LETTER TO THE EDITOR

Prognostic role of metabolic parameters (MTV and TLG) of staging PET/CT in the pediatric population with Hodgkin's lymphoma: an open discussion

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Dear Sir,

I read with interest the article entitled *Baseline PET/CT imaging parameters for prediction of treatment outcome in Hodgkin and diffuse large B cell lymphoma: a systematic review* [1].

However, in this review the authors do not consider the pediatric population and that there is no clear evidence of the prognostic role of baseline metabolic parameters in pediatric Hodgkin lymphoma.

In 2007, in the European protocol EuroNet-PHL-C1 Trial (EudraCT 2006–000,995-33), [18F]FDG PET/CT was a mandatory method in staging and in assessing early response to treatment in pediatric patients with Hodgkin's lymphoma [2].

In the last years, the prognostic role of staging [18F] FDG PET/CT in adult patients with Hodgkin's lymphoma is emerging through the calculation of semi-quantitative parameters such as the volume of the metabolic tumor (MTV) and the total glycolysis of the lesion (TLG). This interest arises from the hypothesis that patients with a higher burden of disease at the baseline [18F]FDG PET/CT have a worse prognosis in terms of disease-free survival (DFS) and overall survival (OS).

Several studies highlighted the prognostic role of baseline MTV in adult patients with Hodgkin's lymphoma (HL). One of these studies is from Cottereau and colleagues. In their series of 258 patients with early clinical stage HL, they demonstrated that MTV has a prognostic role, both in terms of PFS and OS [3].

In the pediatric population, an important study that demonstrated the role of MTV in predicting therapeutic failure was that of Rogasch and colleagues from the University of Berlin. This retrospective study involved 50 children enrolled in experimental therapeutic protocols (42 in the EuroNet protocol PHL-C1 and 8 in the EuroNet protocol PHL-C2), who underwent a [18F]FDG PET/CT study in staging and after 2 cycles of chemotherapy. The metabolic parameters of the staging PET/CT extracted were MTV, TLG, SUVmax, SUVmean, and SUVpeak, and heterogeneity parameters, such as entropy and asphericity. Authors demonstrated that a high tMTV value at staging was the best indicator of therapeutic failure in these patients, in all clinical stages of disease [4].

However, with the exception of this study, there are currently no reliable data on the prognostic role of these metabolic parameters in the pediatric population, compared to adult patients, due to the few studies that have taken into account the role of these parameters in pediatric Hodgkin's lymphoma.

There are different contouring methods to define MTV, and there is still no standardization of the method to be applied. Threshold methods use an SUV cut-off as a threshold (such as 2.5 or 4) or 41% of SUVmax as a threshold. These methods have limitations, as an underestimation of the MTV might occur if many voxels in a tumor mass have low uptake that is less than the threshold. On the other hand, an overestimation might happen if the tumor lies close to anatomical structures with physiological [18F]FDG uptake, which would therefore be erroneously included in the calculation of the disease volume [5, 6].

Each thresholding method has limitations and many software platforms are available for MTV and TLG calculation [6].

It would be of benefit to have a standardization of [18F] FDG PET/CT protocols in prospective multicenter studies, in larger patient cohorts, in order to find out the best

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threshold method and to clarify the role of pre-treatment [18F]FDG PET/CT parameters in pediatric patients affected by Hodgkin lymphoma.

Declarations

Ethical approval This article does not contain any studies with human participants or animals performed by the author.

Conflict of interest The author declares no competing interests.

References

1. Frood R, Burton C, Tsoumpas C, et al. Baseline PET/CT imaging parameters for prediction of treatment outcome in Hodgkin and diffuse large B cell lymphoma: a systematic review. Eur J Nucl Med Mol Imaging. 2021;48:3198–220. https://doi.org/10.1007/s00259-021-05233-2.
2. Kluge R, et al. Current status of FDG-PET/CT in the treatment setting of Hodgkin's lymphoma in childhood and adolescence. Clin Transl Imaging. 2015;3:309–19.
3. Cottereau AS, Versari A, Loft A, et al. Prognostic value of baseline metabolic tumor volume in early-stage Hodgkin lymphoma in the standard arm of the H10 trial. Blood. 2018;131:1456–63.
4. Rogasch JMM, Hundsdoerfer P, Hofheinz F, Wedel F, Schatka I, Amthauer H, Furth C. Pretherapeutic FDG-PET total metabolic tumor volume predicts response to induction therapy in pediatric Hodgkin's lymphoma. BMC Cancer. 2018;18(1):521. https://doi.org/10.1186/s12885-018-4432-4.PMID:29724189;PMCID:PMC5934894.
5. Kobe C, Goergen H, Baues C, et al. Outcome-based interpretation of early interim PET in advanced stage Hodgkin lymphoma. Blood. 2018;132(21):2273–9.
6. Barrington SF, Meignan M. Time to prepare for risk adaptation in lymphoma by standardizing measurement of metabolic tumor burden. J Nucl Med. 2019;60(8):1096–102. https://doi.org/10.2967/jnumed.119.227249.

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