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Research Article

Dual-energy CT-based iodine quantification to differentiate abdominal malignant lymphoma from lymph node metastasis

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ABSTRACT

Purpose: To investigate the value of dual-energy computed tomography (DECT)-derived iodine and fat quantification in differentiating malignant abdominal lymphoma from lymph node metastasis.

Materials and methods: In this retrospective study, 59 patients (39 men; mean age, 62.7 years) with histopathologically-confirmed diagnosis of either malignant lymphoma or lymph node metastasis were included. For each lesion, contrast-enhanced attenuation, as well as DECT-derived iodine density and fat fraction measurements were recorded. Mean attenuation and material density values were compared between malignant lymphomas and lymph node metastases. The receiver operating characteristic (ROC) curve analysis was adopted to estimate the optimal threshold for discriminating between both entities. A control group (n = 60) was analyzed for comparison of attenuation and material density values of normal abdominal lymph nodes.

Results: Assessment of DECT-derived iodine density and fat fraction values revealed significant differences between lymph node metastases (1.7 ± 0.4 mg/ml and 15.5 ± 7.3%) and malignant lymphomas (2.5 ± 0.5 mg/ml and 26.7 ± 12.2%) as well as normal lymph nodes (2.4 ± 0.8 mg/ml and 24.1 ± 10.8%) ($P \leq 0.013$). An iodine concentration of 2.0 mg/ml represented the optimal threshold to discriminate between lymphoma and lymph node metastasis (sensitivity, 87%; specificity, 89%). Moreover, a significant correlation was found between iodine concentration and fat fraction for both lymphomas and lymph node metastases ($P = 0.001$).

Conclusion: DECT enables characterization of abdominal masses as derived iodine and fat fraction values differ significantly between malignant abdominal lymphomas and lymph node metastases.

1. Introduction

The diagnosis of abnormal lymph nodes using computed tomography (CT) is commonly based on the anatomical lymph node size [1]. Larger lymph nodes and lymph node conglomerates are more likely to be malignant [1–3]. However, threshold sizes to define abnormal abdominal lymph nodes vary in the literature [1–5]. In general, lymph nodes with a short axis diameter of ≥10 mm or with a long axis diameter ≥15 mm are considered pathological [2–5]. The integration of positron emission tomography (PET)/CT into routine oncologic imaging has further improved assessment of lymph nodes and facilitated functional evaluation of disease behavior, metabolic response to therapy, and detection of disease recurrence [6]. Therefore, PET/CT is currently considered the most reliable functional imaging technique but it is more expensive and less available than CT. Nevertheless, the differentiation between malignant lymphomas, lymph node metastases, and normal lymph nodes remains difficult.

Dual-energy CT (DECT) allows for material decomposition analysis based on the differences in absorption characteristics for different elements between the two X-ray beam energies [7]. This technique has shown favorable results in oncological imaging regarding tumor characterization and therapy response [8–10]. Iodine quantification provides a more accurate metric of differences in blood supply between different tumors because it is not affected by the confounding factors that affect attenuation measured in Hounsfield units [11,12]. In this context, a recent study showed that iodine measurements can contribute to the differentiation of accessory spleen from lymph nodes [13]. However, this approach has not been investigated for the

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differentiation between malignant lymphoma and lymph node metastasis so far. Moreover, the distinction between malignant lymphoma and lymph node metastasis is of essential clinical importance because the two entities follow diverse diagnostic and therapeutic pathways. Improvements in the characterization of suspect lymph node conglomerates have the potential to avoid additional procedures such as follow-up examinations, imaging with different modalities, or invasive biopsies.

Therefore, the purpose of our study was to investigate whether contrast-enhanced DECT with material decomposition technique is able to distinguish lymphoma from lymph node metastases.

2. Material and methods

2.1. Study population

This retrospective single-center study was approved by the institutional review board of our university hospital and the required written informed consent was waived. A computerized search was performed to find patients with histologically-confirmed abdominal lymphoma or lymph node metastasis who had undergone abdominal DECT on a third-generation dual-source DECT scanner (SOMATOM Force, Siemens Healthcare, Forchheim, Germany) between November 2015 and August 2017. The search yielded data of 83 patients who had undergone contrast-enhanced DECT, with a final diagnosis of malignant lymphoma or lymph node metastasis. None of the patients included in the present study received chemotherapy before the DECT examination. Patients with variations from the standard contrast media injection protocol (n = 6), as well as examinations with a lack of an adequate reference standard (n = 18), were excluded. The final study population consisted of 59 patients (mean age, 62.4 ± 16.3 years; range, 29–95 years) including 39 men (mean age, 62.9 ± 16.6 years; range, 29–95 years) and 20 women (mean age, 61.4 ± 15.8 years; range, 30–84 years). The mean body mass index of our study cohort was 26.2 ± 4.7 kg/m^2 (range, 15.1–35.7 kg/m^2) (Table 1).

