Diagnostic Contribution of Contrast-Enhanced CT as Compared with Unenhanced Low-Dose CT in PET/CT Staging and Treatment Response Assessment of ^{18}F-FDG–Avid Lymphomas: A Prospective Study

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The aim of this study was to assess the added diagnostic value of contrast-enhanced CT (CECT) as compared with unenhanced CT (UECT) in PET/CT staging and treatment response assessment of ^{18}F-FDG–avid lymphomas. **Methods:** 170 PET/UECT scans followed by CECT scans were prospectively performed for staging (n = 85) and for treatment response assessment (n = 85) of ^{18}F-FDG–avid lymphomas, during a single session using an integrated 64-slice PET/CT scanner. CECT and UECT images were evaluated separately by 2 radiologists, whereas PET images were evaluated by 2 nuclear physicians. Nodal and extranodal UECT and CECT findings were classified according to the Lugano criteria and were successively compared with PET/CT results, considered the gold standard. In the analyzed groups, the agreement rate with the disease status determined via PET was calculated separately for UECT and CECT using the McNemar test on paired data. The added value of the contrast medium was shown by the agreement between the PET and CECT results and the lack of agreement between UECT and PET. **Results:** CECT enabled the identification of additional extranodal lesions (hepatic, muscular, and gastric) in only 3 staging group cases (3.5%), indicating different stages as compared with UECT, whereas there was absolute agreement between CECT and UECT in terms of treatment response assessment. The added diagnostic value of CECT was lower than the established threshold for clinical relevance (15%). The McNemar test indicated no statistical significance in either group. The incidental findings detected by CECT but not UECT were important for clinical management but not sufficient to alter lymphoma treatment strategy. **Conclusion:** According to our results, it might be possible to exclude CECT examination of ^{18}F-FDG–avid lymphoma from staging and treatment response assessment, with the consequent advantages of reducing radiation exposure and potential contrast-related risks.

Key Words: PET; CECT; ^{18}F-FDG–avid lymphoma; staging; treatment response

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In the Western world, lymphoma represents the fifth most prevalent tumor, with an incidence of 19–20 cases/100,000 inhabitants, with Caucasian males being at greater risk (*1*,*2*).

A major distinction can be made between Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL), with the most frequent histotypes being diffuse large B-cell lymphoma, follicular lymphoma, and HL (*3*).

In patients with lymphoma, the diagnostic pathway involves multiple radiologic and nuclear imaging examinations and a histotype-dependent follow-up (*4*). Since lymphomas are frequently ^{18}F-FDG–avid, ^{18}F-FDG PET/CT is considered the gold standard for staging and treatment response assessment (*5*), providing absolutely essential functional and metabolic information regarding lymphomatous lesions, whether morphologically altered or normal (*6*). Moreover, treatment guided by PET/CT staging results in better survival of aggressive NHL than does therapy based on contrast-enhanced CT (CECT) (*7*). Intravenous iodine contrast medium in PET/CT protocols improves identification of anatomic structures, detection of pathologic lesions, and their characterization (*8*). The advantages of contrast medium are more evident in several anatomic sites where delineation of disease from muscles, vascular structures, or the bowel is critical (*8*).

Lymphoma Staging and Treatment Response Assessment

According to the International Conference on Malignant Lymphoma (2011) (*4*), staging and treatment response assessment of ^{18}F-FDG–avid lymphomas requires PET/CT examination and baseline CECT, which should be performed during the same session (*9*). These imaging modalities are also helpful for radiation therapy planning and prognostic evaluation (*10*); further imaging is performed during therapy for interim evaluation (*11*).

PET/CT includes first the PET scan and then a low-dose unenhanced CT (UECT) acquisition, aimed to correct the attenuation of PET data and to enable anatomic correlation through image fusion. PET/UECT is then followed by a full-dose diagnostic CECT acquisition (*5*).

PET/CT imaging is interpreted according to the revised Lugano criteria, which combine information about the metabolic activity of the disease furnished by PET with the morphologic data from

CT (*4*). The Lugano criteria recommend the Ann Arbor classification for staging, whereas for the purposes of treatment response assessment they recommend the Deauville criteria for PET and the Cheson criteria for CECT (*4*,*5*,*9*).

This routine diagnostic pathway may generate several disadvantages, primarily a high cumulative radiation dose, with the potential risk of radiation-induced carcinogenesis (*12*) over the course of serial CT (staging, interim, end-of-treatment, follow-up); moreover, the repeated administration of iodinated contrast agents may lead to allergic reactions (*13*), contrast-induced nephropathy (*14*), and transient thyroid dysfunction, with potentially dangerous complications such as atrial fibrillation in hyperthyroidism and myxedema coma in hypothyroidism (*15*).

