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Original Article

Clinical Value of ^{18}F-fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Response Evaluation after Primary Treatment of Advanced Epithelial Ovarian Cancer

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Abstract

Aims: To prospectively evaluate the use of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG-PET/CT) in the definition of the treatment response after primary treatment of advanced epithelial ovarian cancer (EOC).
Materials and methods: Forty-nine patients with advanced EOC had an ^{18}F-FDG PET/CT scan before and after primary treatment. The treatment response was defined with the currently used radiological and serological Response Criteria in Solid Tumors (RECIST1.1/GCIC) criteria and the modified PET Response Criteria in Solid Tumors (PERCIST). The concordance of the two methods was analysed. If the patient had a complete response to primary treatment by conventional criteria, the end of treatment ^{18}F-FDG PET/CT scan (etPET/CT) was not opened until retrospectively at the time of disease progression. The ability of etPET/CT to predict the time to disease recurrence was analysed. The recurrence patterns were observed with an ^{18}F-FDG PET/CT at the first relapse.
Results: The agreement of the RECIST1.1/GCIC and modified PERCIST criteria in defining the primary treatment response in the whole patient cohort was good (weighted kappa coefficient = 0.78). Of the complete responders ($n = 28$), 34% had metabolically active lesions present in the etPET/CT, most typically in the lymph nodes. The same anatomical sites tended to activate at disease relapse, but were seldom the only site of relapse. In patients with widespread intra-abdominal carsinosis at diagnosis, the definition of metabolic response was challenging due to problems in distinguishing the physiological FDG accumulation in the bowel loops from the residual tumour in the same area. The presence of metabolically active lesions in the etPET/CT did not predict earlier disease relapse in the complete responders.
Conclusions: In the present study, etPET/CT revealed metabolically active lesions in complete responders after EOC primary therapy, but they were insignificant for the patient's prognosis. The current study does not favour routine use of ^{18}F-FDG PET/CT after EOC primary treatment for complete responders.

Key words: Epithelial ovarian cancer; FDG; PET/CT; RECIST; response evaluation

Introduction

Epithelial ovarian cancer (EOC) is usually diagnosed at an advanced stage. Primary debulking surgery (PDS) and platinum/taxane-based chemotherapy are the cornerstones of treatment. In widely spread inoperable cases, the primary treatment may start with neoadjuvant chemotherapy (NACT) followed by interval debulking surgery [1,2]. In addition to the FIGO stage and surgical outcome, the response to platinum-based chemotherapy is a significant prognostic factor [3,4]. The response to first-line treatment is measured with radiological and serological parameters

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[5]. A computed tomography (CT) scan is recommended at the end of first-line chemotherapy to define disease status. If the serum tumour marker CA125 is increased at the time of diagnosis, serial CA125 measurements can be useful in monitoring the treatment response [6]. A complete response to first-line therapy requires both normalisation of CA125 during treatment and no signs of residual disease in CT [5–7].

In clinical trials, an objective evaluation of drug response is essential. Tumour shrinkage during treatment and the time of progression are important end points. The Definitions of Objective Endpoints were refined when the World Health Organization criteria [8], first presented in 1981, were followed by the Response Criteria in Solid Tumors (RECIST) criteria in 2000 [9]. These criteria have subsequently been widely adopted by academic research groups and the medical industry for trials where the primary end points are an objectively measured response to treatment or disease progression. The updated RECIST 1.1 criteria [7] published in 2009 clarified some questions and impracticalities in the earlier version. In addition, RECIST 1.1 takes metabolic positron emission tomography (PET) imaging into account when evaluating disease progression.

Treatment response assessment with PET imaging is not included in the current generally accepted guidelines. The PET Response Criteria in Solid Tumors (PERCIST) criteria [10] were introduced in 2009 in order to unify the quality of scanning procedures and the evaluation of metabolic treatment response. The PERCIST categories for response to treatment (complete metabolic response [CMR], partial metabolic response [PMR], stable metabolic disease and progressive metabolic disease) resemble the anatomical RECIST categories. A recent practical guide [11] has helped with the implementation of the proposed criteria into clinical practice. Despite these efforts made to unify metabolic response assessment, a variety of treatment response methods are currently clinically applied.

The present prospective analysis focuses on treatment response evaluation at the end of EOC first-line therapy of advanced EOC. We compared the concordance of the currently used RECIST1.1/GCIC criteria and the modified PERCIST criteria. In addition, we evaluated whether an ^{18}F-fluorodeoxyglucose (^{18}F-FDG) PET/CT scan at the end of first-line therapy could find prognostic subgroups in patients with complete response by conventional criteria. We hypothesised that complete response patients with increased metabolic activity in the end of treatment ^{18}F-FDG PET/CT (etPET/CT) scan would have earlier disease progression.

Materials and Methods

Patients

This study was conducted at the Department of Obstetrics and Gynecology, Turku University Hospital, Finland and was approved by the local ethics committee (ClinicalTrials.gov identifier: NCT01276574). All patients with suspected advanced ovarian, fallopian tube or peritoneal cancer were eligible to participate in this prospective clinical trial. Patients with diabetes mellitus or a history of previous cancer were excluded. Between October 2009 and March 2014, 87 patients were recruited. The present analysis consists of 49 patients with FIGO stage III or IV disease who had an ^{18}F-FDG PET/CT scan at the time of diagnosis and at the end of first-line chemotherapy. All the patients received platinum/taxane-based chemotherapy. Bevacizumab became part of the EOC first-line treatment during the study period and six patients received bevacizumab maintenance therapy. The characteristics of the 49 patients included are presented in Table 1.

PET/CT Scanning Procedure and Imaging Analysis

A pretreatment ^{18}F-FDG PET/CT scan from the base of the skull to mid-thigh was carried out within the 2 weeks before the PDS/diagnostic laparoscopy. The etPET/CT scan was scheduled 3–4 weeks after the six cycles of platinum/taxane chemotherapy in patients who underwent PDS ($n = 22$). For the 27 patients who received NACT, the etPET/CT was taken after a total of six to nine chemotherapy cycles.

The scanning procedure with whole-body contrast-enhanced ^{18}F-FDG PET/CT (with 64-row Discovery STE or VCT; General Electric Medical Systems, Milwaukee, WI, USA) has been described previously [12]. Briefly, all patients fasted for 6 h before the intravenous injection of 4 Mbq/kg ^{18}F-18F-FDG. The low-dose PET/CT (kV 120, Smart mA range 10–80) from skull base to mid-thigh was carried out 50–60 min after the tracer injection. It was followed by a whole-body diagnostic high-dose contrast-enhanced CT scan (kV

Table 1
Patient characteristics

Variables	Patients (n)	%
Total	49	100
Age, median (range)	63 (30–80)	
FIGO stage		
IIIB	2	4%
IIIC	24	49%
IVA	7	14%
IVB	16	33%
Origin		
Ovary	40	82%
Peritoneum	6	12%
Fallopian tube	3	6%
Histology		
High grade serous	43	88%
Low grade serous	5	10%
Clear cell	1	2%
Treatment strategy		
PDS	22	45%
NACT	27	55%
Macroscopic residual tumour in surgery		
No	13	27%
Yes	36	73%

PDS, primary debulking surgery; NACT, neoadjuvant chemotherapy.

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