In addition, a similarly sized control group of patients without a history or diagnosis of malignancy or acute inflammation and non-enlarged (≤ 10 mm diameter) abdominal lymph nodes, (n = 60; mean age, 62.0 ± 15.7; range, 25–89 years) who had been scanned during the same time interval, consisting of 40 men (mean age, 61.8 ± 14.9; range, 25–89 years) and 20 women (mean age, 62.5 ± 17.3; range, 31–85 years), was aggregated to assess iodine density and fat fraction values of normal lymph nodes. The patients were matched by sex, age, body mass index, and clinical inclusion criteria. A flowchart of the study population enrollment following Standards for Reporting Diagnostic Accuracy Studies (STARD) is shown in Fig. 1.

Table 1
Patient characteristics.

Characteristics	Value
Age (years)	62.4 ± 16.3[a]
Male patients (n)	39
Female patients (n)	20
BMI (kg/m^2)	26.2 ± 4.7 [a]
Malignant lymphomas (n)	**23 (92)**
- Non-Hodgkin lymphoma (n)	19 (74)
- Hodgkin lymphoma (n)	4 (18)
Lymph node metastases (n)	**36 (103)**
- Colon cancer (n)	10 (27)
- Prostate cancer (n)	7 (17)
- HCC (n)	5 (12)
- RCC (n)	4 (16)
- Pancreas cancer (n)	3 (10)
- NET (n)	2 (8)
- Gastric cancer (n)	2 (5)
- Ovarian cancer (n)	2 (3)
- Cholangiocarcinoma (n)	1 (5)

[a] Data are means ± standard deviation. The number of investigated lesions is shown in parentheses. HCC = hepatocellular carcinoma; RCC = renal cell carcinoma; NET = neuroendocrine tumor.

2.2. DECT imaging technique

All contrast-enhanced CT examinations were performed on the same third-generation dual-source DECT scanner (SOMATOM Force, Siemens) using a standardized single-phase protocol. After the acquisition of an anteroposterior digital scout radiograph, image acquisition during the portal-venous phase started automatically 70 s after the beginning of the contrast material injection in a craniocaudal direction during inspiratory breath-hold. A nonionic contrast agent (Imeron 350, Bracco, Milan, Italy) at a dose of 1.2 ml per kilogram body weight with a maximum of 120 ml was injected with a flow rate of 3 ml/s through a peripheral vein of the forearm [14,15]. Settings for the DECT mode were as follows: tube A 90 kV, reference current-time product of 190 mAs per rotation; tube B Sn150 kV with tin filter, 95 mAs per rotation. Furthermore, rotation time was 0.5 s, pitch was set to 0.6, and collimation was 2 × 192 × 0.6 mm. Scans were acquired using attenuation-based tube current modulation (CARE Dose 4D, Siemens). The volume CT dose index ($CTDI_{vol}$) and the dose length product (DLP) of each patient were recorded for an estimation of the radiation dose. Images were reconstructed with third-generation advanced modeled iterative reconstruction (ADMIRE, Siemens; strength level, 3) with a medium smooth reconstruction kernel (Br40).

From the dual-energy acquisition, the scanner generates images with a weighted average that are based on data from both detectors by using 60% of the information provided by the low-kilovolt source and 40% from the high-kilovolt spectrum. These images approximate the image quality of a standard 120-kV scan of the abdomen [16,17]. All DECT series were reconstructed as axial and coronal reformats, with 3.0 mm slice thickness and 2.0 mm slice gap on a dedicated DECT workstation (syngo.via, version VB10B, Siemens). DECT material decomposition images were reconstructed on the same workstation to calculate the value of absolute iodine uptake related to tumor size (mg/ml) and fat fraction.

2.3. Reference standard

In patients with malignant lymphoma, the final diagnosis was based on histopathological analysis of lymph node biopsy (n = 15) or lymph node resection (n = 8). In the group of patients with lymph node metastasis, all patients had a history of a primary malignancy (Table 1). In compliance with RECIST 1.1, lymph nodes were only considered abnormal if the short axis exceeded 1.0 cm [2,3,5]. PET/CT data were used as the reference standard for 10 cases of patients with abdominal lymph node metastasis. Furthermore, 26 patients with lymph node metastases were evaluated with follow-up CT examinations. These lesions showed a rapid interval growth defined as an at least 20% increase in size of the transverse maximum diameter within 3 months at follow-up CT (mean follow-up, 4 months; range, 3–10 months). In the control group, patients did not have a history of primary malignancy, suspected malignancy, or acute inflammation. Lymph nodes were considered normal when all radiological and clinical data revealed normal findings and lymph nodes were not enlarged (< 1.0 cm short axis diameter). The final diagnosis was determined by two experienced radiologists with 5 and 7 years of experience in abdominal CT imaging who evaluated all available clinical data and were blinded to the results of the dual-energy CT data analysis.

2.4. Image analysis

All measurements were performed by a radiologist with 4 years of experience in abdominal imaging who was blinded to the final