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# Lactate dehydrogenase levels and <sup>18</sup>F-FDG PET/CT metrics differentiate between mediastinal Hodgkin's lymphoma and primary mediastinal B-cell lymphoma

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**Purpose** This study aims to investigate whether clinical, laboratory, and fluorine-18-fluorodeoxyglucose (<sup>18</sup>F-FDG) PET/CT findings can discriminate between mediastinal Hodgkin's lymphoma and primary mediastinal B-cell lymphoma (PMBCL).

**Patients and methods** This retrospective study included 56 patients (42 with mediastinal Hodgkin's lymphoma and 14 with PBMCL). Differences in clinical, laboratory, and <sup>18</sup>F-FDG PET/CT metrics were assessed between Hodgkin's lymphoma and PMBCL.

Results Lactate dehydrogenase (LDH) and <sup>18</sup>F-FDG PET/ CT-based maximum tumor diameter, lesion-to-liver ratio maximum standardized uptake value (SUV<sub>max</sub>), and lesionto-liver ratio peak standardized uptake value (SUV<sub>peak</sub>) were all significantly higher (P < 0.001) in PMBCL than in Hodgkin's lymphoma, and PMBCL also significantly more frequently (P = 0.001) exhibited necrosis on <sup>18</sup>F-FDG PET/ CT than Hodgkin's lymphoma. LDH, maximum tumor diameter, lesion-to-liver ratio SUV<sub>max</sub>, and lesion-to-liver ratio SUV<sub>peak</sub> yielded areas under the receiver operating characteristic curve of 0.968 [95% confidence interval (CI): 0.923-1.000], 0.866 (95% CI: 0.765-0.968), 0.875 (95% CI: 0.776-0.975), and 0.874 (95% CI: 0.771-0.976), respectively. LDH (with cutoff of 236 U/I) achieved sensitivity and specificity of 81.6 and 100%, respectively; maximum tumor diameter (with cutoff of 9.98 cm) achieved sensitivity and

Introduction

Lymphomas can affect any organ in the body and are in the top 10 of most frequently occurring malignancies worldwide [1,2]. They are traditionally divided into Hodgkin's lymphoma and non-Hodgkin's lymphoma [1,2] and account for ~ 0.5 and 4.3% of all newly diagnosed cancer cases in the western world, respectively [3].

Hodgkin's lymphoma and the more uncommon non-Hodgkin's lymphoma subtype of primary mediastinal B-cell lymphoma (PMBCL, accounting for less than 5% of all non-Hodgkin's lymphomas [4]) are the two types of lymphoma that can both present with an anterior mediastinal tumor mass [2,5]. PMBCL by definition involves the anterior mediastinum [5]. Both diseases have peak specificity of 87.2 and 78.3%, respectively; lesion-to-liver ratio SUV<sub>max</sub> (with cutoff of 7.12) achieved sensitivity and specificity of 94.9 and 64.3%, respectively; lesion-to-liver ratio SUV<sub>peak</sub> (with cutoff of 11.45) achieved sensitivity and specificity of 97.4 and 64.3%, respectively; and the presence of necrosis achieved sensitivity and specificity of 78.6 and 74.4%, respectively, in discriminating PMBCL from Hodgkin's lymphoma.

**Conclusion** LDH levels and several <sup>18</sup>F-FDG PET/CT findings (tumor size, presence of necrosis, and degree of <sup>18</sup>F-FDG uptake) are helpful in discriminating mediastinal Hodgkin's lymphoma from PMBCL. *Nucl Med Commun* 39:572–578 Copyright © 2018 Wolters Kluwer Health, Inc. All rights reserved.

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Keywords: biopsy, <sup>18</sup>F-FDG PET/CT, Hodgkin's lymphoma, primary mediastinal B-cell lymphoma

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incidences in young adults and resemble each other histologically [2,5]. However, they are two different cancer types that are treated differently [2,5]. Because of the proximity of vital structures, mediastinal biopsy is often difficult, has a non-negligible risk of complications, and is sometimes inconclusive owing to sampling errors [1,5]. Timely diagnosis, however, is crucial to avoid both treatment delay and treatment without an established diagnosis (e.g. use of corticosteroids), particularly when the tumor mass compresses surrounding structures such as the superior vena cava and the trachea [5].