In this context, there have been very few studies on the added diagnostic value that iodine contrast injection may bring to staging or treatment response assessment in ^{18}F-FDG–avid lymphomas (*16*–*22*).

The aim of this study was to evaluate the added diagnostic value of contrast injection in staging and treatment response assessment of ^{18}F-FDG–avid lymphomas, comparing CECT with UECT and considering PET as the gold standard. Indeed, if the added diagnostic value of CECT is not clinically and statistically significant, it may be possible to leave it out of the diagnostic pathway without affecting treatment or outcomes, thereby reducing the potential contrast-related risks and superfluous radiation exposure.

MATERIALS AND METHODS

This study was conducted according to the Declaration of Helsinki; Ethics Committee approval for data collection was obtained (protocol 631/2018/Oss/AOUFe), and all subjects gave written informed consent.

The study prospectively enrolled 170 patients referred to our Oncohematology Department with a histologically confirmed diagnosis of ^{18}F-FDG–avid lymphoma over a 2-y period (between December 2017 and August 2019). All patients underwent PET/CT followed by CECT, both performed at a single session using an integrated 64-slice PET/CT scanner (mCT Biograph FlowMotion; Siemens) at our nuclear medicine department in collaboration with the hospital and university radiology unit. The exclusion criteria were an age of less than 18 y, confirmed or suspected pregnancy, breastfeeding, diabetes mellitus, an absolute contraindication for iodized contrast administration, lymphoma not ^{18}F-FDG–avid, and immunotherapy. The enrolled patients were assigned to 1 of 2 groups: a staging group for those with a first diagnosis or relapse of lymphoma, and a treatment response group, in whom the outcome ad interim or at the end of therapy was compared with a baseline examination.

PET/CT Protocol

The patients were invited to drink 500 mL of water and to rest before the scan, fasting for at least 6 h, and blood glucose levels were checked before the examination to ensure glycemia control and to limit bias caused by anomalous uptake of ^{18}F-FDG. The PET acquisition was started 60 ± 5 min after intravenous ^{18}F-FDG injection (an average of 370 MBq, with a range of 200–450 MBq), with a scan area from skull base to proximal thigh. The patients were scanned with an empty bladder and while supine with their arms raised over their head if possible. First, low-dose CT was performed (100–120 kV; 30–100 mAs with automatic tube current modulation; tube rotation time, 0.5 s; pitch, 0.8 s; slice thickness, 3 mm; reconstruction matrix, 512 × 512 at 3 mm for UECT and 5 mm for images fused with PET). Subsequently a 3-dimensional PET scan was acquired via the FlowMotion technique, requiring a total time of 12–15 min with a speed 1.10 mm/s (range, 0.8–1.7 mm/s, depending on body region and administered activity). *syngo*.via software (Siemens) was used to fuse and display PET, PET/CT, and CT scans with a 3-dimensional maximum-intensity-projection PET view. For semiquantitative analysis, a volume of interest was selected, and the contextual SUV was calculated.

CECT Protocol

After the PET/CT scan, a diagnostic CECT scan of the neck, thorax, and abdomen was acquired after a preliminary anteroposterior scout view (100–120 kV; 60–200 mAs with automatic tube current modulation; tube rotation time, 0.5 s; pitch, 0.65 s; slice thickness, 2 mm; reconstruction matrix, 512 × 512; reconstruction thickness, 2 mm) and intravenous administration of iodinated contrast agent (Omnipaque, 350 mg I/mL; GE Healthcare), modulated according to the weight of the patient, with an average flow of 3 mL/s and bolus-tracking mode. Contrast phases were established by the radiologist according to the clinical scenario, always including a whole-body portal venous phase and, when deemed necessary, also arterial or delayed phases.

Image Analysis

Two nuclear physicians evaluated the PET scans independently without knowing the CECT findings, whereas 2 independent radiologists evaluated the CECT and UECT scans without access to the PET/CT data. The operators were, however, informed of the lymphoma diagnosis. They were asked to assess staging group patients on the basis of the revised Ann Arbor/Cotswolds criteria (*4*).

Subsequently, for the treatment response group scans, the Lugano criteria were applied in a masked manner to each imaging modality, comparing the findings with a baseline acquired via the same imaging technique (corresponding to the staging examination). Higher ^{18}F-FDG uptake than background in nonphysiologic locations was considered consistent with lymphomatous tissue, according to the Deauville criteria. Nodal and extranodal findings in UECT and CECT were separately compared with PET/CT results (gold standard) for each study to assess the agreement between methods.

