Ultrasound in Med. & Biol., Vol. ■■, No. ■■, pp. ■■–■■, 2017

0301-5629/$ - see front matter

https://doi.org/10.1016/j.ultrasmedbio.2017.12.001

● *Original Contribution*

ASSESSING RISK CATEGORY OF BREAST CANCER BY ULTRASOUND IMAGING CHARACTERISTICS

Qiang Guo,*,† Lei Zhang,† Zhixin Di,† Chunping Ning,‡ Zhiwu Dong,§ Ziyao Li,† Dongmo Wang,† Chong Liu,† Ming Zhao,† and Jiawei Tian†

* Department of Ultrasound Medicine, Jinshan Branch of Shanghai Sixth People's Hospital, Shanghai Jiaotong University, Shanghai, China; † Department of Ultrasound Medicine, Hospital of Harbin Medical University, Heilongjiang, China; ‡ Department of Ultrasound, Hospital of Qingdao University, Medical College, Qingdao, China; and § Department of Laboratory Medicine, Jinshan Branch of Shanghai Sixth People's Hospital, Shanghai Jiaotong University, Shanghai, China

(*Received* 8 *June* 2017; *revised* 3 *November* 2017; *in final form* 3 *December* 2017)

Abstract—The purpose of our study was to assess the potential clinical value of ultrasound imaging in predicting risk category in patients with breast cancer. Three hundred thirty-six patients were enrolled and divided into a high-risk group (99, 29.5%) and mid- to low-risk group (237, 70.5%) according to the St. Gallen risk criteria. All data were retrospectively collected to analyze correlations between ultrasound features and risk category. The results revealed that the ultrasound features of irregular shape ($p = 0.002$), vertical growth orientation ($p = 0.002$), angular contour ($p = 0.022$) and high color Doppler flow imaging grade ($p = 0.001$) tended to be present in images of the high-risk group. Therefore, tumor ultrasound features should be recognized as an ideal option for determination of risk category in patients with breast cancer. (E-mail: jwtian2004@163.com)

Key Words: **Ultrasonography, Breast neoplasms, Recurrence, Prognosis, St. Gallen, Lymphatic metastasis.**

INTRODUCTION

Even after systemic treatment, patients with breast cancer frequently have a post-operative recurrence or metastasis, which is a disastrous event resulting in a large number of deaths in women worldwide. There were 231,840 newly diagnosed cases of invasive breast cancer and 40,290 breast cancer deaths in the United States in 2015 (DeSantis et al. 2016). Breast cancer recurrence or metastasis reflects tumor aggressiveness and predicts cancer-related death to some extent (Rausei et al. 2010). Patients who have a recurrence or metastasis of breast cancer progress to death five to seven times faster than those without a recurrence or metastasis (Chairat et al. 2014). The 15-y breast cancer mortality rate was 59% in patients with a recurrence of breast cancer (Sopik et al. 2016). Therefore, there is an urgent need to identify the features predicting risk category in breast cancer patients to improve treatment planning and outcomes of these patients (Martei and Matro 2015).

As is known, breast cancer is a heterogeneous disease with diverse pathology and immunohistochemistry (IHC). Today, a variety of information resources help clinicians to make treatment decisions for improving outcomes. Based on the information resources, especially post-operative risk categories, different therapeutic programs can be initiated in patients with breast cancer. The application of post-operative pathology to assessment of clinical outcomes and prognosis gives patients with breast cancer an advantage (Martei and Matro 2015). Other methods, such as gene expression profiles (Chairat et al. 2013; Dowsett et al. 2015; Millar et al. 2009; Sainsbury et al. 1987), Adjuvant! Online (Engelhardt et al. 2017), Oncotype DX Recurrence Score (Nguyen et al. 2014) and the Mamma Print 70-gene expression assay (Saghatchian et al. 2013), have been evaluated and used to improve treatment plans for breast cancer. However, the aforementioned post-operative assessment methods are based mainly on tumor tissue specimens obtained in surgeries that severely harmed patients.