Fluorine-18-fluorodeoxyglucose (<sup>18</sup>F-FDG) PET/CT is a combined molecular-anatomic imaging technique that is increasingly used in lymphoma [6], including PMBCL DOI: 10.1097/MNM.00000000000840

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[7-10]. However, the role of <sup>18</sup>F-FDG PET/CT in the differentiation between mediastinal Hodgkin's lymphoma and PMBCL has not been investigated vet. <sup>18</sup>F-FDG PET/ CT may potentially be of value to noninvasively discriminate these two entities that are not easily accessible for biopsy. Previous work has shown that semiguantitative <sup>18</sup>F-FDG uptake measurements can differentiate Hodgkin's lymphoma from aggressive non-Hodgkin's lymphoma, with higher <sup>18</sup>F-FDG uptake by the latter [11,12]. However, PMBCL has never been evaluated in such analyses. Therefore, it remains unclear whether <sup>18</sup>F-FDG uptake and also other features such as tumor size and the presence of necrosis, can differentiate between mediastinal Hodgkin's lymphoma and PMBCL. If one or more of these <sup>18</sup>F-FDG PET/CT metrics differ between the two entities, <sup>18</sup>F-FDG PET/CT may be used as a noninvasive adjunct to invasive biopsy to steer the diagnosis. In addition, it is unknown if clinical and laboratory parameters differ between mediastinal Hodgkin's lymphoma and PMBCL.

The purpose of this study was therefore to investigate if clinical, laboratory, and <sup>18</sup>F-FDG PET/CT findings can discriminate between mediastinal Hodgkin's lymphoma and PMBCL.

## Patients and methods Study design

This study was approved by the local institutional review board, and because of its retrospective nature, the requirement for written informed consent was waived. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All patients who were newly diagnosed with Hodgkin's lymphoma (with mediastinal involvement according to <sup>18</sup>F-FDG PET/CT) or PMBCL, and who underwent pretreatment <sup>18</sup>F-FDG PET/CT between November 2009 and July 2017 were eligible for inclusion. Patients who underwent <sup>18</sup>F-FDG PET/CT elsewhere, but who were referred to our institution for further diagnostics and/or treatment in the same period, were also eligible for inclusion. Inclusion criteria were patients with newly diagnosed, histologically proven, and treatment-naive Hodgkin's lymphoma with mediastinal involvement or PMBCL, who underwent pretreatment <sup>18</sup>F-FDG PET/CT. Exclusion criteria were patients without a clear histopathological diagnosis of either Hodgkin's lymphoma or PMBCL, previously treated or recurrent Hodgkin's lymphoma or PMBCL, Hodgkin's lymphoma without mediastinal involvement, and imaging performed on a stand-alone PET system.

#### Patient record review

Records of included patients were reviewed to retrieve age, sex, pretreatment hemoglobin (Hb), leukocyte, C-reactive protein (CRP), and lactate dehydrogenase (LDH) levels, and Ann Arbor stage (according to <sup>18</sup>F-FDG PET/CT and available tissue biopsies, including bone marrow biopsy) data.

# <sup>18</sup>F-FDG PET/CT acquisition

Forty-five <sup>18</sup>F-FDG PET/CT scans of patients who were finally included were performed at our institution with an integrated PET/CT system (Biograph mCT PET/CT; Siemens, Knoxville, Tennessee, USA) that was EANM/ EARL (European Association of Nuclear Medicine/ ResEARch 4 Life) accredited [13]. All patients fasted for at least 6 h, after which blood glucose levels were checked to be less than 11 mmol/l, and 3 MBq <sup>18</sup>F-FDG/kg body weight was injected intravenously. Approximately 60 min after <sup>18</sup>F-FDG administration. PET scanning was conducted from midthighs to cranial vertex, with the arms elevated, and with 3 min/bed position. Low-dose computed tomography (CT) with fixed kVp and variable mAs was performed for attenuation correction and anatomical correlation. Data reconstruction was done according to EANM guidelines [13]. Eleven <sup>18</sup>F-FDG PET/CT scans of patients who were finally included were performed in other hospitals before referral to our institution. Although it was unknown whether EANM/EARL-accredited scanners were used in these 11 patients, they all were scanned with integrated PET/CT systems with emission scanning ~60 min after <sup>18</sup>F-FDG injection and a field of view that at least included the region form midthighs to base of skull.