Statistical Analysis

In both staging and treatment response groups, the agreement rate with the disease status determined via PET was calculated separately for UECT and CECT. The Cohen κ-coefficient was applied to assess interrater reliability. The relative frequencies of agreement between PET and both UECT and CECT were compared using the McNemar test on paired data. The added value of contrast medium was considered proven when PET and CECT findings agreed but UECT and PET did not. Data were analyzed using the statistical software Stata, version 13 (StataCorp), and a P value of less than 0.05 was considered statistically significant.

RESULTS

Study Population

The study comprised 170 PET/CT and CECT scans, of which 85 were assigned to the staging group and 85 to the treatment response group. In the treatment response group, of the total of 85 patients, 50 were evaluable for interim treatment response analysis and 35 for end-of-treatment assessment. The participants in the study comprised 97 men and 73 women with a mean age of 53 y (range, 20–82 y): 41 diagnosed with HL and 129 with NHL. A deeper analysis of the population characteristics and histotypes is reported in Table 1.

Staging Group

Agreement with PET was 80% for CECT and 76.5% for UECT ($P < 0.001$ in both cases). In 82 of 85 patients (96.5%), CECT provided the same Ann Arbor stage as assigned by low-dose

TABLE 1
Characteristics of Staging and Treatment Response Groups

Characteristic	Staging (n = 85)	Treatment response (n = 85)
Mean age (y)	57.6 (range, 24–82)	48.2 (range, 20–81)
Sex		
Male	50 (59%)	47 (55%)
Female	35 (41%)	38 (45%)
HL	15 (18%)	26 (31%)
NHL	70 (82%)	59 (69%)
Diffuse large B-cell lymphoma	30 (35%)	28 (33%)
Follicular	17 (20%)	9 (11%)
Mantle cells	8 (9%)	7 (8%)
Marginal zone	2 (2%)	5 (6%)
Burkitt lymphoma	2 (2%)	7 (8%)
Others*	11 (13%)	3 (3%)
Performance status (ECOG)		
0	73 (86%)	79 (93%)
1	8 (10%)	4 (5%)
2	2 (2%)	1 (1%)
Missing	2 (2%)	1 (1%)
International Prognostic Index		
0	10 (12%)	5 (6%)
1	8 (9%)	8 (9%)
2	9 (11%)	9 (11%)
3	7 (8%)	13 (15%)
4	1 (1%)	4 (5%)
Missing	50 (59%)	46 (54%)
Lactate dehydrogenase		
Less than or equal to ULN	53 (63%)	54 (64%)
Greater than ULN	25 (29%)	29 (34%)
Missing	7 (8%)	2 (2%)
Bulky mass	13 (15%)	7 (8%)

*Peripheral T-cell lymphoma, gastric lymphoma, nasal natural-killer/T-cell lymphoma, anaplastic large cell lymphoma, indolent B-cell lymphomas, angioimmunoblastic lymphoma, high-grade B-cell lymphoma, nonspecific high-grade lymphoma.

ECOG = Eastern Cooperative Oncology Group; ULN = upper limit of normal.

UECT, and nodal findings were detected equally by CECT and UECT. In only 3 patients (3.5%) did CECT identify further extranodal lesions (hepatic, muscular, and gastric), assigning a different Ann Arbor stage to low-dose UECT. The first of these patients had HL, and CECT revealed a paravertebral, intramuscular hypodense nodular area, indicating stage IV, whereas the same area was not visible under UECT, which indicated stage III. On the PET scan, that lesion was hypermetabolic and therefore indicative of stage IV (Fig. 1). The second patient also had HL and showed several intrahepatic, hypodense nodular areas on CECT (indicating stage IV) that were not visible on UECT (which indicated stage III). At PET examination, those hepatic nodules appeared as hypermetabolic foci, indicating stage IV and thus confirming the CECT results (Fig. 2). In the last patient, who had NHL (diffuse large B-cell lymphoma), CECT revealed heterogeneous thickening of the gastric wall, indicating stage I, which was confirmed by radiotracer uptake in PET images. Conversely, since gastric wall thickening was not evident without iodine contrast medium, this patient was classified as without any abnormality on the UECT examination (Fig. 3). In all 3 patients, PET and CECT staging were concordant whereas UECT slightly underestimated the disease stage (Table 2; Fig. 4). The main reason for the discordance between CT imaging and the gold standard, PET, was that PET showed ^{18}F-FDG uptake in bone lesions that were not visible under either UECT or CECT.

Our results indicate that the added diagnostic value of CECT was very small because there was a 3.5% lack of agreement (95% CI, 0%–7.5%) between CECT and UECT staging (Table 3). This value is under the threshold considered clinically relevant (15%), and furthermore, the McNemar test showed no statistical significance ($P = 0.083$).

