3D time-of-flight magnetic resonance angiography combined with high resolution T2-weighted imaging in preoperative evaluation of microvascular decompression

Liang C et al. MRI combined sequence for judging NVC
Abstract

BACKGROUND

Neurovascular compression (NVC) is the main cause of primary trigeminal neuralgia (TN) and hemifacial spasm (HFS). Microvascular decompression (MVD) is an effective surgical method for the treatment of TN and HFS caused by NCV. The judgement of NVC is a critical step in the preoperative evaluation of MVD, which is related to the effect of MVD treatment. Magnetic resonance imaging (MRI) technology has been used to detect NVC prior to MVD for several years. Among the many MRI sequences, 3D time-of-flight magnetic resonance angiography (3D TOF MRA) is the most widely used. However, 3D TOF MRA has some shortcomings in detecting NVC. Therefore, 3D TOF MRA combined with high resolution T2-weighted imaging (HR T2WI) is considered to be a more effective method to detect NVC.

AIM

To determine the value of 3D TOF MRA combined with HR T2WI in the judgment of NVC, and thus to assess its value in the preoperative evaluation of MVD.

METHODS

Related studies published from inception to September 2022 based on PubMed, Embase, Web of Science and the Cochrane Library were retrieved. Studies that investigated 3D TOF MRA combined with HR T2WI to judge NVC in patients with TN or hydrosalpinx fluid (HSF) were included according to the inclusion criteria. Studies without complete data or not relevant to the research topics were excluded. The Quality Assessment of Diagnostic Accuracy Studies (QUADAS) checklist was used to assess the quality of included studies. The publication bias of the included literature was examined by Deeks’ test. An exact binomial rendition of the bivariate mixed-effects regression model was used to synthesize data. Data analysis was performed using the MIDAS module of statistical software Stata 16.0. Two independent investigators extracted patient and study characteristics, and discrepancies were resolved by
consensus. Individual and pooled sensitivities and specificities were calculated. The \( P \) and Q test were used to test heterogeneity. The study was registered on the website of PROSERO (registration no. CRD42022357158).

RESULTS

Our search identified 595 articles, of which 12 (including 855 patients) fulfilled the inclusion criteria. Bivariate analysis showed that the pooled sensitivity and specificity of 3D TOF MRA combined with HR T2WI for detecting NVC were 0.96 [95% confidence interval (CI): 0.92-0.98] and 0.92 (95%CI: 0.74-0.98), respectively. The pooled positive likelihood ratio was 12.4 (95%CI: 3.2-47.8), pooled negative likelihood ratio was 0.04 (95%CI: 0.02-0.09) and pooled diagnostic odds ratio was 283 (95%CI: 50-1620). The area under the receiver operating characteristic curve was 0.98 (95%CI: 0.97-0.99). The studies showed no substantial heterogeneity (\( I^2 = 0, Q = 0.001, P = 0.50 \)).

CONCLUSION

Our results suggest that 3D TOF MRA combined with HR T2WI has excellent sensitivity and specificity for judging NVC in patients with TN or HSF. This method can be used as an effective tool for preoperative evaluation of MVD.

Key Words: 3D time-of-flight magnetic resonance angiography; High resolution T2 weighted imaging; Neurovascular compression; Microvascular decompression; Meta-analysis

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Core Tip: This meta-analysis included a total of 855 patients from 12 studies. The results indicated that 3D time-of-flight magnetic resonance angiography combined with
high resolution T2-weighted imaging has excellent diagnostic accuracy for judging neurovascular compression in patients with trigeminal neuralgia or hemifacial spasm. It can be used as an effective tool for preoperative evaluation of microvascular decompression.

INTRODUCTION

Neurovascular compression (NVC) is considered the main cause of primary trigeminal neuralgia (TN) and hemifacial spasm (HFS), which usually occurs in the root entry zone (REZ) of the trigeminal nerve or facial nerve\[^{1-2}\]. Microvascular decompression (MVD) is an effective surgical method for treating TN and HFS caused by NVC\[^{3-4}\]. Although this operation is safe and effective for skillful and experienced neurosurgeons, it does not seem to be the best choice for patients with TN or HFS not caused by NVC\[^{5}\]. Therefore, the judgement of NVC is a critical step in the preoperative evaluation of MVD, which is related to optimal decision-making for neurosurgeons and the effect of MVD treatment.

