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Diagnostic accuracy of ultrasound superb microvascular imaging for parotid tumors
A protocol for systematic review and meta-analysis

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Abstract
Background: As a novel ultrasound technique, superb microvascular imaging (SMI) can quickly, simply, and noninvasively study the microvascular distribution in the tumor and evaluate the microvascular perfusion. Studies suggested that SMI is helpful for the differentiation between benign and malignant parotid tumors. However, the results of these studies have been contradictory. Therefore, the present meta-analysis aimed at determining the accuracy of SMI in the differential diagnosis between benign and malignant parotid tumors.

Methods: We will search PubMed, Web of Science, Cochrane Library, and Chinese biomedical databases from their inceptions to September 30, 2020, 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 Stata14.0 software will be used for data analysis.

Results: This systematic review will determine the accuracy of SMI in the differential diagnosis between benign and malignant parotid tumors.

Conclusion: Its findings will provide helpful evidence for the accuracy of SMI in the differential diagnosis between benign and malignant parotid tumors.

Systematic review registration: INPLASY2020100093

Abbreviation: SMI = superb microvascular imaging.

Keywords: meta-analysis, parotid tumors, superb microvascular imaging

1. Introduction

Parotid tumors account for 80% of salivary gland tumors in clinical practice, of which 80% to 85% are benign tumors and 15% to 20% are malignant tumors.[1] There are great differences in treatment and long-term prognosis between benign tumors and malignant tumors patients. Patients with benign tumors commonly undergo superficial

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parotidectomy/total parotidectomy and preservation of facial nerves. malignant tumors patients are usually treated with total parotidectomy (with postoperative chemo/radiotherapy), which can result in complete facial paralysis if the facial nerve needs to be resected along with the parotid lobes.[2,3] Therefore, it is very important to diagnose benign and malignant parotid tumors. High-frequency ultrasound can not only show the size, shape, and internal echo of parotid tumors, but also show the blood flow distribution.[4] As a novel ultrasound technique, superb microvascular imaging (SMI) can quickly, simply, and noninvasively study the microvascular distribution in the tumor and evaluate the microvascular perfusion.[5] The SMI adopts a multidimensional filter to eliminate only the clutter and to preserve low-velocity flow signals, whereas conventional Doppler systems use a single-dimension filter and, accordingly, can exhibit a loss of low-velocity flow signals that overlap with clutter.[6] Studies suggested that SMI is helpful for the differentiation between benign and malignant parotid tumors.[7–10] However, the results of these studies have been contradictory. Therefore, the present meta-analysis aimed at determining the accuracy of SMI in the differential diagnosis between benign and malignant parotid tumors.

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 (INPLASY2020100093).

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 parotid tumors.

2.1.3. Intervention and comparison.
This study compares SMI with pathology for diagnosing parotid 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 inceptions to July 31, 2020, 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 X[9]. 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, "gold standard," and diagnostic accuracy. The true positives, true negatives, false positives, and false negatives in the fourfold (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 Cochrans 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 sub-group 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. Discussion

High-frequency ultrasound is a first-line examination method for the diagnosis of parotid gland tumor, which can provide information such as the location, size, shape, internal echo, and the relationship with surrounding tissues, etc.[13] As an important component of tumor stroma, blood vessels interact with tumor cells to form a complete microenvironment. SMI can clearly and completely show the shape and distribution of vascular network of parotid tumors without injection of contrast agent.[14] These studies suggest that SMI can accurately detect the pixel ratio of blood flow signal in parotid gland tumors, and truly reflect the distribution density of low-velocity blood flow signal in the tumors, so as to intuitively reflect the microvascular condition of the tumor and to differentiate benign and malignant parotid tumors.[15] However, the results of these studies have been contradictory. To clarify, we will perform a systematic review to summarize high-quality studies and to provide evidence on the evidence-based medical support for clinical practice.

Author contributions

Conceptualization: Xiukun Hou, Jialing Wu.
Data curation: Xiukun Hou, Jili Zhang, Jialing Wu.
Formal analysis: Xiukun Hou.
Funding acquisition: Xiukun Hou.
Investigation: Jialing Wu.
Methodology: Jili Zhang, Jialing Wu.
Project administration: Jili Zhang, Jialing Wu.
Software: Jili Zhang.
Supervision: Jili Zhang.
Validation: Jialing Wu.
Writing – original draft: Jili Zhang, Jialing Wu.
Writing – review & editing: Jili Zhang, Jialing Wu, Xiukun Hou.

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Table 1

Search strategy sample of PubMed.

Number	Search terms
1.	Parotid tumors, parotid gland or parotid gland neoplasms.
2.	Pathology
3.	Superb microvascular imaging or superb micro-vascular imaging or SMI
4.	and 1–3

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