CT and 18-FDG PET/CT for the assessment of treatment response in Hodgkin's and Non-Hodgkin lymphoma

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Abstract

Introduction: The assessment of lymphoma response to treatment is based on imaging studies. **Objective:** To correlate the assessment of lymphoma treatment response by computed tomography (CT) and by positron emission tomography/computed tomography (PET/CT). **Method:** Cross-sectional, observational study, where records of patients with lymphoma under surveillance by CT and PET/CT were reviewed. **Results:** The study population consisted of 43 patients with a mean age of 32.7 ± 22.4 years; 26 (60.5 %) had a diagnosis of Hodgkin's lymphoma and 17 (9.5 %) had non-Hodgkin lymphoma. By CT, 34 (79.1 %) were diagnosed with disease and nine (20.9 %) without disease. The criteria used to assess the response was radiologist experience in 39 (90.7 %) and RECIST 1.1 criteria in four (9.3 %). The diagnosis by 18-FDG PET/CT was no response to treatment or partial response-recurrence in 32 (74.4 %) and response to treatment in 11 (25.6 %); with PERCIST criteria in 13 (30.2 %) and Deauville criteria in 30 (69.8 %). When the diagnosis by CT versus 18-FDG PET/CT was compared, out of 11 patients with complete response on PET/CT, three had a similar CT diagnosis. Of the 34 patients with data consistent disease diagnosed by CT, 26 had similar results by 18-FDG PET/CT ($p = 0.54$). **Conclusion:** The value of lymphoma treatment response on CT does not agree with that obtained by 18-FDG PET/CT.

KEY WORDS: Lymphoma. Computed tomography. Positron-emission tomography. Conventional tomography.

Introduction

The World Health Organization International Classification of Diseases (2008) recognizes more than 50 types of lymphoma based on histopathological, immunohistochemical, cytogenetic and molecular analysis.¹ Many lymphomas are potentially curable when treated with chemotherapy alone or in combination with radiotherapy, as well as with stem cell transplant.^{2,3} The Ann Arbor staging system applies to both Hodgkin's and non-Hodgkin lymphoma.^{4,5} Staging with this system is based on the extension of lymph node groups involvement.^{6,7}

The treatment of lymphoma depends on subtype and clinical stage. The therapeutic goal in Hodgkin's

and non-Hodgkin lymphoma is total cure of the disease.^{8,9} Cure can be achieved with chemotherapy, radiation therapy or combined immunotherapy.¹⁰

Computed tomography (CT) performed with 5-mm slices in multiplanar images is an appropriate method to assess treatment response according to the Response Criteria in Solid Tumors (RECIST) 1.1, based on unidimensional measurements with a pre-treatment baseline examination that should record two to five malignant lesions, representative of tumor burden, and that will be assessed in subsequent follow-up examinations. To classify a lymph node lesion as "target", its diameter should be larger than 15 mm in its short axis. Any additional non-measurable lesion (< 10 or < 15 mm, pleural effusion, etc.) is recorded as a non-target lesion and is qualitatively

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assessed. Lytic, blastic or mixed metastases are measurable when the soft tissue component meets measurable lesion criteria.^{11,12} Tumor volume measurement is an alternative to unidimensional and two-dimensional measurement procedures, given that a large number of neoplasms are not spherical and grow or shrink irregularly.^{13,14}

In 1999, the international working group for non-Hodgkin lymphoma therapeutic response assessment standardization established follow-up based on a combination of markers, clinical findings and radiological evaluation by computed tomography (CT) according to two-dimensional size criteria. In 2007, the International Harmonization Project incorporated the use of positron-emission tomography (PET)/CT with 18-FDG and immunohistochemistry criteria for the management of Hodgkin's disease.¹⁵

In 2009, the PET-Response Criteria in Solid Tumors (PERCIST), which combine anatomical and functional information, limiting to five the number of target lesions and a maximum of two per organ, were published. In addition, the percentage of change required to determine the metabolic response was established and the use of standardized uptake value (SUV) was adopted, recommending the use of maximum SUV corrected for lean mass (SUL), calculated in a volumetric region of interest (ROI) of 1 to 2 cm of the tumor.¹⁶