Magnetic resonance imaging (MRI) technology has been used to detect NVC prior to MVD for several years. However, the routine T1-weighted (T1W) and T2-weighted (T2W) images do not adequately delineate neurovascular relationships at the REZ of the nerve\[^{6}\]. Continuous advancements in MRI scanning sequence and imaging technology have enabled clear visualization of the cerebrovascular and intracranial segments of cranial nerves. Among the many MRI sequences, 3D time-of-flight magnetic resonance angiography (3D TOF MRA) is the most widely used. TOF MRA selectively demonstrates fast-flowing blood and provides visualization of arteries and nerves\[^{7}\]. However, the shortcoming of TOF MRA is that veins are insufficiently visualized\[^{8}\]. High resolution T2WI (HR T2WI) can be obtained by different technologies, including 3D balanced steady state gradient echo and 3D fast turbo spin echo\[^{7}\]. Different manufactures have different names for these technologies, such as Constructive Interference Steady State (CISS), Fast Imaging Employing Steady-state Acquisition (FIESTA), balanced-Fast Field Echo, Sampling Perfection with Application optimized Contrast using different flip angle Evolution (SPACE), balanced Steady State Free
Precession (bSSFP), and TSE Driven Equilibrium (DRIVE). HR T2WI has an excellent contrast between structures, including cerebrospinal fluid, nerves and adjacent blood vessels. Therefore, 3D TOF MRA combined with HR T2WI is considered to be a more effective method to detect NVC. These two MRI techniques may be used to accurately visualize the fine anatomical structures at the REZ of the trigeminal nerve and facial nerve and differentiate vein from artery. The present meta-analysis was designed to determine the value of 3D TOF MRA combined with HR T2WI in the judgment of NVC, and thus to assess its value in preoperative evaluation of MVD.

**MATERIALS AND METHODS**

**Search strategy and selection criteria**

PubMed, Embase, Web of Science and the Cochrane Library were systematically searched. The medical subject heading (MeSH) or Emtree terms were “Magnetic Resonance Angiography” and “Microvascular Decompression Surgery”. The search query was “((Microvascular Decompression Surgery) OR (Decompression Surgeries, Microvascular) OR (Decompression Surgery, Microvascular) OR (Microvascular Decompression Surgeries) OR (Surgeries, Microvascular Decompression) OR (Surgery, Microvascular Decompression) OR (Microvascular Decompression) OR (Decompression, Microvascular) OR (Decompressions, Microvascular) OR (Microvascular Decompressions)) AND ((Magnetic Resonance Angiography) OR (MRI Angiography) OR (Angiographies, MRI) OR (Angiography, MRI) OR (MRI Angiographies) OR (MRI Angiographies) OR (MRI Angiographies) OR (Angiographies, Magnetic Resonance) OR (Magnetic Resonance Angiographies) OR (Perfusion Magnetic Resonance Imaging) OR (Perfusion Weighted MRI) OR (MRI, Perfusion Weighted) OR (time-of-flight))”. Studies published from inception to September 2022 based on these databases were retrieved.

After deleting duplicate publications, reasonable inclusion criteria and exclusion criteria were developed to review the remaining studies. The inclusion criteria were: (1) The purpose of the study was to investigate 3D TOF MRA combined with HR T2WI to judge NVC in patients with TN or hydrosalpinx fluid (HSF); (2) The study design was
prospective or retrospective; and (3) The intraoperative findings were used as the reference standard for NVC diagnosis. The exclusion criteria were: (1) Reviews, case reports, editorials, correspondence, comments, or meeting abstracts/meeting minutes; (2) 3D TOF MRA combined with HR T2WI was not used as a method to judge NVC; (3) The patients in the study received only MRI evaluation and did not receive MVD; and (4) Studies without sufficient data to construct the 2 × 2 contingency table.

Data extraction
Two investigators (Li RC, Zhang BB) independently extracted data, including the quality assessment from the retrieved studies. Discrepancies were resolved in a consensus meeting or, if agreement could not be reached, they were resolved by referral to a third investigator (Guo SW). The extracted data included: (1) Basic research information, including the first author, the publication year, the country of the first author, sample size and the type of the research design; (2) The characteristics of the patients, including their age and diagnosis; (3) The MRI sequences used; and (4) The research results, including the number of true positives (TP), false positives (FP), false negatives (FN), and true negatives (TN).

Literature quality assessment
The methodological quality of the included studies was assessed by two researchers on the basis of the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) checklist. Review Manager 5.4.1 software (The Cochrane Collaboration, United Kingdom) was used to generate a methodological quality graph and methodological quality graph summary.

