

Diagnostic accuracy of ultrasound shear wave elastography combined with superb microvascular imaging for breast tumors

A protocol for systematic review and meta-analysis

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Abstract

Background: Shear wave elastography (SWE) is a new ultrasonic elastography technique for evaluating the hardness of living tissue by measuring the propagation velocity of shear wave in tissue, which is characterized by real-time, non-invasive and quantitative. The SWE technique can be used to diagnose the lesions of different tissues and organs, and the quantitative measurement of SWE is considered as more objective information about breast masses. Superb microvascular imaging (SMI) is a new noninvasive Doppler ultrasound imaging method, which can display blood flow information with high spatial resolution and high frame rate, while keeping the minimum low-speed blood flow components. Therefore, SMI can diagnose diseases closely related to angiogenesis at a relatively early stage. However, the results of these studies have been contradictory. The present meta-analysis aimed at determining the accuracy of SWE combined with SMI in the differential diagnosis between benign and malignant breast lesions.

Methods: We will search PubMed, Web of Science, Cochrane Library, and Chinese biomedical databases from their inception to the April 18, 2021, without language restrictions. Two authors will independently carry out searching literature records, scanning titles and abstracts, full texts, collecting data, and assessing risk of bias. Review Manager 5.2 and Stata 14.0 software will be used for data analysis.

Results: This systematic review will determine the accuracy of shear wave elastography combined with superb microvascular imaging in the differential diagnosis between benign and malignant breast tumors.

Conclusion: Its findings will provide helpful evidence for the accuracy of shear wave elastography combined with superb microvascular imaging in the differential diagnosis between benign and malignant breast tumors.

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Abbreviations: OR = odds ratio, SMI = superb microvascular imaging, SWE = shear wave elastography, SWV = shear wave velocity.

Keywords: breast tumors, meta-analysis, shear wave elastography, superb microvascular imaging

The authors report no conflicts of interest.

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1. Introduction

Breast cancer is one of the most common malignant tumors of women in the 21st century, and it is also the main cause of cancer-related deaths for women in the world. The early manifestation of breast cancer is atypical and easy to be misdiagnosed or missed. Thus, how to accurately distinguish benign and malignant breast lesions is the focus of the development of breast ultrasound technology.^[1,2] In breast tumors, tissue hardness is related to the risk of malignant tumor: the harder the tumor, the higher the risk of malignant tumor. The basic principle of Shear wave elastography is that the vibration of tissue particles is caused by the acoustic radiation pulse generated by focused ultrasonic beam, displacement is induced at the focus and transverse shear wave is generated. The shear wave velocity (SWV) of the detected tissue can be measured accurately and quantitatively, and the SWV can be color-coded and superimposed on the 2-dimensional anatomical image, thus forming a real-time shear wave velocity map of living tissue. Therefore, shear wave elastography (SWE) can be used to diagnose the lesions of different tissues and organs, and the quantitative measurement of SWV is considered as more

objective information about breast masses.^[3–5] However, there is no uniform standard for the elastic parameters and their limits in diagnosing benign and malignant breast lesions, and more clinical research is needed. Tumor angiogenesis plays an important role in the development, growth, and metastasis of breast cancer, and the number of microvessels in the lesion is closely related to the malignancy of the tumor.^[6] Superb microvascular imaging (SMI) is a new noninvasive Doppler ultrasound imaging method, which uses a new clutter suppression algorithm to identify and eliminate the movement of tissue itself, extract blood flow signals at a relatively high frame rate, and provide high-resolution details of vascular branches without ultrasound contrast agent. SMI can display blood flow information with high spatial resolution and high frame rate, while keeping the minimum low-speed blood flow components so that diagnoses diseases closely related to angiogenesis at a relatively early stage.^[7–9]

Studies indicate that SWE combined with SMI is of great value in differential diagnosis of benign and malignant breast masses.^[10] However, the results of these studies have been contradictory. Thus, the current meta-analysis aims at determining the accuracy of SWE combined with SMI in the differential diagnosis between benign and malignant breast lesions to provide reference for the diagnosis and clinical treatment of breast cancer.

2. Materials and methods

This study was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta Analyses) guidelines and the protocol was registered in the INPLASY (INPLASY202150075).