## <sup>18</sup>F-FDG PET/CT analysis

All <sup>18</sup>F-FDG PET/CT scans were evaluated by an experienced nuclear medicine physician (W.N.) using a dedicated workstation and Syngo.via software (Siemens Healthcare, Erlangen, Germany). This observer knew the age and sex of each patient, but was unaware of the type of lymphoma (Hodgkin's lymphoma or PMBCL) under evaluation, and all other clinical, laboratory, pathological, and follow-up findings. All <sup>18</sup>F-FDG PET/CT scans were visually assessed for tumor size (i.e. longest diameter in the axial plane on <sup>18</sup>F-FDG PET/CT), presence of necrosis (defined as photopenic areas within the tumor on <sup>18</sup>F-FDG PET), and presence of calcifications (defined as areas that approach the density of bone on CT). Maximum standardized uptake value (SUV<sub>max</sub>, representing the value of the single voxel with the highest SUV) and peak standardized uptake value (SUV<sub>peak</sub>, representing the mean SUV of a 12-mm sphere encompassing the SUV<sub>max</sub>) [13] of mediastinal tumor and mean standardized uptake value (SUV<sub>mean</sub>) of liver were measured using volume of interest analysis (Fig. 1). Mediastinal tumor <sup>18</sup>F-FDG uptake was semiquantified as the ratio of tumor <sup>18</sup>F-FDG uptake to liver <sup>18</sup>F-FDG uptake for both tumor  $SUV_{max}$  and  $SUV_{peak}$  (lesion-to-liver ratio SUV<sub>max</sub> and lesion-to-liver ratio SUV<sub>peak</sub>, respectively).

#### Statistical analysis

Differences in age, sex, pretreatment Hb, leukocyte, CRP, and LDH levels, Ann Arbor stage, tumor size,





<sup>18</sup>F-FDG PET/CT in a 40-year-old woman with PMBCL, who presented with an LDH level of 431 U/I. Coronal maximum intensity projection 18F-FDG PET (a) shows a mediastinal mass (arrow) and three lung lesions (arrowheads). Maximum axial diameter of the mediastinal mass was 13.6 cm. Axial 18F-FDG PET images show volumes of interest for SUV<sub>max</sub> and SUV<sub>peak</sub> measurements of the mediastinal mass (b) and liver (c). Lesion-to-liver ratio SUV<sub>max</sub> and lesion-to-liver ratio SUV<sub>peak</sub> were 9.8 and 9.9, respectively. Axial fused <sup>18</sup>F-FDG PET/CT images show a central photopenic area in the mediastinal mass (d, arrow), in keeping with necrosis, and some of the lung lesions (e, arrowheads). There were no calcifications in the tumor mass. CT, computed tomography; 18F-FDG, fluorine-18-fluorodeoxyglucose; LDH, lactate dehydrogenase; SUV<sub>max</sub>, maximum standardized uptake value; SUV<sub>peak</sub> peak standardized uptake value.

presence of necrosis, presence of calcifications, lesionto-liver ratio SUV<sub>max</sub>, and lesion-to-liver ratio SUV<sub>peak</sub> between Hodgkin's lymphoma and PMBCL were assessed using two-tailed unpaired *t*-tests for normal distributed data, Mann-Whitney tests for non-normal distributed data, and  $\chi^2$ -tests for dichotomous data. Before this analysis, Shapiro-Wilk tests were first used to check whether continuous variables were normally distributed. In case of any significant differences for any of the aforementioned parameters, corresponding sensitivity and specificity were calculated for differentiating mediastinal Hodgkin's lymphoma from PMBCL. For continuous measures, receiver operating characteristic analysis was first performed to determine the optimal cutoff values. All data were presented with 95% confidence intervals. P values less than 0.05 were considered statistically significant. All statistical analyses were performed using IBM Statistical Package for the Social Sciences, version 24 (SPSS Inc., Chicago, Illinois, USA).