Statistical analysis
An exact binomial rendition of the bivariate mixed-effects regression model was used to synthesize data. The data analysis was performed using the MIDAS module of STATA 16.0 software (StataCorp LLC, United States). The pooled sensitivity, specificity,
positive likelihood ratio (PLR), negative likelihood ratio (PNR), diagnostic odds ratio (DOR), the area under the receiver operating characteristic curve (AUROC) and 95% confidence intervals (CIs) were calculated. The \( P \) and \( Q \) test were used to assess heterogeneity. The publication bias of the included literature was examined by Deeks’ test on Stata 16.0. The clinical application value of 3D TOF MRA combined with HR T2WI in the judgment of NCV was evaluated by the Fagan nomogram and likelihood ratio scatter plot. Graphs were produced with the MIDAS module for STATA 16.0 and Review Manager 5.4.1 software. This meta-analysis was registered on the website of PROSPERO (registration no. CRD42022357158).

RESULTS

Articles included

We identified 595 articles after the search, and 391 articles remained after deleting duplicate records. Full-text analysis was performed on the 52 articles remaining after screening by titles and abstracts, of which 12 articles without complete data and 28 articles using different MRI sequences were excluded. Finally, 12 articles were included in this analysis (Figure 1).

Basic characteristics of the included literature

The basic characteristics of the literature included in this study are shown in Table 1. A total of 855 patients were included in the 12 studies. Among them, 8 studies focused on TN\(^9-16\), 2 on HFS\(^17,18\), and 2 on both\(^19,20\). Three of the 12 studies were performed with 3D TOF MRA combined with 3D CISS\(^9,16,17\), 6 with 3D TOF MRA combined with 3D FIESTA\(^10-13,18,19\), 1 with 3D TOF MRA combined with 3D SPACE\(^20\), 1 with 3D TOF MRA combined with bSSFP/FSE\(^14\) and 1 with 3D TOF MRA combined with 3D TSE DRIVE\(^15\). Four of the 12 were prospective studies and the remaining 8 were retrospective studies\(^10-12,13,17\). According to the methodological quality assessment conducted using the QUADAS checklist, the quality of the literature included in this study was acceptable (Figure 2).
**Meta-analysis results**

**Heterogeneity of the meta-analysis:** The $I^2$ and $Q$ tests were used to assess heterogeneity. The results indicated that the studies in this meta-analysis had no substantial heterogeneity ($I^2 = 0$, $Q = 0.001$, $P = 0.50$). The same result can be observed from the Galbraith plot (Figure 3A).

**Summary effect size:** Bivariate analysis revealed that the pooled sensitivity and specificity of 3D TOF MRA combined with HR T2WI for the detection of NVC were 0.96 (95% CI: 0.92-0.98) and 0.92 (95% CI: 0.74-0.98), respectively (Figure 4A). The pooled PLR was 12.44 (95% CI: 3.24-47.83), pooled PNR was 0.04 (95% CI: 0.02-0.09) (Figure 4B) and pooled DOR was 283.26 (95% CI: 49.53-1619.90) (Figure 4C). The AUROC was 0.98 (95% CI: 0.97-0.99) (Figure 4D).

**Publication bias:** Deeks’ funnel plot asymmetry test was conducted to assess the publication bias of the studies in the meta-analysis, with $P = 0.97$ indicating no significant publication bias in the included literature (Figure 3B).

**Sensitivity analysis:** Sensitivity analysis was performed by removing each included study one by one and calculating the summary effect size. The pooled sensitivity and AUROC were used as evaluation indicators. The results showed that excluding any study did not significantly change the pooled sensitivity and AUROC (Table 2), which suggested that the results of this meta-analysis were robust and reliable.

**Assessment of clinical application value:** The likelihood ratio scatter plot based on summary PLR and NLR was in the left upper quadrant (Figure 5A). According to the data of this meta-analysis, it is estimated that the incidence rate of NVC in TN and HFS patients was 89.47%, which was consistent with the reported results[2]. Therefore, given
a pretest probability of 0.89, the Fagan nomogram showed that the positive post-test probability was 99% and negative post-test probability was 26% (Figure 5B).

