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Interim ^{18}FDG PET/CT during radiochemotherapy in the management of pelvic malignancies: A systematic review

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ABSTRACT

^{18}F-fluorodeoxyglucose PET/CT (^{18}F-FDG-PET/CT) is widely applied in oncology for disease staging, assessment of therapy response, relapse diagnosis, follow-up and target volume delineation. In particular, it can detect early response during chemoradiotherapy (interim) because functional modifications usually precede morphological ones. This ability is crucial to the radiation oncologist for the management of patients, to avoid persisting with ineffective therapy – often leading toxicity – and to shift to potentially more effective alternatives.

Interim ^{18}F FDG-PET imaging in rectal and cervical cancer, the main malignancies of the pelvic district, has been applied and a broad literature is available, although some results are discordant. This systematic review summarizes the application of ^{18}F FDG-PET/CT during the chemoradiotherapy of locally advanced

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pelvic malignancies in order to clarify its capability to predict response and prognosis and its potential role to tailor therapy, which seems to be validated in rectal cancer, whilst less conclusive in cervical cancer.

1. Introduction

In the past decade imaging in oncology has developed an expanding role in diagnosis, staging, treatment selection, response evaluation and follow up – broadly grouped into anatomical and functional. Anatomical imaging techniques in particular computed tomographic (CT) imaging and magnetic resonance imaging (MRI) provide the everyday assessment, but more recent techniques such as fluorodeoxyglucose-positron emission tomography (FDG-PET) and functional MRI may provide intriguing insights into tumour biology and behaviour in the face of treatment.

Rectal carcinoma is the third most frequent tumour and the second most common cause of death in western world in both sexes (Delbeke and Walker, 2010; Gil-delgado and Khayat, 2008), showing an increased incidence due to aging and alimentary habits changes (Delbeke and Walker, 2010). The standard treatment is curative surgery in early stages and neo-adjuvant chemo-radiotherapy (CRT) in locally advanced rectal cancer (LARC) aiming to reduce the tumour volume and stage, in order to increase the resectability and the sphincter conservation (Murcia Durendez et al., 2013). Fifty to sixty percent of patients are down-staged following CRT with about 20% reaching pathological complete response (pCR) (Goldberg et al., 2012).

The histopathological analysis is based on a standardized protocol that includes the evaluation of the (y)pTNM categories (according to the International Union against Cancer), the number of resected and tumour-involved lymph nodes, and tumour infiltration of the circumferential resection margins. Histopathological tumour regression is categorized according to different classification criteria (Becker et al., 2003; Mandard et al., 1994; Dworak et al., 1997).

Uterine cervical cancer is a curable disease treated with external beam radiotherapy (RT) and/or brachytherapy and chemotherapy (CHT). Randomized clinical trials have shown that combined CRT – the standard treatment for advanced cancer of the cervix – is superior to RT alone (Green et al., 2005). The presence of lymph nodes metastases is the most important prognostic factor in patients with cervical cancer, most of all at early stage (Gien and Covens, 2009; Parker et al., 2009). Indeed, the survival rate at 5 years for cervical cancer with no evidence of lymph nodes metastasis ranges from 70% to 95% compared with 40% to 68% for patients with positive lymph nodes (Chyong-Huey et al., 1999).

Positron Emission Tomography (PET) is widely applied imaging modality in oncological field for disease staging, assessment of therapy response, relapse diagnosis, follow-up and target volume delineation (Lee et al., 2015).

Fluorodeoxyglucose (^{18}F-FDG) is a radiotracer able to accumulate in glucose consuming cells (i.e. cancer cells) in an early phase before morphological changes occur. The ^{18}F FDG is detected in human body through a dedicated device called PET scanner that in the last decades has been evolved in the hybrid machine PET/Computed Tomography (PET/CT). PET/CT is a full-ring-detector PET scanner combined with a multi-detector row helical CT scanner, which allows contemporaneous and coregistered acquisition of both PET and CT images (Ak et al., 2000).

In the pelvic region rectal and gynaecological cancer are the two main malignancies where ^{18}F FDG-PET/CT is employed to detect the extension of the neoplasm (tumour and lymph nodes) before, and most of all, during neoadjuvant treatment. Other malignancies, such as prostate, anal and endometrial cancer are not routinely evaluated by ^{18}F FDG-PET/CT either in staging or in the therapy response setting.

In rectal cancer ^{18}F FDG-PET is not superior to other imaging techniques in tumour and lymph nodes staging but some data have demonstrated greater sensitivity than CT in hepatic and extra-hepatic disease diagnosis (Poeppel et al., 2009; Chowdhury et al., 2010). The uptake of the cervical cancer detected by ^{18}F FDG-PET is predictive of local tumour response and prognostic of survival outcomes (Xue et al., 2006; Kidd et al., 2007). Moreover, PET has demonstrated its increased accuracy in lymph nodes staging (Gouy et al., 2013).

The ability to evaluate therapy response at an early stage is crucial to the radiation oncologist for the management of patients, to avoid persisting with ineffective therapy – often leading toxicity – and to shift to potentially more effective alternatives. Among these, the adaptive RT represents an important option, but, to date, few data have been published in this field.

^{18}F-FDG-PET/CT during (*interim*) CRT (^{18}F-FDG-PET$_{int}$/CT) imaging in rectal and cervical cancer has been applied and a broad literature is now available. However, discordant results about the prediction of response have been reported in relation to non-homogenous timing of PET imaging.

The aim of this comprehensive review is to analyse the application of ^{18}F FDG-PET$_{int}$/CT in the management of rectal and cervical cancer. In particular, we explore its capability to predict response and prognosis, and consequently, its possible role in tailoring therapy to the individual. This strategy could open the way to define new standard protocols based on PET imaging in the guidelines for pelvic cancers.

2. Materials and methods

We searched in PUBMED Library with specific keywords to identify studies involving ^{18}F FDG-PET$_{int}$/CT during CRT in patients affected by rectal and gynaecological cancer. Different search terms were combined using Boolean operators (and, or), as indicated in Table 1a and Table1b, for rectal and gynaecological cancer, respectively. All results were evaluated for adequacy to the scope of this review. The exclusion criteria were: publication before January 2005 or after June 2016; editorial letters; other than English language; only PET scanner (not PET/CT) to avoid non-uniform, less recent and accurate data; patient population with other cancer types besides rectum or cervical cancer; neoadjuvant chemotherapy only; only baseline acquisition and lack of response analysis other than PET/CT images to allow response comparison with a gold standard. Reviews were not utilized in the analysis, but their references were also checked.

3. Results

Table 1a and Table 1b summarize the results obtained from the literature research for the rectal and the cervical cancer, respectively.