Examining the cases of HL (15 cases) and NHL (70 cases) separately, the respective agreement of CECT and UECT with PET was 93% and 80% in HL and 77% and 76% in NHL; for both CECT and UECT, the agreement with PET was statistically significant ($P < 0.001$). Analysis of the HL and NHL subgroups showed no difference in results (Table 4). In fact, 2 of the 3 cases of discordance between CECT and UECT staging were HL, and the use of contrast medium in these patients would not have modified the treatment strategy. Conversely, in the case of gastric NHL, CECT showing an additional lesion led to a change in treatment. In the HL group, on the other hand, the additional diagnostic value of contrast administration (13.3%; 95% CI, 0%–30.5%) was just under the threshold considered clinically relevant (15%), although the McNemar test indicated a lack of statistical significance ($P = 0.157$).

Treatment Response

In the 85 patients evaluated according to the Lugano criteria ad interim and at the end of treatment, there was absolute agreement (100%) between CECT and low-dose UECT (32 cases with complete response, 49 with partial response, and 4 with stable disease), with both being equally comparable to PET, even in the 2 different HL and NHL histotypes (Table 5). Consequently, CECT did not contribute to the therapy response assessment and may therefore be considered superfluous for this purpose. However, as expected, agreement with PET was low for both CECT and UECT (38.8%), but the difference was not statistically significant in either case ($P = 0.104$). Bone lesions were the main reason for discordance between PET and UECT/CECT, since they were not visible on CT but were revealed by ^{18}F-FDG uptake, and the enlarged lymph nodes were devoid of ^{18}F-FDG uptake. Therefore, there is no added value of CECT over UECT in terms of directing the lymphoma treatment strategy, regardless of histotype.

Incidental Findings

Finally, CECT detected some incidental findings that were not recognizable at UECT alone. These included portal vein

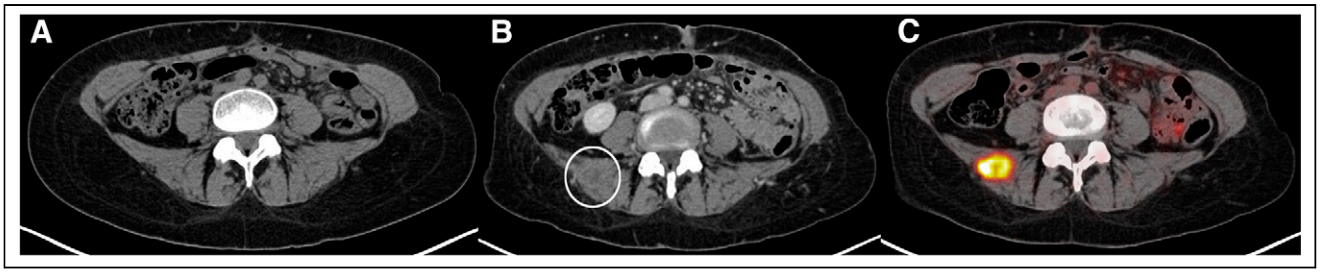

FIGURE 1. In patient with HL, UECT did not detect lesion in right paravertebral muscles (A), revealed as hypovascular nodular area (circle) by CECT (B), thereby indicating Ann Arbor stage III instead of stage IV as suggested by CECT (C) and evident as hypermetabolic focus on ^{18}F-FDG PET (C).

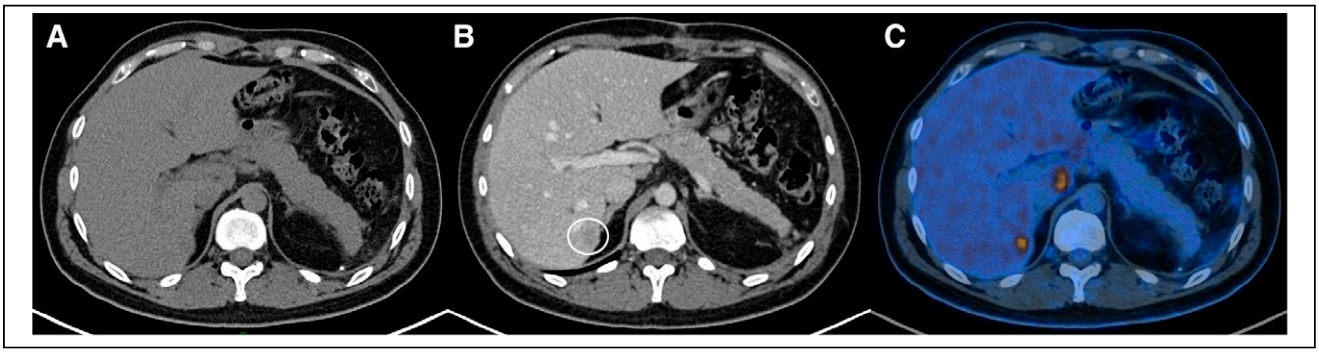

FIGURE 2. In patient with HL, UECT did not detect hepatic lesion in right lobe (A), revealed as hypodense nodular area (circle) by CECT (B), thereby indicating Ann Arbor stage III instead of stage IV as suggested by CECT and evident as hypermetabolic focus on ^{18}F-FDG PET (C).