#### Post-hoc analysis

Associations between variables that were found to be significantly different between mediastinal Hodgkin's lymphoma and PMBCL were assessed using Pearson's correlation coefficient for Gaussian data, Spearman's correlation coefficient for non-Gaussian data, and the point-biserial correlation coefficient (for any dichotomous data). Correlations were classified as very weak (coefficients of 0.00–0.19), weak (coefficients of 0.20–0.39), moderate (coefficients of 0.40–0.59), strong (coefficients of 0.60–0.79), and very strong (coefficients of 0.80–1.0).

#### Results

#### Patients

A total of 70 patients were potentially eligible for inclusion. Of these 70 patients, eight patients with Hodgkin's lymphoma were excluded owing to the absence of lymphoma in the mediastinum, three patients were excluded owing to the administration of corticosteroids before <sup>18</sup>F-FDG PET/CT scanning, one patient was excluded because of an unclassifiable B-cell lymphoma with characteristics of both diffuse large B-cell lymphoma and classical Hodgkin's lymphoma (mediastinal gray zone lymphoma), one patient was excluded because of recurrent PMBCL, and one patient was excluded because of lack of pretreatment <sup>18</sup>F-FDG PET/CT. Thus, 56 unique patients (42 with mediastinal Hodgkin's lymphoma and 14 with PBMCL, 30 men and 26 women, with mean age  $\pm$  SD of 36.5  $\pm$  15 years) remained and were finally included. Four patients only had mediastinal involvement (three with PMBCL and one with Hodgkin's lymphoma), whereas 49 patients had both

Table 1 Characteristics of all included patients and comparison between patients with Hodgkin's lymphoma and those with primary mediastinal B-cell lymphoma

Parameters	All patients ( $n = 56$ )	Hodgkin's lymphoma ( $n = 42$ )	PMBCL $(n = 14)$	P value
Age (mean ± SD)	36.5±15.9	36.9±17.4	35.4±10.7	0.77 <sup>h</sup>
Sex (male/female)	30/26	22/20	8/6	> 0.999 <sup>j</sup>
Hb (mean $\pm$ SD) (mmol/l)	$7.9 \pm 1.2^{\circ}$	$7.9 \pm 1.2^{a}$	8.3±0.91 <sup>b</sup>	0.268 <sup>h</sup>
Leukocytes [median (interguartile range)] (10 <sup>9</sup> /l)	9.6 (7.8–10.5) <sup>c</sup>	9.6 (7.65-10.8) <sup>a</sup>	9.2 (7.9–10.3) <sup>b</sup>	0.566 <sup>i</sup>
CRP [median (interguartile range)] (mg/l)	35.5 (9.75–71.25) <sup>9</sup>	31.5 (9.75–69) <sup>d</sup>	45.5 (12.0-72.50) <sup>e</sup>	0.685 <sup>i</sup>
LDH [median (interguartile range)] (U/I)	201.5 (158.75-264.75) <sup>f</sup>	192.5 (144.8–218.75) <sup>d</sup>	424.5 (277.75-721.25) <sup>d</sup>	< 0.001 <sup>i</sup>
Ann Arbor stage (I/II/III/IV)	6/23/11/16	2/19/10/11	4/4/1/5	0.479 <sup>i</sup>
Maximum tumor diameter [median (interguartile range)] (cm)	6.25 (3.0–11.4) <sup>c</sup>	4.34 (2.52–8.62) <sup>c</sup>	12.66 (9.95–14.49)	< 0.001 <sup>i</sup>
Necrosis (present/absent)	21/32 <sup>c</sup>	10/29 <sup>c</sup>	11/3	0.001 <sup>j</sup>
Lesion-to-liver ratio SUV <sub>max</sub> [median (interguartile range)]	4.50 (3.008–6.49) <sup>c</sup>	3.88 (2.52–5.19) <sup>c</sup>	8.61 (5.06-9.95)	< 0.001 <sup>i</sup>
Lesion-to-liver ratio SUV <sub>peak</sub> [median (interquartile range)]	7.78 (5.04–9.72) <sup>c</sup>	5.91 (3.91-8.47) <sup>c</sup>	12.93 (8.06–17.39)	< 0.001 <sup>i</sup>