PET/CT has revolutionized the definition of measurable tumor and introduced metabolism-based criteria into imaging.¹⁷ Lugano's criteria indicate the use of 18-FDG PET/CT as an imaging method recommended both for staging and follow-up of lymphomas. When not available, and in cases where lymphomas show variability or no 18-FDG uptake, using CT as the diagnostic and follow-up method is recommended. Contrasted CT allows a more accurate measurement of the nodule size and sometimes helps identify adenopathy from surrounding soft tissue structures that PET/CT fails to detect.¹⁸ Evaluation of response with 18-FDG PET/CT is based on metabolic activity, indicated by 18-FDG uptake. SUV serves as a semi-quantitative marker of metabolic activity and response evaluation is based on 18-FDG uptake visual assessment and is classified according to the "five-point scale".^{19,20}

The purpose of this investigation was to analyze the consistency between computed tomography and 18-FDG PET/CT for treatment response assessment in the follow-up of patients with Hodgkin and non-Hodgkin lymphoma.

Method

Cross-sectional study carried out from May 2016 to July 2018. CT and PET/CT diagnoses were reviewed after management with chemotherapy, radiotherapy and autologous transplantation in patients with Hodgkin and non-Hodgkin lymphoma confirmed by histopathology. Adult and pediatric patients of both genders, who underwent CT and PET/CT, who received previous treatment with chemotherapy, radiotherapy or autologous transplant for a period of more than three months and less than 12 months, were included. The variables used were age, gender, radiologic criteria (qualitative method), RECIST criteria, type of response according to CT, nuclear medicine criteria, PERCIST criteria and Deauville criteria.

CT imaging reports, which were carried out by medical specialists in radiology and imaging with more than 10 years of experience, were reviewed, as well as PET/CT reports, which were issued by two doctors, one specialist in nuclear medicine and another in radiology and imaging.

Descriptive statistics and central tendency and dispersion measures were used, as well as the kappa value for diagnostic concordance and chi-square tests for nominal variables' association.

This investigation was approved by the Committee of Research of the participating unit and complied with the ethics in medical research guidelines. Participant patients' anonymity was preserved at all times and informed consent was not required.

Results

The study included 43 patients. Mean age was 32.7 years, with a minimum of six and maximum of 77 years (SD = 22.4); 20 patients (46 %) were females and 23 (53 %), males; 26 (60.5 %) had been diagnosed with Hodgkin's lymphoma and 17 (9.5 %), with non-Hodgkin lymphoma. The reason for conducting the study was follow-up in four (9.3 %), disease activity or current status assessment in 30 (69.8 %), treatment response assessment in five (11.6 %) and surveillance in four (9.3 %). Disease was diagnosed by CT in 34 cases (79.1%) and no disease in nine (20.9 %). Response assessment was mainly based on the qualitative characteristics described in the report by the imaging specialist physician (experience) in 39 cases (90.7 %) and based on RECIST 1.1 criteria in four (9.3 %).

18-FDG PET/CT diagnosis was indicated with no response in 32 patients (74.4 %) in whom partial

treatment response or recurrence was identified, with treatment response being reported in 11 (25.6 %). The nuclear physician's report referred that the qualitative method (experience) was used in 37 cases (86 %). In 13 cases (30.2 %), the response was assessed based on PERCIST criteria and in 30 (69.8%) on Deauville criteria, as recommended in current guidelines.

Among the patients who were initially diagnosed with Hodgkin's and non-Hodgkin lymphoma and underwent tomographic treatment response assessment, seven with Hodgkin's lymphoma and two with non-Hodgkin lymphoma were found to be free of disease; disease recurrence was identified in 19 cases with Hodgkin's lymphoma and in 15 with non-Hodgkin lymphoma, $p = 0.23$ (a p -value ≤ 0.05 was considered statistically significant) (Table 1).

Among the patients who were initially diagnosed with Hodgkin and non-Hodgkin lymphoma and underwent treatment response evaluation with PET/CT, seven with Hodgkin and four with non-Hodgkin lymphoma were found to be free of disease; 19 patients with Hodgkin's lymphoma and 13 with non-Hodgkin lymphoma were found with disease, $p = 0.80$. The comparison of patients diagnosed by computed tomography and with 18-FDG PET/CT showed that, among the 11 patients with complete response, three had a similar diagnosis on CT. On the other hand, among the 34 patients with data consistent with disease diagnosed by tomography, only 26 had the same results on 18-FDG PET/CT, $p = 0.54$ (Table 2).