2.1. Eligibility criteria

2.1.1. Type of study. This study will only include high-quality clinical cohort or case–control studies.

2.1.2. Type of patients. The patients should be those who had undergone breast tumors.

2.1.3. Intervention and comparison. This study compared the diagnostic value of SWE combined with SMI and pathology in breast tumors.

2.1.4. Type of outcomes. The primary outcomes include sensitivity, specificity, positive and negative likelihood ratio, diagnostic odds ratio, and the area under the curve of the summary receiver-operating characteristic.

2.2. Search methods

PubMed, Web of Science, Cochrane Library, and Chinese biomedical databases will be searched from their inception to May 18, 2021, without language restrictions. The search strategy

for PubMed is shown in Table 1. Other online databases will be used in the same strategy.

2.3. Data extraction and quality assessment

Two authors will independently select the trials according to the inclusion criteria, and import into Endnote X9. Then remove duplicated or ineligible studies. Screen the titles, abstracts, and full texts of all literature to identify eligible studies. All essential data will be extracted using previously created data collection sheet by 2 independent authors. Discrepancies in data collection between 2 authors will be settled down through discussion with the help of another author. The following data will be extracted from each included research: the first author’s surname, publication year, language of publication, study design, sample size, number of lesions, source of the subjects, instrument, “criterion standard,” and diagnostic accuracy. The true positives, true negatives, false positives, and false negatives in the 4-fold (2 × 2) tables were also collected. Methodological quality was independently assessed by 2 researchers based on the quality assessment of studies of diagnostic accuracy studies (QUADAS) tool. The QUADAS criteria included 14 assessment items. Each of these items was scored as “yes” (2), “no” (0), or “unclear” (1). The QUADAS score ranged from 0 to 28, and a score ≥22 indicated good quality. Any disagreements between 2 investigators will be solved through discussion or consultation by a 3rd investigator.^[11]

2.4. Statistical analysis

The STATA version 14.0 (Stata Corp, College Station, TX) and Meta-Disc version 1.4 (Universidad Complutense, Madrid, Spain) soft wares were used for meta-analysis. We calculated the pooled summary statistics for sensitivity, specificity, positive and negative likelihood ratio, and diagnostic odds ratio with their 95% confidence intervals. The summary receiver operating characteristic curve and corresponding area under the curve were obtained. The threshold effect was assessed using Spearman correlation coefficients. The Cochran’s Q-statistic and *I* test were used to evaluate potential heterogeneity between studies. If significant heterogeneity was detected (Q test $P < .05$ or *I* test $>50\%$), a random-effects model or fixed-effects model was used.^[12] We also performed subgroup and meta-regression analyses to investigate potential sources of heterogeneity. To evaluate the influence of single studies on the overall estimate, a sensitivity analysis was performed. We conducted Beggs funnel plots and Eggers linear regression tests to investigate publication bias.

2.5. Ethics and dissemination

We will not obtain ethic documents because this study will be conducted based on the data of published literature. We expect to publish this study in a peer-reviewed journal.

3. Discussions

At present, high-frequency ultrasound is a cost-effective and widely used breast cancer screening tool which detects tumors through sound waves reflected from breast tissues. However, this technique is subjective and ambiguous, with high sensitivity and low specificity in differentiating benign and malignant breast

Number	Search terms
1	Breast tumors, breast lesions, or breast cancer.
2	Pathology
3	Shear wave elastography or SWE
4	Superb microvascular imaging or SMI

cancer, and is easy to be misdiagnosed and missed in atypical lesions.^[13] Generally speaking, the hardness of breast tissue is malignant, benign, and normal in order from large to small. Young's modulus is a physical quantity to evaluate the elasticity of tissue, which is proportional to the square of the measured tissue density and the propagation velocity of the shear wave. Studies have shown that the Young's modulus of malignant breast lesions is higher than that of benign breast lesions. SWE can measure Young's modulus to analyze the elastic heterogeneity of breast lesions, and then distinguish benign and malignant lesions. Therefore, SWE can achieve acoustic palpation, objectively and quantitatively evaluate the hardness of lesions, and provide sufficient information for the differential diagnosis of benign and malignant lesions of breast cancer.^[14,15] The vascular morphology and distribution characteristics of tumor are closely related to the nature of tumor, which is an important basis for differentiating benign and malignant tumors. Specifically, malignant breast tumors secrete related growth factors to accelerate the formation of new blood vessels, so the shape of blood vessels is irregular and uneven. The venous return and lymphatic reticulum of benign breast tumors are in normal state, so the blood vessels walk naturally and are of equal thickness. Therefore, the state of tumor microvessels can be displayed by SMI, and the Adler method can be used to observe and evaluate the blood supply of the tumor from a certain plane to qualitatively analyze the benign and malignant breast tumors.^[16]