CRP, C-reactive protein; Hb, hemoglobin; LDH, lactate dehydrogenase; PMBCL, primary mediastinal B-cell lymphoma; SUV<sub>max</sub>, maximum standardized uptake value; SUV<sub>peak</sub>, peak standardized uptake value.

<sup>a</sup>One missing/unavailable data.

<sup>b</sup>Two missing/unavailable data. <sup>c</sup>Three missing/unavailable data. <sup>d</sup>Four missing/unavailable data. <sup>e</sup>Six missing/unavailable data. <sup>f</sup>Eight missing/unavailable data. <sup>h</sup>Unpaired *t*-test.

<sup>i</sup>Mann–Whitney test.  $_{j}^{j}\chi^{2}$ -test.

mediastinal involvement and disease elsewhere according to <sup>18</sup>F-FDG PET/CT. Distribution of Ann Arbor stages was I (n=6), II (n=23), III (n=11), and IV (n=16). Further patient characteristics are displayed in Table 1. Note that <sup>18</sup>F-FDG PET/CT scans of three patients with Hodgkin's lymphoma could not be retrieved from the institutional archives anymore, but these patients were not excluded from the other (non-<sup>18</sup>F-FDG PET/CT) comparative analyses. Of the remaining 53 patients, 43 <sup>18</sup>F-FDG PET/CT scans were performed at our institution and 10 <sup>18</sup>F-FDG PET/CT were performed elsewhere before referral. Representative examples are shown in Figs 1 and 2.

# Comparison of clinical and laboratory parameters between Hodgkin's lymphoma and PMBCL

LDH in PMBCL was significantly higher (P=0.000) than in Hodgkin's lymphoma, whereas age, sex, Hb, leukocytes, CRP, and Ann Arbor stage were not significantly different between the two entities (P=0.268-0.999) (Table 1). The area under the curve of LDH in discriminating PMBCL from Hodgkin's lymphoma was 0.968 [95% confidence interval (CI): 0.923-1.000], and an optimal cutoff of 236 U/l yielded sensitivity and specificity values of 81.6 and 100%, respectively (Fig. 3a).

# Comparison of <sup>18</sup>F-FDG PET/CT metrics between Hodgkin's lymphoma and PMBCL

Maximum tumor diameter, lesion-to-liver ratio  $SUV_{max}$ , and lesion-to-liver ratio  $SUV_{peak}$  were significantly higher (P < 0.001) in PMBCL than in Hodgkin's lymphoma, and necrosis was also significantly more frequent (P=0.001) in PMBCL than in Hodgkin's lymphoma (Table 1). AUCs of maximum tumor diameter, lesion-to-liver ratio SUV<sub>max</sub>, and lesion-to-liver ratio SUV<sub>peak</sub> were 0.866 (95% CI: 0.765-0.968), 0.875 (95% CI: 0.776-0.975), and 0.874 (95% CI: 0.771-0.976), respectively (Fig. 3b-d). Optimal cutoff values for maximum tumor diameter, lesion-to-liver ratio SUVmax, and lesion-to-liver ratio SUV<sub>peak</sub> were 9.98 cm (with sensitivity of 87.2 and specificity of 78.3%), 7.12 (with sensitivity of 94.9 and specificity of 64.3%), and 11.45 (with sensitivity of 97.4 and specificity of 64.3%), respectively. The presence of necrosis yielded sensitivity and specificity of 78.6 and 74.4%, respectively, in discriminating PMBCL from Hodgkin's lymphoma. Calcifications were present in only one patient with PMBCL and in none of the patients with Hodgkin's lymphoma, and were thus not relevant for further analysis.