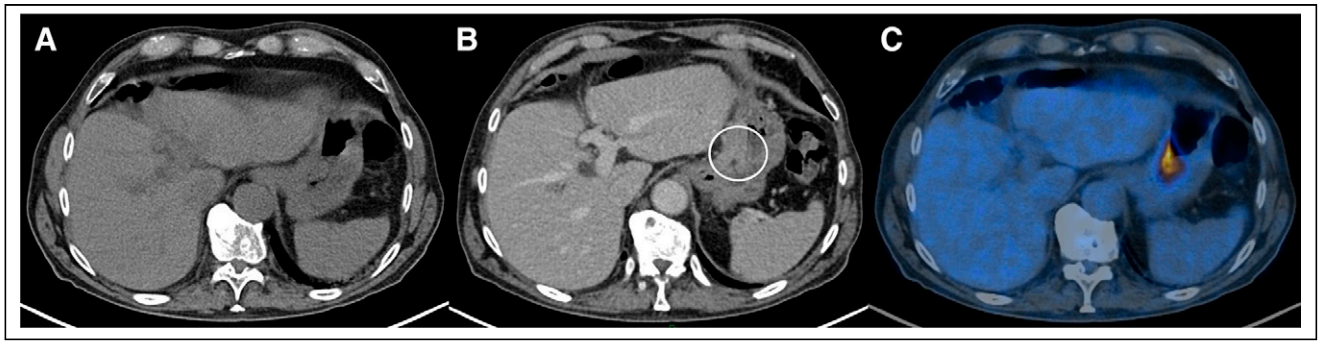

FIGURE 3. In patient with NHL, UECT did not show gastric lesion (A), revealed as thickened gastric wall (circle) by CECT (B), thereby indicating no detected abnormality instead of stage I as suggested by CECT and evident as hypermetabolic focus on ^{18}F-FDG PET (C).

thrombosis (Fig. 5), pulmonary thromboembolism (Supplemental Fig. 1; supplemental materials are available at http://jnm.snmjournals.org), and spleen infarction (Supplemental Fig. 2). None of these influenced lymphoma staging or treatment response assessment, but for obvious reasons, they did influence the overall clinical management of the affected patients.

DISCUSSION

This study investigated the additional value of CECT in comparison to UECT for both staging and treatment response assessment purposes in a group of 170 patients with ^{18}F-FDG–avid lymphoma, considering PET as the gold standard. In the staging group, CECT and UECT displayed 80% and 76.5% agreement with PET, respectively, and agreement was statistically significant in both cases. Lack of agreement was ascribable to the higher sensitivity of PET for some types of lymphomatous bone lesions as compared with UECT and CECT (*17*,*23*). Muscular, hepatic, and gastric lesions, on the other hand, were detected by both PET and CECT but were not recognizable via UECT in the patients assessed for staging. In discrimination between HL and NHL, the agreement with PET was always significantly greater than 75% for both CECT and UECT.

On closer analysis of the 3 cases (3.5%) of lack of agreement between CECT and UECT in the staging group, in the 2 HL patients the correct staging provided by CECT would not have changed the treatment strategy, whereas in the third case (i.e., NHL) the correct CECT staging led to a change in clinical management with respect to what would have been prescribed on the basis of UECT findings alone. In this light, in the HL subgroup the added diagnostic value of CECT for staging purposes was 13.5%, close to the clinically relevant threshold (15%), but this

