Radiotherapy and Oncology 113 (2014) 158–165

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Systematic Review

The role of diffusion-weighted MRI and ^{18}F-FDG PET/CT in the prediction of pathologic complete response after radiochemotherapy for rectal cancer: A systematic review

Ines Joye [a,b,*], Christophe M. Deroose [c], Vincent Vandecaveye [d], Karin Haustermans [a,b]

[a] Department of Radiation Oncology, University Hospitals Leuven; [b] Department of Oncology, KU Leuven; [c] Department of Nuclear Medicine, University Hospitals Leuven; and [d] Department of Radiology, University Hospitals Leuven, Belgium

ARTICLE INFO

Article history:
Received 29 September 2014
Received in revised form 13 November 2014
Accepted 13 November 2014

Keywords:
Rectal cancer
Diffusion-weighted MRI
^{18}F-FDG PET/CT
Pathological complete response
Radiochemotherapy

ABSTRACT

After neoadjuvant radiochemotherapy (RCT) for locally advanced rectal cancer, 15–27% of the patients experience a pathological complete response (pCR). This observation raises the question as to whether invasive surgery could be avoided in a selected cohort of patients who obtain a clinical complete response after preoperative RCT. In this respect, there has been growing interest in functional imaging techniques to improve clinical response assessment. This systematic review focuses on the role of diffusion-weighted imaging (DWI) and ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) in the prediction of pCR after RCT for rectal cancer.

A total of 14 publications on DWI and 25 on ^{18}F-FDG PET/CT were retrieved. Pooled analysis of individual patient data shows both imaging modalities have a low positive predictive value in the prediction of pCR (mean PPV of 54% and 39% for DWI- and ^{18}F-FDG PET/CT-based parameters respectively). Especially pre-RCT imaging is unable to predict pCR with overall accuracies of 68–72% for DWI and 44% for ^{18}F-FDG PET/CT. Qualitative DWI assessment 5–10 weeks after the end of RCT may outperform apparent diffusion coefficient (ADC)-based DWI-parameters (overall accuracy of 87% vs. 74–78%). Although few data are available, early changes in FDG-uptake seem promising in the prediction of pCR and the role of ^{18}F-FDG PET/CT during RCT should be further investigated. Quantitative and qualitative ^{18}F-FDG PET/CT measurements are equally effective in the assessment of pCR after RCT.

The major strength of DWI and ^{18}F-FDG PET/CT lies in the identification of non-responders who are not candidates for organ preservation. Up to now, DWI and ^{18}F-FDG PET/CT are not accurate enough to safely select patients for organ-sparing strategies. Future research must focus on the integration of functional imaging with clinical data and molecular biomarkers.

Neoadjuvant radiochemotherapy (RCT) followed by total mesorectal excision (TME) surgery is currently the standard treatment for locally advanced rectal carcinoma [1–3]. The tumoral response to this preoperative treatment is very heterogeneous: while 15–27% of the patients achieve a pathological complete response (pCR), a partial response is seen in 54–75% and others show no response at all [4]. Patients who achieve a pCR have a favorable long-term outcome with excellent local control and disease-free survival regardless of their initial T- and N-stages [4–6]. Retrospective studies from Brazil have highlighted the 'wait-and-see' policy in such patients [7]. More recent series support the feasibility of this approach [8,9]. Adopting a non-operative strategy for clinical complete responders will avoid the risks of surgical morbidity and mortality, and will spare them the need for a stoma [10–12]. However, before a 'wait-and-see' policy could be safely implemented, a precise selection of the eligible patients is mandatory.

The gold standard for assessing the tumoral response to preoperative RCT is conventional histopathological analysis. This method, however, is only applicable in the postoperative setting and consequently cannot be used for the preoperative selection for an individualized treatment. Computed tomography (CT), endorectal ultrasound (EUS) and conventional magnetic resonance imaging (MRI) have shown to lack accuracy for restaging after RCT [13–16]. In recent years, there has been growing interest in functional imaging techniques to improve clinical response assessment. These imaging modalities depict the microstructural and metabolic characteristics of the tumor, allowing assessment of treatment-induced changes before morphological changes become apparent. In this

* Corresponding author at: Leuven Cancer Institute, University Hospitals Leuven, Herestraat 49, 3000 Leuven, Belgium.
E-mail address: ines.joye@uzleuven.be (I. Joye).

http://dx.doi.org/10.1016/j.radonc.2014.11.026
0167-8140/

respect, diffusion-weighted imaging (DWI) and ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) have emerged as powerful tools in the response prediction before, during and after neoadjuvant RCT for rectal cancer.

DWI is a non-invasive imaging modality, providing functional information on the microstructure of tissues through the assessment of differences in water proton mobility [17]. Water diffusion characteristics depend on several factors such as cell density, vascularity, viscosity of the extracellular fluid and cell membrane integrity. By quantifying these properties as the apparent diffusion coefficient (ADC), DWI can be used as an imaging biomarker to monitor and predict tumoral response to RCT [18,19].

^{18}F-FDG PET semi-quantitatively assesses tumor glucose metabolic activity through changes in FDG-uptake. A decrease in FDG-uptake after radiotherapy and/or chemotherapy has been correlated with pathological response in several tumor types [20–22].

In this systematic review, we collect the current evidence of the role of DWI and ^{18}F-FDG PET/CT in the prediction of pCR after preoperative RCT for locally advanced rectal cancer.