#### Association between discriminatory variables

Correlations between LDH, tumor size, necrotic status, and <sup>18</sup>F-FDG uptake metrics (without considering lesion-to-liver ratio SUV<sub>max</sub> versus lesion-to-liver ratio SUV<sub>peak</sub>) were significantly (P < 0.001-0.037) weak to strong (correlation coefficients ranging between 0.309 and 0.692) (Table 2). Correlation between lesion-to-liver ratio SUV<sub>max</sub> and lesion-to-liver ratio SUV<sub>peak</sub> was significantly (P < 0.001) very strong (correlation coefficient of 0.955).

#### Discussion

The results of this study show that several noninvasive laboratory and <sup>18</sup>F-FDG PET/CT parameters are of value in differentiating mediastinal Hodgkin's lymphoma from PMBCL. Increased LDH values, larger tumor size,





<sup>18</sup>F-FDG/PET-CT in a 66-year-old woman with Hodgkin's lymphoma, who presented with an LDH level of 110 U/I. Coronal fused <sup>18</sup>F-FDG PET/CT (a) shows a mediastinal mass (arrow). Maximum axial tumor diameter was 8.1 cm. Lesion-to-liver ratio SUV<sub>max</sub> and lesion-to-liver radio SUV<sub>peak</sub> were 5.1 and 6.1, respectively. Axial fused <sup>18</sup>F-FDG PET/CT images (b–d) show the mass (arrows) without any signs of necrosis and no calcifications. CT, computed tomography; 18F-FDG, fluorine-18-fluorodeoxyglucose; LDH, lactate dehydrogenase; SUVmax, maximum standardized uptake value; SUVpeak, peak standardized uptake value.

presence of necrosis, and increased <sup>18</sup>F-FDG uptake were all found to favor PMBCL over Hodgkin's lymphoma, and are likely to reflect the more aggressive tumor biology of the former compared with the latter. Although biopsy will remain the mainstay to establish a final diagnosis, LDH level testing and <sup>18</sup>F-FDG PET/CT are routinely performed in these patients as part of their standard pretreatment workup and as part of the prognostic score [4,5]. As such, they are readily available, and may aid in the discrimination between mediastinal Hodgkin's lymphoma and PMBCL, which may particularly be useful when biopsy is inconclusive or contraindicated owing to whatever reason. Of note, although their exact interplay is still a topic of ongoing research, LDH, tumor size, necrosis, and <sup>18</sup>F-FDG uptake are biologically interconnected [14,15], which may explain why these metrics emerged in this study. In a post-hoc analysis (and not considering the expected high correlation between lesion-to-liver ratio SUV<sub>max</sub> and lesion-to-liver ratio SUV<sub>peak</sub>), significant weak to strong correlations were found between these aforementioned parameters. However, none of the correlation coefficients exceeded 0.7, which suggests that LDH, tumor size, necrosis, and <sup>18</sup>F-FDG uptake still may have independent value in differentiating mediastinal Hodgkin's lymphoma from PMBCL. Future larger studies are necessary to perform a robust multivariate analysis.

So far, there has been a lack of studies on the noninvasive differentiation between mediastinal Hodgkin's lymphoma and PMBCL. Previous work has already shown that <sup>18</sup>F-FDG uptake of aggressive non-Hodgkin's lymphoma is significantly higher than that of Hodgkin lymphoma [11,12], but although these studies enrolled 255 and 121 patients with lymphoma [11,12], they did not include any patient with PMBCL, reflecting the relative rarity of this entity. Nevertheless, the results of the present study are in line with these previous works [11,12], in that PMBCL as an aggressive non-Hodgkin's lymphoma indeed exhibits higher <sup>18</sup>F-FDG uptake than Hodgkin's lymphoma. Other new and previously unreported findings of the present study are the diagnostic value of LDH levels, tumor size, and necrosis in this setting, as mentioned previously.

