

Letter to the Editor

The radiation oncologist point of view on “Predictive value of 18F-FDG PET/CT on survival in locally advanced rectal cancer after neoadjuvant chemoradiation”

Dear Editor,

In the recent paper “Predictive value of 18F-FDG PET/CT on survival in locally advanced rectal cancer after neoadjuvant chemoradiation” Niccoli Asabella et al¹ evaluate the prognostic value of 18-FDG PET/CT in terms of survival in a series of 58 patients with locally advanced rectal cancer (LARC) patients who underwent to surgery preceded by neoadjuvant chemo-radiotherapy (nCRT). The correlation between overall survival (OS) and disease-free survival (DFS) with pathological staging ((y)pTNM and TRG) was also investigated.

Niccoli Asabella et al¹ “highlight the predictive and prognostic potential role of 18F-FDG PET/CT to personalize decision in the selective risk-adapted treatment strategy, and to schedule the correct follow-up approach”. We have appreciated the study; so, we offer here some considerations and comments to the discussion, focused on the “Radiation oncologist point of view”. According to the NCCN Guidelines Version 3.2018, PET scan is not indicated for preoperative staging of rectal cancer². It should only be used to evaluate an equivocal finding, or in patients with a strong contraindication to intravenous (IV) contrast. However, 18-FDG PET/CT is being investigated for its ability to accurately determine response to neoadjuvant treatment, to detect distant metastases that would change the treatment strategy, and to plan the surgical approach. PET/TC can be applied in many other fields. It may be considered in select cases of oligometastatic patients if a surgical cure of M1 disease is feasible. Furthermore, in the post-treatment surveillance scenario with an elevated CEA and with negative CT scans, 18F-FDG PET/TC can be considered indicated thanks to the high sensitivity and a specificity rate (about 88%) for the detection of recurrence². According to the last Italian Association of Radiation Oncology (AIRO) Guidelines, PET/CT may be used for the definition of occult synchronous tumors or M1. From our point of view, it can also be useful for the delineation of the Biological Target Volume, the Gross Tumor or Nodal Volume and for the RT planning, especially using sophisticated technique as Intensity Modulated RT^{3,4}.

Radiation Oncologists are particularly interested in the improvements image registration, fusion algorithms, evaluation strategies of autosegmentation approaches for metabolic, biological and imaging PET data in order to reduce the inter/intraobserver variability and to permit adaptive planning RT treatments⁵⁻⁷. Finally, PET/CT offers a good performance in the early evaluation of the response to radio-chemotherapy (RTCHT) treatment. As underscored in the paper by Niccoli Asabella et al¹, pure morphological imaging techniques alone may not be sufficient to predict treatment response, because often functional tissue changes precede anatomical changes. In the last decade five reviews have been published in the literature⁸⁻¹². All these reviews conclude that data on the role of 18F-FDG PET/CT in response prediction before, during and after RTCT for locally advanced rectal cancer are emerging.

In general, a SUV (Standardized Uptake Value) decrease is associated with better response to RCT; moreover the early changes in FDG-uptake seem promising. Multicenter studies, using large patient populations, are needed to validate the role of functional imaging in order to identify those patients who may benefit from a less or a more aggressive therapeutic approach after RTCHT. Up to now, 18F-FDG PET/CT is not accurate enough to safely select patients for organ

preservation⁸⁻¹². Future research must focus on the integration of functional imaging with clinical data and molecular biomarkers.

In 2014 Van Stiphout Ruud et al¹³ have detailed and validated a “Nomogram predicting response after chemoradiotherapy in rectal cancer using sequential PETCT imaging” in a multicentric prospective study (Thunder Trial). This nomogram can be used to distinguish three types of patients: complete responders, good responders and non-responders, for which respectively a wait-and-see policy, radiotherapy boost and additional chemotherapy can be administered. This personalized treatment approach is expected to promote more complete responders, to reduce the number of surgical procedures and related complications, and to avoid unnecessary toxicities¹³. Extremely promising and exciting is to study and assess the role of the 18F-FDG PET/CT Quantitative Imaging (QI) in Radiation Oncology and the potential of radiomic-based phenotyping in precision medicine^{14,15}. The most common applications for these tools are for treatment planning, risk stratification, guidance of dose escalation, and characterization of post-treatment effects. By collaborating across disciplines, the 18F-FDG PET/CT QI could be integrated into the radiation oncology clinical workflow, including identification and standardization of clinically significant QI parameters and optimization of existing imaging methods for RT planning and response assessment. From the Radiation Oncologist point of view, these data, when validated, may be used to introduce the concept of “Sequential 18F-FDG PET/CT based RTCHT neoadjuvant treatment” in rectal cancer. In conclusion, these important investigations are necessary for the robust integration of individual patients’ anatomic, biological, physiological, and genomic imaging characteristics into radiation oncology decision-making and treatment design, thereby enabling truly personalized cancer care. Then, we thank the editorial board and the Authors of the study for giving us data and considerations that, if confirmed, could become very useful in the extensive oncological vision and in the multidisciplinary clinical practice.

Conflict of interest

The authors declare no conflicts of interest.

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