Discussion

In developed countries, assessment of the response to Hodgkin or non-Hodgkin lymphoma treatment is based on 18-FDG PET/CT, since glucose labeled with a radioactive tracer has higher concentration in tissues with high active cellular component; uptake of this radiotracer it is the "gold standard".^{9,17} The assessment is based on PERCIST and Deauville criteria, which have as key point the determination of background SUV and its comparison with the lymph nodes that show higher uptake.^{13,14} The disadvantage of this method is its poor accessibility in Mexico; however, in international literature, CT is suggested as an alternative method,¹⁸ given the availability of the RECIST 1.1 criteria, which are specific for treatment response assessment according to lymph nodes localization, size and morphology.¹⁹

In this study, the sample was found to have an age and gender distribution similar to those reported in

Table 1. Type of lymphoma in 43 patients and treatment response as determined by computed tomography

	Without disease on CAT	With disease on CAT	χ^2	p
Hodgkin's lymphoma	7	19	1.427	0.23
Non-Hodgkin lymphoma	2	15		

CAT = computed axial tomography

Table 2. Association of treatment response assessment determined by computed tomography and PET/CT

	Without disease on CAT	With disease on CAT	χ^2	p
Without disease on PETCT	3	8	0.35	0.54
With disease on PETCT	6	26		

PET/CT = Positron-emission tomography combined with tomography, CAT = computed axial tomography.

publications of the World Health Organization in patients with lymphoma. As for the type of lymphoma, it was Hodgkin's type in 26 (60.5 %).

In 30 patients (69.8%), the reason for assessment was to determine tumor activity and disease status, which indicates that doctors of the hemato-oncology department look for the best method to assess treatment response.^{9,10}

Imaging systems play a highly important role in this assessment, since in the works by Barrington, Meignan and Kulkarni, the comparison of imaging studies before and after treatment was shown to be vital in order to not have false positive or false negative results.^{16,17,20}

Now, for the assessment of response, the imaging specialist of the CT department used a qualitative method in 39 (90.7 %) and a systematized quantitative method (RECIST 1.1) only in four (9.3 %) subjects, which is not in agreement with international guidelines recommendations, which suggest a systematization of tumor assessment supported by a digital imaging system,^{11,12,13} in contrast to that which was observed in the doctors of the PET/CT department, who reported their results based on PERCIST or Deauville criteria, which are indicated in Lugano's criteria to assess treatment response.¹⁷ PERCIST criteria were used in 13 cases (30.2 %) and Deauville criteria in 30 (69.8 %), taking into account that the five-point classification is the most commonly used in this department and that it correlates with the National Comprehensive Cancer Network guidelines recommendation.²¹

The results of Hodgkin's lymphoma patients response were found to be similar with both imaging methods (CT and PET/CT), but in the assessment of non-Hodgkin lymphoma with CT, only two patients showed absence of disease, and when it was carried out with PET/CT, four were identified. Even when the statistical result was not significant, the above reflects that two patients were incorrectly evaluated (Table 1).

In the CT evaluation, a lack of standardization on the method was systematically observed. When the statistical analysis of the reports of treatment response assessment by 18-FDG PET/CT was performed, no significant relationship showing agreement with the CT assessment was identified, which means that the radiology report is not providing sufficient information and that it is outperformed by the imaging study with the 18-FDG radiopharmaceutical (Table 2).^{17,18-21}

Conclusions

The data herein presented show that the diagnostic value of treatment response assessment by means of computed tomography in patients with Hodgkin and non-Hodgkin lymphoma has no significant agreement with currently recommended evaluation method, 18-FDG PET/CT. On the other hand, this study shows that CT diagnostic veracity would be of greater impact if the imaging expert would carry out response assessment based on RECIST 1.1 criteria, with a digital imaging storage system and relate it to the National Comprehensive Cancer Network international guidelines.

To homogenize previous agreement criteria with international guidelines recommendations, a digital imaging system should be available, in addition to a standardized quantitative system, applicable to the assessment of lymphoma treatment response, based on recommended criteria, in order to enable the performance of a comparative study of topographic images at retreatment and post-treatment stages.

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