (25%) patients; four patients received EFRT in combination with cisplatin chemotherapy instead of standard pelvic field radiotherapy in combination with cisplatin chemotherapy.

Conclusion. Our results, despite our study group is small, suggest that PET/CT is an effective imaging technique in the evaluation of LACC with negative CT findings. It may help planning the management especially selecting radiation field. However, larger controlled studies are needed to recommend PET/CT as an alternative to pre-treatment surgical staging.

Keywords: Locally advanced cervical cancer; Para-aortic lymph node metastasis; PET/CT

Introduction

Cervical cancer has continued to become one of the most common cancers in women particularly living in developing countries. Despite the advances in screening and treatment programs of preinvasive cervical lesions, the mortality from cervical cancer has not decreased in the last three decades [1].

The treatment of cervical cancer depends on various factors such as the International Federation of Gynecology and Obstetrics (FIGO) stage of disease, histological subtype, depth of invasion and lymph node status [2,3]. The most important limitation of FIGO clinical staging for cervical cancer is that this system does not provide any information about retroperitoneal lymph node status especially para-aortic nodal metastasis. Para-aortic lymph node metastasis, which is significantly related to the progression-free survival and recurrence, has been observed in approximately one in third of locally advanced (FIGO stage IIB–IVA) cervical cancer (LACC) patients [4–10]. Also, in order to choose ideal treatment method, it is needed to know para-aortic nodal status actually. Invasive surgical staging procedures using laparotomy

* Corresponding author.
E-mail address: dr.yusufyildirim@yahoo.com.tr (Y. Yildirim).

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and laparoscopy have recently been performed to obtain this knowledge [11,12]. However, the feasibility and the survival advantage of surgical staging applications have also been discussed and non-invasive methods have been looked for detecting nodal status in LACC.

Various imaging methods such as computed tomography (CT) and magnetic resonance (MR) imaging have traditionally been used in order to determine the extent of disease in cervical cancer [13,14]. The detection of lymph node metastasis with the use of both CT and MR imaging techniques remains difficult because the identification of metastatic lymph nodes with these morphologic imaging modalities is based on the measurement of node size, with greater than 1 cm short-axis diameter being the most accepted criterion for the diagnosis of cancer involvement [15,16]. These morphologic imaging studies are also not ideal exactly and remain insufficient to demonstrate nodal involvement because only 10% of the metastatic retroperitoneal nodes are markedly enlarged [17]. Although CT is a non-invasive and easily available method for clinical staging of cervical cancer, its overall sensitivity reported for retroperitoneal nodal metastasis is approximately 44% [13]. A study by Gynecologic Oncology Group (GOG) demonstrated that the sensitivity of CT in the detection of para-aortic nodal metastasis was only 34% [4].

In the last two decades, the invention of positron emission tomography (PET) using the radionuclide-labeled analogue of glucose "2-[18F] fluoro-2-deoxy-D-glucose (18F-FDG)", which is one of the major source of energy in cancer cells, makes possible for us to detect regional metabolism in metabolically overactive tumor foci more accurately than with that of morphologic imaging techniques [18,19]. According to available data, PET detects lymph node metastases of cervical cancer more accurate than does CT and PET results are better predictor of treatment outcome [20–23]. However, the anatomical landmarks on PET may be limited due to the low soft-tissue background activity [24]. Recently, PET/CT integrating morphologic data of CT with functional data of PET has widely been used in order to evaluate locoregional and distant spreads in cervical cancer, as well as in many solid cancers. Previous studies have suggested that PET/CT is useful technique to identify lymph node metastasis and recurrence in patients with LACC [25–27].

The objective of this study is to evaluate the usefulness of integrated PET/CT in evaluating para-aortic nodal status and to test whether PET/CT change management strategy in patients with LACC with negative conventional CT findings.

