European Journal of Radiology 85 (2016) 48–54

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Qualitative, quantitative and combination score systems in differential diagnosis of breast lesions by contrast-enhanced ultrasound

YongMei Wang[a], Wei Fan[b], Song Zhao[a], Kai Zhang[a], Li Zhang[c], Ping Zhang[c], Rong Ma[a,*]

[a] Department of Breast Surgery, Qilu Hospital of Shandong University, Jinan, China
[b] Department of Gastroenterology, Qilu Hospital of Shandong University, Jinan, China
[c] Department of Health Care Ultrasound, Qilu Hospital of Shandong University, Jinan, China

ARTICLE INFO

Article history:
Received 7 August 2015
Received in revised form 14 October 2015
Accepted 27 October 2015

Keywords:
Breast diseases
Differential diagnosis
Score system
Contrast-enhanced ultrasound

ABSTRACT

Objective: To assess the feasibility of score systems in differential diagnosis of breast lesions by contrast-enhanced ultrasound (CEUS).
Methods: CEUS was performed in 121 patients with 127 breast lesions by Philips iU22 with Sonovue as contrast agent. Pearson Chi-square χ^2 test, binary logistic regression analysis and Student's *t*-test are used to identify significant CEUS parameters in differential diagnosis. Based on these significant CEUS parameters, qualitative, quantitative and combination score systems were built by scoring 1 for benign characteristic and scoring 2 for malignant characteristic. Receiver operating characteristic (ROC) curve was applied to evaluate the diagnostic efficacy of different analytical methods.
Results: Pathological results showed 41 benign and 86 malignant lesions. Qualitative analysis and logistic regression analysis showed that there are significant differences in enhancement degree, enhancement order, internal homogeneity, enhancement margin, surrounding vessels and enlargement of diameters ($P < 0.05$) between benign and malignant lesions. Quantitative analysis indicated that malignant lesions tended to show higher peak intensity (PI), larger area under the curve (AUC) and shorter time to peak (TTP) than benign ones ($P < 0.05$). Qualitative score systems showed higher diagnostic efficacy than single quantitative CEUS parameters. The corresponding area under the ROC curve for qualitative, quantitative and combination score systems were 0.897, 0.716 and 0.903 respectively. *Z* test showed that area under the ROC curve of quantitative score system was statistically smaller than that of other score systems.
Conclusions: Quantitative score system helps little in improving the diagnostic efficacy of CEUS. While qualitative score system improves the performance of CEUS greatly in discrimination of benign and malignant breast lesions. The application of qualitative could develop the diagnostic performance of CEUS which is clinically promising.

1. Introduction

Despite advances in diagnosis and treatment, breast cancer is still one of the leading causes of death for women [1,2]. Early diagnosis is crucial to determine the future therapy and prognosis for patients [3]. Angiogenesis plays an important role in the development of breast cancer, including growth and metastasis [4]. Contrast-enhanced ultrasound (CEUS) imaging with microbubble contrast agents has created a significant opportunity for visualization of the microcirculation within the lesion, and thus makes it possible to improve the diagnostic accuracy of breast cancer preoperatively and non-invasively [5–7].

Previous studies have proven many characteristics detected by CEUS being helpful in breast disease diagnosis and correlated to some prognostic factors of breast cancer [8–10]. Qualitative assessment concerns enhancement patterns, including enhancement degree, enhancement order, the presence of blood perfusion defect, internal homogeneity and so on [8,11,12]. Quantitative analysis mainly concerns time–intensity curves made by special software. The curves reflect the enhancement progress by parameters such as time to peak, and peak intensity [6,10,11]. However, the significance of some CEUS characteristics is still controversial and

Abbreviations: CEUS, contrast-enhanced ultrasound; BI-RADS, breast imaging reporting and data system; RT, rising time; PI, peak intensity; MTT, mean transit time; AUC, area under the curve; WIS, wash-in slope; TTP, time to peak; ROC, receiver operating characteristic.

* Corresponding author. Fax: +86 531 82959051.
E-mail addresses: wangyongmei-123@163.com (Y. Wang), fanweitanzhen@sina.com (W. Fan), wshsongsong@126.com (S. Zhao), zk0827019@163.com (K. Zhang), 15063397202@163.com (L. Zhang), zpql_2014@126.com (P. Zhang), marongw2000@163.com (R. Ma).

http://dx.doi.org/10.1016/j.ejrad.2015.10.017
0720-048X/

the effectiveness of breast CEUS remains unsatisfying. Lack of clear and systematic diagnostic criteria limits the clinical application of breast CEUS.

In our opinion, an objective score system is essential because one parameter cannot completely reflect the variable aspects of breast lesions. The incorporation of different and related significant CEUS characteristics might allow for the development of a better metric to improve the diagnostic performance of breast CEUS. The purpose of our study was to build score system based on single CEUS parameter and compare the diagnostic efficacy between them. We then attempted to provide a practical evaluation system for clinical assessment of breast tumor by CEUS.

2. Materials and methods

2.1. Patient population

Approval was obtained from the ethics committee of our hospital for this study. All patients involved were informed of the possible complications of CEUS and signed an informed consent before the CEUS examinations.