DISCUSSION

In the present meta-analysis, we analyzed the sensitivity, specificity, PLR, NLR, DOR and AUROC of 3D TOF MRA combined with HR T2WI for detecting NVC. The results showed high diagnostic ability of this combination method with high sensitivity and specificity. In a meta-analysis in 2015, the authors reported that 3D TOF MRA had a sensitivity rate of 95% (95% CI: 0.93-0.96) and a specificity rate of 77% (95% CI: 0.66-0.86) in identifying NVC in TN patients[21]. According to our results, when combined with HR T2WI, the specificity of 3D TOF MRA could be significantly improved in diagnosing NVC. Higher specificity means less FP. This is very important for MVD when using MRI findings as the main basis for preoperative diagnosis. Fewer FP can reduce the potential risk of unnecessary MVD surgery in TN or HFS patients without NVC. For these patients, alternative procedures such as balloon compression, radiofrequency lesioning, glycerol injection, or stereotactic radiotherapy are less invasive and might be preferable to MVD[16]. Likelihood ratio and DOR are composite indicators that can simultaneously reflect sensitivity and specificity. According to a previous report, the DOR of 3D TOF MRA in diagnosing NCV was 52.92 (95% CI: 26.39-106.11)[21]. Compared with 3D TOF MRA, combined 3D TOF MRA and HR T2WI had higher PLR and lower NLR, and its DOR reached 283 (95% CI: 50-1620). These results suggested that combining 3D TOF MRA and HR T2WI has more advantages in diagnosing NVC in terms of diagnostic accuracy. Similar results were also shown by the AUROC. The AUROC value is correlated with the overall performance of the diagnostic test with larger AUROC values (closer to 1) indicating greater accuracy, sensitivity and specificity[22]. The AUROC of 3D TOF MRA combined with HR T2WI in diagnosing NVC was 0.98 (95% CI: 0.97-0.99), showing high utility performance in the clinical diagnosis of NVC.
The post-test probabilities are also relevant for clinical diagnosis\cite{23}. They provide information on the probability of whether the patient has NCV after obtaining the test results. In the present study, the post-test probability was also excellent. The post-test probability for a positive test result was 99\%, indicating high clinical application value of 3D TOF MRA combined with HR T2WI in diagnosing NVC. The likelihood ratio scatter plot is a qualitative effect size rating approach for diagnostic test accuracy, which divides the effects rating of the diagnostic test by quadrant\cite{24}. The likelihood ratio scatter plot based on summary PLR and NLR was in the left upper quadrant, indicating high clinical validity. This means that 3D TOF MRA combined with HR T2WI has the ability to exclude and confirm the diagnosis of NVC and the diagnostic accuracy of this test has a “Substantial” effect rating.

There are still some limitations in this meta-analysis: (1) NVC can also cause glossopharyngeal neuralgia (GN), but due to the lack of relevant clinical research data, patients with GN were not included in this meta-analysis; (2) Due to the small number of HFS cases, subgroup analysis was not performed for different diseases (TN/HFS); and (3) Of the 12 included studies, 8 were retrospective studies, which might cause more potential bias and confounding results than prospective studies.

CONCLUSION

Our results suggest that 3D TOF MRA combined with HR T2WI has excellent sensitivity and specificity for judging NVC in patients with TN or HSF. This method can be used as an effective tool for preoperative evaluation of MVD.

ARTICLE HIGHLIGHTS

Research background

The judgement of neurovascular compression (NVC) is a critical step in the preoperative evaluation of microvascular decompression (MVD). 3D time-of-flight magnetic resonance angiography (3D TOF MRA) combined with high resolution T2-
weighted imaging (HR T2WI) is considered to be a more effective method to detect NVC.

**Research motivation**

To assess the value of 3D TOF MRA combined with HR T2WI in the preoperative evaluation of MVD.

**Research objectives**

To determine the diagnostic value of 3D TOF MRA combined with HR T2WI in the judgment of NVC.

**Research methods**

Related studies published from inception to September 2022 based on PubMed, Embase, Web of Science and the Cochrane Library were retrieved. A meta-analysis was performed using the MIDAS module of STATA 16.0 software. The pooled sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (PNR), diagnostic odds ratio (DOR), the area under the receiver operating characteristic curve (AUROC) and 95% confidence intervals (CIs) were calculated.

**Research results**

Our search identified 595 articles, of which 12 (including 855 patients) fulfilled the inclusion criteria. The pooled sensitivity and specificity of 3D TOF MRA combined with HR T2WI for detecting NVC were 0.96 (95%CI: 0.92-0.98) and 0.92 (95%CI: 0.74-0.98), respectively. The pooled PLR was 12.4 (95%CI: 3.2-47.8), pooled PNR was 0.04 (95%CI: 0.02-0.09) and pooled DOR was 283 (95%CI: 50-1620). The AUROC was 0.98 (95%CI: 0.97-0.99).

**Research conclusions**
3D TOF MRA combined with HR T2WI has excellent sensitivity and specificity for judging NVC in patients with trigeminal neuralgia or hydrosalpinx fluid.

*Research perspectives*

3D TOF MRA combined with HR T2WI can be used as an effective tool for preoperative evaluation of MVD.
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