This study had several limitations. First, other <sup>18</sup>F-FDGavid anterior mediastinal tumors than mediastinal Hodgkin lymphoma and PMBCL, such as germ cell tumors, thymomas, and thymic carcinomas [16,17], were not included. However, clinical and laboratory findings



ROC curves for LDH (a), maximum axial diameter of the mediastinal mass (b), lesion-to-liver ratio SUV<sub>max</sub> (c), and lesion-to-liver radio SUV<sub>peak</sub> (d), in discriminating PMBCL from Hodgkin's lymphoma. AUCs were 0.968 (95% CI: 0.923–1.000), 0.866 (95% CI: 0.765–0.968), 0.875 (95% CI: 0.776–0.975), and 0.874 (95% CI: 0.771–0.976), respectively. AUC, area under the curve; CI, confidence interval; LDH, lactate dehydrogenase; PMBCL, primary mediastinal B-cell lymphoma; ROC, receiver operating characteristic; SUV<sub>max</sub>, maximum standardized uptake value; SUV<sub>peak</sub>, peak standardized uptake value.

are known to be useful to differentiate between these entities, with the presence of B-symptoms (fever, night sweats, and weight loss) favoring the diagnosis of lymphoma, elevated serum  $\alpha$ -fetoprotein levels being suggestive of germ cell tumors, and thymoma and thymic

carcinoma commonly being associated with myasthenia gravis [16,17]. On the contrary, it should be noted that other rare lymphoma subtypes that may involve the mediastinum such as T cell, lymphoblastic, and mediastinal gray zone lymphomas were not included in this

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	Tumor size	Presence of necrosis	Lesion-to-liver ratio $\text{SUV}_{\text{max}}$	Lesion-to-liver ratio $SUV_{peak}$
LDH	0.489 <sup>a</sup> (0.001)	0.401 <sup>b</sup> (0.006)	0.321 <sup>a</sup> (0.030)	0.309 <sup>a</sup> (0.037)
Tumor size	_	0.640 <sup>b</sup> (< 0.001)	0.692 <sup>a</sup> (<0.001)	0.687 <sup>a</sup> (< 0.001)
Presence of necrosis	_	<u> </u>	0.515 <sup>b</sup> (< 0.001)	0.550 <sup>b</sup> (<0.001)
Lesion-to-liver ratio $SUV_{max}$	-	-	-	0.955 <sup>a</sup> (<0.001)

Table 2 Correlation coefficients (with *P* values between parentheses) between variables that were found to be significantly different between mediastinal Hodgkin's lymphoma and primary mediastinal B-cell lymphoma

LDH, lactate dehydrogenase; SUV<sub>max</sub>, maximum standardized uptake value; SUV<sub>peak</sub>, peak standardized uptake value.

<sup>a</sup>Spearman's correlation coefficient.

<sup>b</sup>Point-biserial correlation coefficient

study. In the rare cases where biopsy is contraindicated, the LDH and <sup>18</sup>F-FDG PET/CT findings might therefore not lead to the final diagnosis. Second, because several patients underwent <sup>18</sup>F-FDG PET/CT outside of our hospital with PET/CT systems that were possibly not EANM/EARL accredited, tumor SUV<sub>max</sub> and SUV<sub>peak</sub> had to be normalized relative to liver uptake. Third, optimal diagnostic cutoff values for LDH, maximum tumor diameter, lesion-to-liver ratio SUV<sub>max</sub>, and lesionto-liver ratio SUV<sub>peak</sub> were retrospectively determined, and may yield lower sensitivity and specificity when applied to other patients outside the current study population.

# Conclusion

LDH levels and several <sup>18</sup>F-FDG PET/CT findings (tumor size, presence of necrosis, and degree of <sup>18</sup>F-FDG uptake) are helpful in discriminating mediastinal Hodgkin's lymphoma from PMBCL.

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#### **Conflicts of interest**

There are no conflicts of interest.

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