From January 2013 to March 2015, CEUS was performed to a total of consecutive 121 patients. All patients were selected on the basis of suspicion of breast lesions classified as BI-RADS 3–5, according to the Breast Imaging Reporting and Data System (BI-RADS) of the American College of Radiology, on conventional ultrasound or mammography. When a patient had more than one lesion in the same breast, only the largest one or most suspicious one on conventional ultrasound was evaluated. Exclusion criteria: patients with contraindications to contrast medium, such as a history of cardiac failure, respiratory disorders and hypersensitivity. Pregnant or nursing women were also excluded.

Among these 121 patients (age range, 26–74 years; mean ± SD, 47.6 ± 9.1 years), 115 patients had a unilateral lesion and 6 patients had bilateral tumors. Thus, the final analysis included 127 solid breast masses (diameter range, 0.5–5.7 cm; mean ± SD, 2.0 ± 0.9 cm). The diagnoses for all these 127 lesions were confirmed by histopathologic examination with specimens obtained by a surgical resection or biopsy.

2.2. Contrast-enhanced ultrasound examination

All patients were detected by conventional ultrasound, observing the diameter, shape, boundary, echoing feature and color Doppler flow imaging information of breast lesions. During conventional ultrasound scanning, the maximal tumor diameter was chosen as the ideal plane for CEUS, with the patient in a supine position and the probe stabilized manually.

A Philips iU22Color Ultrasound system (Philips, Seattle, WA, USA) with Philips C5-1 probe was used in this study. Machine parameters were adjusted so that the mechanical index was 0.06. Contrast agent SonoVue (Bracco, Plan-Les-Ouates, Switzerland) was reconstituted by the addition of 5 ml sterile normal saline and 25 mg of lyophilized powder. Every patient received an injection of 2.4 ml of contrast agent as a bolus followed by a flush of 5 ml saline solution through a 21-G catheter and a three-way connector via the antecubital vein in every examination. The entire CEUS process for each patient was recorded from the start of the injection until no apparent agent could be observed.

2.3. Image analysis

All examinations were recorded in a compute and analyzed both qualitatively and quantitatively by two investigators with more than two years of experience with breast CEUS. When these two investigators disagreed in some point, another investigator was invited to make the final decision. The qualitative characteristics included enhancement degree, enhancement order, internal homogeneity, enhancement margin, enhancement shape, local blood perfusion defect, surrounding vessels and enlargement of diameters.

(1) Enhancement degree (2 types): Compared with surrounding normal breast tissue at the peak time, classified into hypo-enhancement or iso-enhancement, and hyper-enhancement.
(2) Enhancement order (2 types): Centrifugal enhancement (enhancement originating from the center of the lesion and developing centrifugally) or diffused enhancement, and centripetal enhancement (enhancement originating from the periphery of the lesion and developing centripetally).
(3) Internal homogeneity (2 types): Homogeneous enhancement, heterogeneous enhancement.
(4) Enhancement margin (2 types): Well defined (>50% of the lesion circumference was clearly visible), poorly defined (<50% of the lesion circumference was clearly visible).
(5) Enhancement shape: Regular and irregular.
(6) Presence or absence of blood perfusion defects (Fig. 2c,e).
(7) Surrounding vessels: Presence or absence of peripheral and penetrating vessels.
(8) Enlargement of diameter: Compared with the corresponding values measured in conventional ultrasound, when both the length and the width measured in CEUS enlarged, or either of them enlarged for 3 mm or more, we defined it as enlarged.

Quantitative analysis includes wash-in and wash-out patterns of the contrast agent which were analyzed with quantification software. For each lesion, the video from the 1 s to the 120 s second was taken into study. The region of interest was depicted along the boundary of each lesion. The parameters of the time-intensity curve, obtained with Philips built-in analysis software (QLAB 9.0^{TM} Philips Medical System, Seattle, WA, USA), were rising time (RT), peak intensity (PI), mean transit time (MTT), area under the curve (AUC), time from peak to one half, wash-in slope (WIS) and time to peak (TTP).

2.4. Histopathology

All the lesions underwent surgical resection or biopsy, followed by the histopathological examination. The histopathological diagnosis was considered as the gold standard. CEUS findings were analyzed and compared with the final histopathological diagnoses.

2.5. Statistical analysis

SPSS Version 20.0 software was used for statistical analysis. Qualitative data were analyzed with the Pearson Chi-square χ^2 test and binary logistic regression analysis with stepwise forward variable selection was used to choose the final qualitative parameters which were included in the qualitative score system (P value for entry and removal were 0.05 and 0.1 respectively). The Student's t-test for independent samples was applied to check for a statistical difference of the quantitative parameters between benign and malignant breast lesions. Qualitative, quantitative and combination score systems were built to incorporate different parameters together in differential diagnosis. We evaluate lesions from all characteristics which are included in the score system and score 1 or 2 for each one. Score 1 was given if the lesion showed signs of benign, otherwise a score of 2 was given. The diagnostic values of scoring systems were evaluated by receiver operating characteristic (ROC) curve analysis. The areas under the 3 curves were compared using