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# Original article

# Retrospective evaluation of ultrasound-indeterminate renal multilocular cystic masses by using neutrophil-lymphocyte ratio and computed tomography

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#### Abstract

**Purpose:** To evaluate the clinical usefulness of neutrophil-lymphocyte ratio (NLR) in differentiating the ultrasound-indeterminate renal multilocular cystic masses (RMCM) in comparison with computed tomography (CT) and whether NLR has additional benefits to CT on sensitivity of detecting the malignant.

Materials and methods: Overall, 93 patients who underwent normal ultrasound with a conclusion of indeterminate RMCM were examined by NLR and CT within 30 days before surgery or follow-up from March to September 2014 at PLA General Hospital and enrolled in this retrospective study. Logistic regression model was performed to find independent predictors for differentiating true nature of RMCM; differences in the validity parameters and diagnostic power of CT, NLR, and their combination were compared using McNemar tests and AUC model, respectively.

**Results:** The final diagnoses of the 93 patients consisted of 36 patients with benign complex cysts, 16 with multilocular cystic renal cell carcinoma, 9 with multilocular cystic nephroma, and 32 with clear cell renal cell carcinoma. Higher NLR were strongly associated with malignant masses. Multivariate logistic regression analysis revealed that NLR could be an independent predictor for differentiating true nature of these masses (OR = 3.617; 95% CI: 1.219-10.727; P = 0.020). For detecting the malignant masses, the sensitivity, specificity, and accuracy were 71.9%, 80.6%, and 75.3% for CT and 57.9%, 88.9%, and 69.9% for NLR under cutoff value of 2.31, respectively, whereas those of CT + NLR were 89.5%, 69.4%, and 81.7%. No significant difference was found between CT and NLR in sensitivity (P = 0.185), specificity (P = 0.549), and accuracy (P = 0.428). But the sensitivity of CT + NLR was significantly higher than those of CT (P = 0.002) and NLR (P < 0.001), respectively; AUC model analysis indicated that CT + NLR got the largest area of 0.795 (P < 0.001, 95% CI: 0.693–0.896) in comparison with those of CT (area = 0.795, P < 0.001, 95% CI: 0.661–0.864) and NLR (area = 0.734, P < 0.001, 95% CI: 0.631–0.836).

Conclusions: Given that NLR, under cutoff value of 2.31, had no diagnostic difference with CT in evaluating the ultrasound-indeterminate RMCM. However, combination of CT and NLR could increase the sensitivity of detecting malignant masses and acquire the best diagnostic power. Prospectively larger cohort and multicenter studies are still necessary. © 2016 Elsevier Inc. All rights reserved.

Keywords: Renal multilocular cystic masses; Ultrasound; Neutrophil-lymphocyte ratio; CT; Diagnosis

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#### 1. Introduction

Most renal multilocular cystic masses (RMCM) are asymptomatic [1] and are usually found incidentally during regular physical examinations. The Bosniak classification system is routinely used to define these masses through imaging studies [2]. However, this classification system is limited by several anthropic factors and nonanthropic factors in clinical work. For example, in ultrasound tests, differences in the criteria adopted, ages and skills of physicians, and sensitivity levels for recognizing pathological appearances, particularly for similar multilocular complex masses, result in challenges in identifying whether a mass is benign or malignant [3]. Even if computed tomography (CT) can improve diagnostic rate and discriminate parts of RMCM according to their CT values, enhanced, and unenhanced phases, it cannot clearly detect a slight enhancement in low-grade renal cell carcinoma (RCC); some small simple cysts may present pseudoenhancement, and some benign hemorrhagic and inflammatory cysts may exhibit complex appearances resembling those of malignant masses [4-6]. In addition, CT is still unobtainable for most primary community medical facilities. Therefore, another convenient and efficient predictor is imperative to improve the evaluation of the true nature of RMCM and avoid treatment delays.

According to Coussens and Werb [7], and Whiteside [8], systemic inflammatory responses are closely related to the carcinogenesis and to the development and prognosis of cancers; they can also be used to independently predict the clinical state and outcome of various neoplasms. In particular, neutrophil-lymphocyte ratio (NLR) has been proposed as a reliable and easily accessible marker for evaluating and differentiating between benign masses and malignant masses, presenting such advantages as low cost and absence of radiation and nephrotoxicity [9,10]. Viers et al. [11] conducted a study involving 2,402 patients with RCC and found that an elevated NLR was associated with RCC pathology, high-grade tumors, and aggressive histological subtypes of cancer and could be useful in predicting malignancy and guiding cancer management. Sejima et al. [12] also found that the NLRs of the late recurrence group were significantly lower than those of the early recurrence group, indicating that NLRs were higher among patients with advanced RCC; they also found that patients with low NLRs tended to have a late recurrence and relatively longer survival. However, the study of Viers et al. [11] was unable to accurately rule out other influential factors that could significantly affect the inflammatory profiles of the patients. Moreover, only few studies have directly compared the diagnostic difference among NLR, CT, and even their combination, which could provide information of RMCM from totally different perspectives and help us know and diagnose these masses more accurately.

Therefore, the aim of our study was to assess the clinical usefulness of NLR in differentiating the ultrasound-indeterminate RMCM in comparison with CT and whether

NLR has additional benefits to CT on sensitivity of detecting the malignant.

#### 2. Materials and methods

#### 2.1. Patients

This study is a single-institution retrospective study approved by the institutional review board of PLA General Hospital. In this study, the following selection criteria were adopted: (1) the patient was RMCM-specific; (2) the lesion of patient was incidentally found by physical examination, or the patient had focal malaise around the kidneys; (3) the patient had no acute or chronic inflammation in any system within latest 2 weeks; (4) the patient had not taken antibiotics within latest 2 weeks; (5) the patient had no immune diseases; and (6) the patient had no hematological diseases. We searched the radiological and pathological databases and medical records from the Urology Department of the PLA General Hospital to identify 122 patients with original indeterminate diagnoses on ultrasound findings. Final diagnosis obtained by histology or contrast enhanced ultrasound plus CT with a follow-up at least 12 months. However, 1 patient with missing pathological slide, 5 patients without contrast-enhanced CT images, 2 patients with acute nonspecific inflammation, 2 patients with hematologic system diseases, 6 patients without regular blood tests, and 13 patients without complete follow-up and conclusive diagnoses were excluded from this study. Therefore, only 93 patients were enrolled and all of them have sporadic, unilateral masses; regular blood tests and CT examinations were done within 30 days before partial nephrectomy or followup. All regular blood tests and CT results were provided by a single laboratory and department of radiology, respectively. The pathological features of the patients were studied according to the staging system of the American Joint Committee on Cancer [13] and reviewed by a single pathologist/genitourinary pathology specialist who was blinded to the radiological outcomes and NLR results.

#### 2.2. Imaging techniques

## 2.2.1. Ultrasound technique

Ultrasound was performed with a Philips iU Elite or iU22 ultrasound machine. The baseline of the kidneys was presented in the fundamental mode and in grayscale with a multifrequency C5-1 convex array probe with harmonics (scanning parameters: 3–5 MHz; MI = 1.1; TIS = 1.2) to identify the nodules. Color Doppler examination (scanning parameters: color frequency = 2.5 MHz, color gain = 80%) was performed to evaluate intratumoral vascularity.

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