If a patient's risk category can be predicted before surgery, especially with a non-invasive method, that patient may benefit from an early pre-treatment plan. Ultrasound

Address correspondence to: Jiawei Tian, Department of Ultrasound Medicine, Second Affiliated Hospital of Harbin Medical University, No. 246 Xuefu Road, Nangang District, Harbin, 150086, Heilongjiang Province, China. E-mail: jwtian2004@163.com

Conflicts of Interest: The authors have no conflict of interests to declare.

is an important imaging modality that can vividly reflect the characteristics of breast tumor growth and differentiate malignant from benign lesions (Shi et al. 2015). The correlation between molecular biological expression and ultrasound features of breast cancer has also been studied (Au-Yong et al. 2009; Li et al. 2014, 2016; Zhang et al. 2015). Several studies have revealed that some ultrasound imaging features of breast cancer are significantly related to molecular markers such as estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) (Cao et al. 2014; Lamb et al. 2000) and even the molecular subtypes of luminal A, luminal B and basal-like (Li et al. 2016; Zhang et al. 2015). However, to date, a correlation between ultrasound features and risk category in breast cancer has not been illustrated.

Since 1978, the St. Gallen International Expert Consensus has provided the general principles and guidelines for the adjuvant therapy of breast cancer. In recent decades, the recommendations updated every 2 y by St. Gallen meetings have been increasingly considered key criteria in the treatment of breast cancer (Jackisch et al. 2015). St. Gallen risk categories were issued by the St. Gallen meeting in 2007. Patients with breast cancer are classified into high-, intermediate- and low-risk categories based on age, histologic grade, IHC, axillary lymph node status, and other factors (Goldhirsch et al. 2007). Risk categorization is convenient, accurate and practical for patients with breast cancer, improving management of treatment and serving clinicians worldwide as a valuable method for determining prognosis (Bauer et al. 2010; Goldhirsch et al. 2007; Koornstra et al. 2015; Rabaglio et al. 2007; Shimizu et al. 2015). Therefore, the St. Gallen risk criteria were employed as a reference standard for categorization of patients. In this study, we evaluated the correlation between ultrasound features of breast cancer and St. Gallen risk categories and established a regression model based on the ultrasound features.

METHODS

Ethical approval

All procedures performed in this study were in accordance with the ethical standards of the 1964 Helsinki Declaration and were approved by the ethics committee of the Second Affiliated Hospital of Harbin Medical University. Formal consent by the ethics committee was not required owing to the retrospective study design, noninvasive nature and use of anonymous data.

Written informed consent was obtained from all patients recruited in this study.

Patients

The retrospective study comprised 336 consecutive patients who underwent mastectomy and axillary clearance at the Second Affiliated Hospital of Harbin Medical University from May 2009 to August 2011. Postoperatively, adjuvant radiotherapy, chemotherapy or hormone treatment was administered based on tumor stage and pathology results. The following criteria were used to include patients: (i) a single and unilateral breast cancer; (ii) complete results of pathologic diagnosis, immunohistochemical molecular markers and ultrasound examinations; (ii) telephone numbers or e-mail addresses and follow-up data for physical examinations, laboratory tests, and imaging. Patients who have undergone treatment before surgery or who had metastases in multiple organs were excluded. Patients were divided into a high-risk group and a mid- to low-risk group according to the St. Gallen criteria.

St. Gallen risk criteria

Patients assigned to the high-risk category had ≥4 positive axillary nodes (≥4 N^+) or 1–3 positive axillary nodes (1–3 N^+), and were either ER^-/PR^- or $HER2^+$. Those assigned to the mid- to low-risk category were node negative or had 1–3 positive nodes (1–3 N^+), and were ER^+ and/or PR^+ and $HER2^-$ (Goldhirsch et al. 2007).

Survival analysis

The 5-y overall survival rate was calculated for 60 mo from the date of surgery to the date of last follow-up or death. Patients who died from breast cancer recurrence or metastasis were considered in the overall survival rate, whereas patients who died of other causes or were still alive at the last date of follow-up were censored. Tumor recurrence and metastasis were identified by blood tests, tumor markers, mammography, ultrasound, chest radiography, bone scan, computed tomography imaging and other auxiliary examinations.

Ultrasound examination

Pre-operative ultrasound examinations were performed by two sonographers with more than 5 y of experience in breast ultrasound using the Hitachi Vision 900 system (Hitachi Medical Systems, Tokyo, Japan) or S2000 (Siemens Medical Solutions, Mountain View, CA, USA) with a 5- to 12-Hz linear-array transducer. B-Mode ultrasound imaging, color Doppler flow imaging (CDFI) and elasticity data for each lesion, including cine clips through the masses and static images with at least a longitudinal axis and a transverse axis, were saved in the database for subsequent application. For interpretation of ultrasound image features, double-blind analysis was performed by the other two sonographers with more than 5 y experience of breast ultrasound. In cases of disagreement, a consensus conclusion was arrived at by consultation. Based on the Breast Imaging Report and Data System