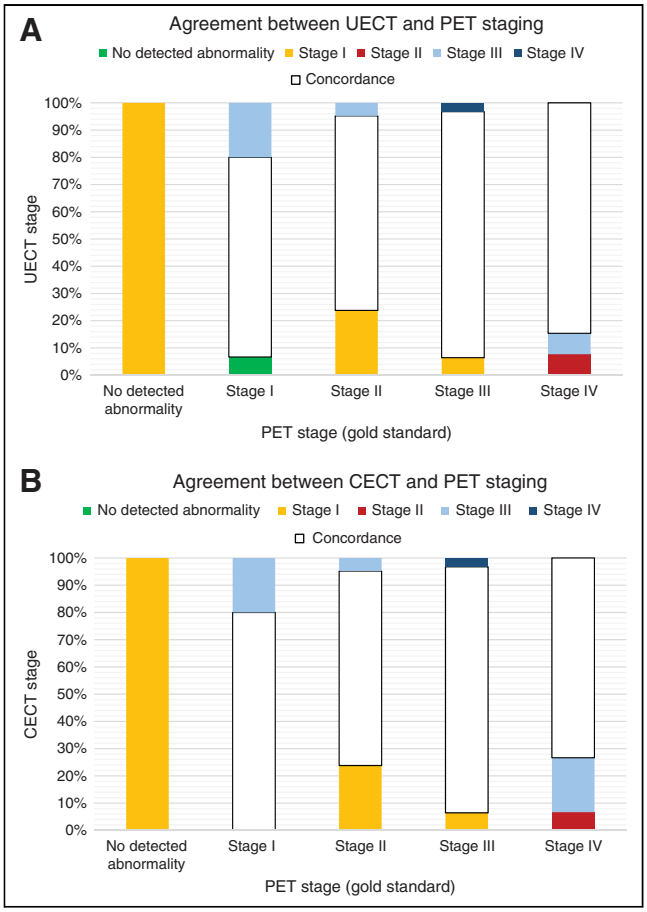

FIGURE 4. White bars representing agreement between Ann Arbor stages assigned on basis of PET as compared with 2 CT techniques: UECT (A) and CECT (B).

TABLE 2
Agreement Between CT and PET Staging According to Ann Arbor Classification

	PET					
CT	NA	I	II	III	IV	Total
UECT						
NA	0*	1	0	0	0	1
I	1	11*	5	2	0	19
II	0	0	15*	0	1	16
III	0	3	1	28*	5	37
IV	0	0	0	1	11*	12
Total	1	15	21	31	17	85
CECT						
NA	0*	0	0	0	0	0
I	1	12*	5	2	0	20
II	0	0	15*	0	1	16
III	0	3	1	28*	3	35
IV	0	0	0	1	13*	14
Total	1	15	21	31	17	85

*Case of agreement.
NA = no abnormality detected.
In 65 of 85 cases, UECT agreed with PET (76.5% agreement; 95% CI, 66.0%–85.0%; $P < 0.001$ and k = 0.676). In 20 of 85 cases, UECT disagreed with PET: in 6 patients (7%), UECT overstaged; in 14 patients (16.5%), UECT understaged. These data are plotted in Figure 4A. In 68 of 85 cases, CECT agreed with PET (80% agreement; 95% CI, 69.9%–87.9%; $P < 0.001$ and k = 0.726). In 17 of 85 cases, CECT disagreed with PET: in 6 patients (7%), CECT overstaged; in 11 patients (13%), CECT understaged. These data are plotted in Figure 4B.

value was influenced by the limited number of patients (n = 15),whereas in the larger subgroup, NHL (n = 70), this value was clearly lower than the threshold (1.4%). Therefore, a potential increased diagnostic value of CECT in HL compared with NHL should be demonstrated in a larger sample group.

On the basis of our findings, however, PET/UECT should be suggested as the imaging modality of choice for staging of ^{18}F-FDG–avid lymphomas. This conclusion is in line with that by van Hamersvelt et al. (*16*), who recommended ^{18}F-FDG PET/UECT as the primary imaging modality for staging ^{18}F-FDG–avid lymphomas after a similar study, comparing the staging findings of ^{18}F-FDG PET/UECT and CECT in a group of 29 patients newly diagnosed with ^{18}F-FDG–avid lymphoma. In that study, the stage indicated by CECT differed from that indicated by UECT on the basis of the Ann Arbor classification in 7% of patients, but without changes in therapeutic approach, thus supporting the hypothesis that iodinated contrast medium is unnecessary for staging purposes.

Indeed, another prospective study, by Rodríguez-Vigil et al. (*24*), found no difference between unenhanced low-dose ^{18}F-FDG PET/CT and contrast-enhanced full-dose ^{18}F-FDG PET/CT in 47 patients newly diagnosed with lymphoma, except that the latter technique showed fewer indeterminate findings and a higher number of extranodal lesions. UECT and CECT correlated well in terms of nodal and extranodal lesion detection, and the authors therefore concluded that unenhanced low-dose PET/CT could be used for initial imaging in lymphomas, reserving CECT for only selected cases. However, similarly to our results, they found that contrast-enhanced full-dose ^{18}F-FDG PET/CT detected important incidental findings in 2 patients (4.3%)—findings that were not observed via unenhanced low-dose ^{18}F-FDG PET/CT (*24*).

In this regard, another study, by Pinilla et al. (*25*), found comparable results regarding nodal involvement and parenchymal evaluation, bone marrow included. In unenhanced low-dose and contrast-enhanced full-dose ^{18}F-FDG PET/CT obtained for 101 patients with newly diagnosed lymphoma, the authors showed that CECT revealed important incidental findings in 6 patients (5.9%). They also concluded that there were no significant differences between the modalities in terms of initial lymphoma staging accuracy but that CECT enabled the detection of incidental findings not revealed using UECT.