Materials and methods

Patients

Patients with LACC with negative CT findings for para-aortic nodal metastasis at the Aegean Obstetrics and Gynecology Training and Research Hospital, Gynecologic Oncology Department, between March 2006 and November 2006 were eligible to enter this prospective study. Age >70 years, concurrent or previous malignant disease, previous radiation therapy, adenocarcinoma or adenosquamous carcinoma histology, World Health Organization (WHO) performance status ≥3, inadequate renal, hepatic and cardiac functions and BMI >40 were excluded. During this period mentioned above, a total of 54 cervical cancer patients were diagnosed and treated but only 16 of them (29.6%) met our selection criteria (Fig. 1).

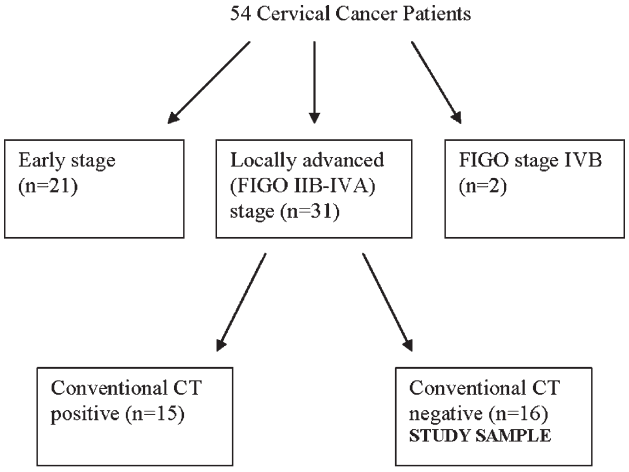

Fig. 1. Flow chart of the study sample.

The study protocol was approved by the Institutional Review Board (IRB) of our center. Detailed information about the study nature was given to all participants and the verbal informed consent was taken from all of them.

Prior to study entry, all patients underwent laboratory work-up, ECG, chest X-ray, complete physical and gynecological examination, upper abdominal and pelvic ultrasonography and chest CT. After their disease was clinically staged, all patients enrolled in the study underwent PET/CT and were subsequently scheduled for surgery (extraperitoneal para-aortic lymphadenectomy). There was no neo-adjuvant chemotherapy administration in any patients. The time interval between PET/CT and surgery was 5–14 days (mean, 8.3 days). Before surgery, mechanical bowel preparation, venous thrombosis prophylaxis with low molecular weight heparin (LMWH) (starting 1 h before the operation) and antibiotic prophylaxis with single dose of a first generation cephalosporin were performed to all patients.

Data collected involved patient age, cancer diagnosis, histology and stage, WHO performance status, medical history, serum cancer antigen 125 (CA-125) levels, results of surgical exploration and PET/CT, surgical complications and treatment methods.

^{18}F-FDG-PET/CT procedure

Patients were instructed to fast at least for 4 h before injection of ^{18}F-FDG (except for glucose-free oral hydration). Patients voided prior to administration of ^{18}F-FDG and over again prior to image obtaining. Sterile ^{18}F-FDG was given intravenously followed by a tracer uptake phase of approximately 60 min. The injection doses of ^{18}F-FDG were between 370 and 555 MBq (10–15 mCi). After injection, patients were kept lying comfortably. No urinary bladder catheterization was applied and no oral muscle relaxants were given. No intravenous diuretics and hydration were given [28].

The hybrid PET/CT system combining a third generation multislice spiral CT with a PET scanner was used. All PET/CT images were evaluated by visual interpretation of the experienced nuclear medicine and radiology physicians who were blinded to the FIGO clinical staging and conventional CT results.

Surgical procedure

A right J-shaped (hockey-stick) incision, which is routinely preferred incision by our surgical team, was used in order to carry out pelvic and para-aortic extraperitoneal lymphadenectomy. The skin, the subcutaneous tissue, the external and internal oblique muscles, transverse abdominal muscle and their fascia were dissected to enter the pre-peritoneal space. By positioning the peritoneum medially, cecum and ascending colon were mobilized medially and the retroperitoneal space was exposed for allowing clear visualization of the pelvic lymphatic tissue. Pelvic lymphadenectomy was performed by resection of the entire lymphatic tissue overlying the major pelvic vessels and the obturator