Materials and methods

Search strategy and selection criteria

The MEDLINE and Embase databases were searched for the terms (“rectal cancer” AND “diffusion magnetic resonance imaging” AND “response”) and for (“rectal cancer” AND “positron emission tomography” AND “response”) (29 September 2014) [23]. These initial searches yielded 155 and 222 publications respectively. Only papers published in English, German, and French were included, resulting in 153 and 216 articles. All titles and abstracts were screened and only studies reporting on the role of DWI or ^{18}F-FDG PET in the assessment of pCR after RCT for locally advanced rectal cancer were retained. Reviews, general overview articles and congress abstracts were excluded. To identify additional relevant studies, the reference lists of the retrieved studies were checked manually. A total of 14 relevant DWI and 25 ^{18}F-FDG PET/CT papers were identified. Selected studies were evaluated for methodological quality using the quality assessment of diagnostic accuracy studies (QUADAS) criteria [24]. Literature selection results are depicted in Fig. 1. A meta-analysis was not performed due to the wide heterogeneity between the included studies.

Data extraction

We extracted all available data on the performance of following quantitative DWI parameters: pretreatment ADC (ADC_{pre}), ADC during RCT (ADC_{during}), posttreatment ADC (ADC_{post}), change in ADC during RCT (ΔADC_{during}) and change in ADC after RCT (ΔADC_{post}). Additionally, volumetric data and data on qualitative DWI assessment were collected. Following ^{18}F-FDG PET/CT parameters were retained: the mean and maximum standardized uptake value (SUV) measured before ($SUVmean_{pre}$, $SUVmax_{pre}$), during ($SUVmean_{during}$, $SUVmax_{during}$) and after RCT ($SUVmean_{post}$, $SUVmax_{post}$). The absolute change in SUVmax (ΔSUVmax) and the response indices were also extracted (RI SUV_{mean}, RI SUV_{max}), as was the total lesion glycolysis (TLG) and the metabolic tumor volume (MTV). The visual response score (VRS) was retained as a qualitative parameter.

Some papers used receiver operating characteristic (ROC) analysis to calculate cutoff values for the individual response parameters. A ROC curve plots the true positive rate against the false positive rate at various threshold settings, thereby allowing to calculate optimal cutoff values. If cutoff values were provided, 2×2 contingency tables were constructed and the sensitivity, specificity, positive and negative predictive values of DWI and ^{18}F-FDG PET/CT in the prediction of pCR were calculated (Suppl Fig. 1). We defined the sensitivity for pCR prediction as the fraction of patients with pCR that is correctly identified as such by imaging. The specificity is the fraction of patients without pCR correctly identified as such by DWI or ^{18}F-FDG PET/CT. The positive predictive value (PPV) reflects the probability that a complete response on imaging is confirmed by pathological examination. Conversely, the negative predictive value (NPV) reflects the probability that an incomplete response on imaging is confirmed by pathology. Finally, when available, individual patient data (i.e. true positives, false positives, true negatives and false negatives) were extracted

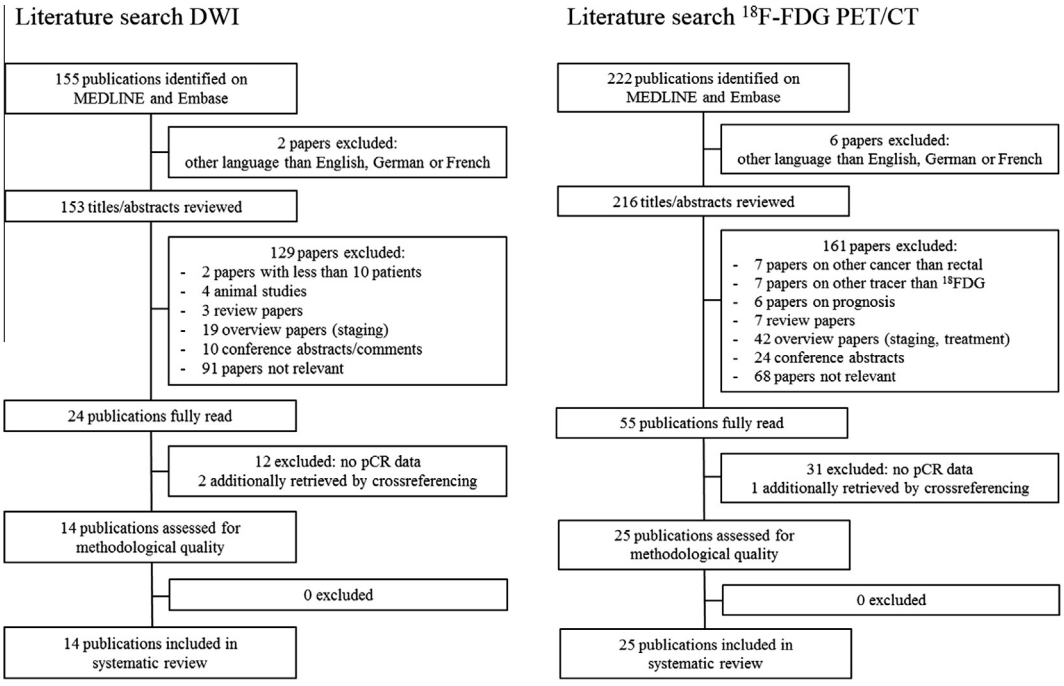

Fig. 1. Literature search.