However, Sabaté-Llobera et al. (*19*), who studied 28 patients with diffuse large B-cell lymphoma assessed for staging purposes via ^{18}F-FDG PET/UECT and CECT, found disagreement between the 2 techniques in 21% of cases, in half of which the treatment strategy would have been impacted. In particular, they concluded that PET/UECT is more sensitive than CECT in detecting nodal and extranodal lesions and therefore suggested that contrast administration might be avoidable. Alnouby et al. (*23*), analyzing a group of 144 patients with various lymphoma histotypes

TABLE 3
Agreement Between CECT and UECT Staging According to Ann Arbor Classification

	UECT					
CECT	NA	I	II	III	IV	Total
NA	0*	0	0	0	0	0
I	1	19*	0	0	0	20
II	0	0	16*	0	0	16
III	0	0	0	35*	0	35
IV	0	0	0	2	12*	14
Total	1	19	16	37	12	85

*Case of agreement.
NA = no abnormality detected.

TABLE 4
Agreement Between PET and UECT or CECT Staging According to Ann Arbor Classification in NHL and HL

	PET					
CT	NA	I	II	III	IV	Total
UECT						
NHL						
NA	0*	1	0	0	0	1
I	1	9*	5	2	0	17
II	0	0	10*	0	1	11
III	0	3	1	25*	2	31
IV	0	0	0	1	9*	10
Total	1	13	16	28	12	70
HL						
NA	0*	0	0	0	0	0
I	0	2*	0	0	0	2
II	0	0	5*	0	0	5
III	0	0	0	3*	3	6
IV	0	0	0	0	2*	2
Total	0	2	5	3	5	15
CECT						
NHL						
NA	0*	0	0	0	0	0
I	1	10*	5	2	0	18
II	0	0	10*	0	1	11
III	0	3	1	25*	2	31
IV	0	0	0	1	9*	10
Total	1	13	16	28	12	70
HL						
NA	0*	0	0	0	0	0
I	0	2*	0	0	0	2
II	0	0	5*	0	0	5
III	0	0	0	3*	1	4
IV	0	0	0	0	4*	4
Total	0	2	5	3	5	15

*Case of agreement.
NA = no abnormality detected.
Overstaging of 4 NHL patients on CECT and UECT compared with PET, with consequent therapeutic planning change, was due to enlarged nodes (longest diameter in axial plane > 1.5 cm) localized on both sides of diaphragm without significant PET uptake.

including those weakly avid for ^{18}F-FDG, also reported results indicating that PET/UECT assessment is more sensitive for extranodal involvement than CECT (respective sensitivity of 97% and 89.6% and respective accuracy of 91.7% and 87.5%), especially in the spleen, bone, and bone marrow, since ^{18}F-FDG highlights metabolically active areas in structures of normal morphology. Similarly, Panebianco et al. (*17*), in their study of 62 cases of newly diagnosed HL, found that CECT was less sensitive than ^{18}F-FDG PET/CT in the detection of some bone marrow lesions but more reliable in assessing hepatic tumors, whereas no difference emerged between the 2 imaging modalities in terms of detecting lung involvement; they confirmed that PET/CT allows better staging in HL through the detection of nodal lesions. Furthermore, Paone et al. (*18*) investigated the advantage of using contrast medium in end-of-treatment low-dose PET/CT to detect sites of disease in 30 patients with follicular lymphoma (agreement rate between CECT and UECT, 87%) and concluded that the clinical impact of CECT was limited to cases with suspected residual disease in mesenteric and iliac nodal stations.

Similarly, in our study the additional diagnostic value of contrast medium in staging and treatment response assessment in ^{18}F-FDG–avid lymphomas was limited to very few cases, in which CECT would have assigned a less advanced Ann Arbor stage than the gold standard low-dose ^{18}F-FDG PET/CT, and in only 1 case would it have affected the treatment pathway. The added diagnostic value, 3.5%, that we found for CECT is not statistically significant, suggesting that it may be possible to omit CECT from the process of staging ^{18}F-FDG–avid lymphomas, irrespective of their histotype. Nonetheless, should our results be confirmed in a larger sample, CECT could still have a role in HL staging, because the added value of contrast medium was close to the threshold of clinical significance.