Compared with conventional ultrasound, SWE provides a standard quantitative result for assessing tissue hardness, and SMI shows more subtle blood flow information in benign and malignant breast masses. These studies suggest that combining all quantitative values of SWE and SMI with B-type ultrasound can improve the diagnostic ability of benign and malignant breast lesions. To clarify this point, we will conduct a systematic review, summarizing high-quality studies and providing evidence-based medicine to support clinical practice.

Author contributions

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References

- [1] Torre LA, Siegel RL, Ward EM, et al. Global cancer incidence and mortality rates and trends—an update. *Cancer Epidemiol Biomarkers Prev* 2016;25:16–27.
- [2] Wu C, Li M, Meng H, et al. Analysis of status and countermeasures of cancer incidence and mortality in China. *Sci China Life Sci* 2019;62:640–7.
- [3] Bercoff J, Tanter M, Fink M. Supersonic shear imaging: a new technique for soft tissue elasticity mapping. *IEEE Trans Ultrason Ferroelectr Freq Control* 2004;51:396–409.
- [4] Carlsen J, Ewertsen C, Sletting S, et al. Ultrasound elastography in breast cancer diagnosis. *Ultraschall Med* 2015;36:550–63.
- [5] Xue Y, Yao S, Li X, et al. Value of shear wave elastography in discriminating malignant and benign breast lesions: A meta-analysis. *Medicine (Baltimore)* 2017;96:e7412.
- [6] Zhu YC, Zhang Y, Deng SH, et al. Diagnostic performance of superb microvascular imaging (SMI) combined with shear-wave elastography in evaluating breast lesions. *Med Sci Monit* 2018;24:5935–42.
- [7] Park AY, Seo BK, Woo OH, et al. The utility of ultrasound superb microvascular imaging for evaluation of breast tumour vascularity: comparison with colour and power Doppler imaging regarding diagnostic performance. *Clin Radiol* 2018;73:304–11.
- [8] Mack LM, Mastrobattista JM, Gandhi R, et al. Characterization of placental microvasculature using superb microvascular imaging. *J Ultrasound Med* 2019;38:2485–91.
- [9] Dubinsky TJ, Revels J, Wang S, et al. Comparison of superb microvascular imaging with color flow and power doppler imaging of small hepatocellular carcinomas. *J Ultrasound Med* 2018;37:2915–24.
- [10] Lee EJ, Chang YW. Combination of quantitative parameters of shear wave elastography and superb microvascular imaging to evaluate breast masses. *Korean J Radiol* 2020;21:1045–54.
- [11] Ouyang YL, Zhou ZH, Wu WW, et al. A review of ultrasound detection methods for breast microcalcification. *Math Biosci Eng* 2019;16:1761–85.
- [12] Zhao Q, Sun JW, Zhou H, et al. Pre-operative conventional ultrasound and sonoelastography evaluation for predicting axillary lymph node metastasis in patients with malignant breast lesions. *J Ultrasound Med Biol* 2018;44:2587–95.
- [13] Wang L. Early diagnosis of breast cancer. *Sensors (Basel)* 2017;17:1572.
- [14] Huang Y, Li F, Han J, et al. Shear wave elastography of breast lesions: Quantitative analysis of elastic heterogeneity improves diagnostic performance. *Ultrasound Med Biol* 2019;45:1909–17.
- [15] Youk JH, Gweon HM, Son EJ. Shear-wave elastography in breast ultrasonography: the state of the art. *Ultrasonography* 2017;36:300–9.
- [16] Fu Z, Zhang J, Lu Y, et al. Clinical applications of superb microvascular imaging in the superficial tissues and organs: a systematic review. *Acad Radiol* 2021;28:694–703.