In assessing treatment response, on the other hand, CECT did not demonstrate any advantage over UECT in ^{18}F-FDG–avid lymphomas, confirming that UECT should be the first-choice low-dose ^{18}F-FDG PET/CT imaging mode in this type of disease. The main additional information provided by contrast enhancement was the detection of extranodal involvement, which was, however, always revealed by the gold standard, PET. Although CECT allowed the detection of additional incidental findings unrelated to the lymphoma, these were clinically significant in only a few cases and did not affect lymphoma staging or treatment response assessment. Consequently, these findings did not increase the diagnostic value of CECT in the assessment of ^{18}F-FDG–avid lymphomas, with the addition of a consistent increase in radiation exposure (*26*). An advantage of our study is the use of a standardized protocol in which CECT was performed after PET/CT, preventing inaccuracies in SUV quantification due to the artifacts of iodine contrast attenuation (*26*). Both exams were executed in a single session, allowing a better overlapping of the acquired images. Some limitations of the study should be also acknowledged. First,

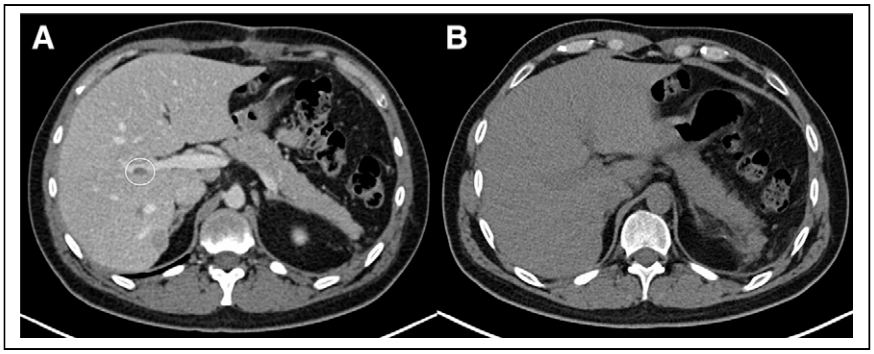

FIGURE 5. NHL patient presenting with portal vein thrombosis (circle) detected by venous-phase CECT (A) but not recognizable on UECT (B).

it was a single-center study. Second, the protocol did not estimate the effective dose delivered by PET/CT and CECT for each acquisition. Finally, the different numbers of patients in the HL and NHL subgroups make the diagnostic added value of CECT difficult to compare based on the different histotypes: in particular, in the HL population, the diagnostic added value of CECT should be calculated on a more representative sample size to confirm our data.

TABLE 5
Agreement Between PET and UECT or CECT Response Classes According to Lugano Criteria in Treatment Response Group and in HL and NHL Groups

	PET				
UECT/CECT	CR	PR	SD	PD	Total
Treatment response					
CR	31*	0	0	1	32
PR	44	2*	1	2	49
SD	4	0	0*	0	4
PD	0	0	0	0*	0
Total	79	2	1	3	85
HL					
CR	22*	0	0	1	23
PR	32	1*	1	0	34
SD	2	0	0*	0	2
PD	0	0	0	0*	0
Total	56	1	1	1	59
NHL					
CR	9*	12	2	0	23
PR	0	1*	0	0	1
SD	0	0	0*	0	0
PD	0	2	0	0*	2
Total	9	15	2	0	26

*Case of agreement.

CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease.

In 33 of 85 cases, UECT and CECT agreed with PET (38.8% agreement; 95% CI, 28.4%–50.0%), a value that is not statistically significant ($P = 0.104$ and $k = 0.038$).

CONCLUSION

According to our data, it is conceivable that, in the ^{18}F-FDG–avid lymphoma examination, CECT should be justifiable only in patients with negative PET findings and equivocal UECT findings and in patients with PET findings suspected of being nonlymphomatous lesions.

Since the most important benefit of CECT data as part of the combined PET/CT examination relates to more precise anatomic localization of disease by differentiation of the lesion from its surrounding structures, CECT might be useful for planning radiotherapy, interventional procedures, and surgery.

Limiting the field of application of CECT to the aforementioned cases could prevent undue exposure of patients, both young and elderly, to the drawbacks of repeated irradiation and iodinated contrast medium. Furthermore, this approach could also lessen the financial burden, allowing better management and more efficient distribution of resources. However, further studies are required to confirm these results in a larger cohort, in order to better select those patients who really need CECT examination, especially in cases of suspected extranodal disease.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

KEY POINTS

QUESTION: Does CECT have an added value over UECT in PET/CT staging and in assessment of response to treatment of ^{18}F-FDG–avid lymphomas?

PERTINENT FINDINGS: In this prospective study of 85 patients who underwent PET/UECT followed by CECT for staging, and 85 patients who underwent treatment response assessment of ^{18}F-FDG–avid lymphomas, in only 3.5% of patients did CECT indicate a stage different from that indicated by UECT, whereas there was absolute agreement between CECT and UECT in the assessment of treatment response.

IMPLICATIONS FOR PATIENT CARE: CECT examination in PET/CT staging and in treatment response assessment of ^{18}F-FDG–avid lymphoma may be useless.

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