Original Articles/นิพนธ์ต้นฉบับ

# Comparison of Contrast-Enhanced 3D Spoiled Gradient-Echo High-Resolution T1-Weighted Sequences Versus Contrast-Enhanced MR Venography for Detection of Dural Venous Sinus Thrombosis

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## Abstract

**Background:** Cerebral venous thrombosis (CVT) has diverse clinical presentations that are often nonspecific. Early diagnosis is crucial because early intervention, including anticoagulation and systemic or catheter-directed thrombolysis, is associated with favorable clinical outcomes. Magnetic resonance imaging (MRI) and MR venography (MRV) have become preferred techniques because of noninvasiveness with high image resolution.

**Objectives:** To compare the diagnostic accuracy of contrast-enhanced 3D T1-weighted high-resolution isotropic volume excitation (THRIVE) MRI sequences versus contrast-enhanced MRV for the detection of dural venous sinus (DVS) thrombosis.

**Methods:** Contrast-enhanced 3D THRIVE and contrast-enhanced MRV sequences of 98 patients, acquired between August 2010 and November 2012, were retrospectively reviewed by neuroradiologists for detection of DVS thrombosis in each of eight venous sinus segments (total, 784 venous segments). Diagnostic performance values were calculated for contrast-enhanced 3D THRIVE MRI sequences.

**Results:** Eleven patients (30 venous segments) had definite DVS thrombosis on contrast-enhanced MRV, according to neuroradiologists. Compared with contrast-enhanced MRV, the 3D THRIVE had a per-patient sensitivity and specificity of 81.8% and 92%, respectively, and a per-segment sensitivity and specificity of 90% and 98.4%, respectively. The positive predictive value of 3D THRIVE in detecting DVS thrombosis was 56.3% per patient and 69.2% per venous segment; the negative predictive value was 97.6% per patient and 99.6% per venous segment.

**Conclusions:** Contrast-enhanced 3D spoiled gradient-echo high-resolution T1-weighted MRI sequences (contrast-enhanced 3D THRIVE at our institution) have high diagnostic accuracy in detecting DVS thrombosis and are reliable for excluding DVS thrombosis in clinically suspected patients.

**Keywords:** MRV, THRIVE, Venous sinus thrombosis

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## Introduction

Cerebral venous thrombosis (CVT) has diverse clinical presentations that are often nonspecific.[1] The most common presenting symptom is headache, which is present in 70 - 90% of patients,[2] and which may be the only complaint in 25% of cases. Other common presentations include focal neurologic deficits, seizures, and altered consciousness.[1] The presence and severity of symptoms depend on the location and extent of the thrombus.[3]

CVT is a relatively uncommon disorder, with an estimated incidence of 0.2 to 0.5 per 100,000 per year.[4] CVT is the cause of 0.5 - 1% of ischemic stroke cases.[5] Early diagnosis is crucial because early intervention, included are anticoagulation and systemic or catheter-directed thrombolysis, is associated with favorable clinical outcomes.[6]

Though angiography remains the gold standard for diagnosing CVT, magnetic resonance imaging (MRI) and MR venography (MRV) have become preferred techniques because they are non-invasive.[7] MRI is frequently performed to detect CVT because of its superiority over computed tomography (CT) for evaluating not only venous sinus thrombosis, but also cerebral parenchymal pathology. Furthermore, MRI does not require radiation exposure or iodinated contrast medium. The most commonly used MRI techniques are conventional sequences, time-of-flight and contrast-enhanced MRV. The appearance of thrombosis on conventional MRI sequences can vary according to its stage. On spin-echo T1-weighted images, an acute thrombus may appear isointense, whereas subacute thrombus may be hyperintense. On spin-echo T2-weighted images, CVT may appear hypointense (resembling flow void) or hyperintense. A filling defect or empty delta sign caused by thrombus may also be seen on MRV.[8-11]

Contrast-enhanced volumetric three-dimensional (3D) gradient-recalled echo (GRE) T1-weighted images are generally the best MRI sequence for evaluating venous structures and have become a standard part of the routine brain MRI protocol at many centers. GRE MR sequences allow acquisition of T1-weighted 3D datasets of the brain that can be post-processed in multiplanar reconstruction. The GRE nature of the technique allows acquisition of images with high spatial resolution and fewer flow artifacts in a reasonable time for clinical use.[7, 8, 12]

At our institution, contrast-enhanced 3D T1-weighted high-resolution isotropic volume excitation (THRIVE) has been included in the brain MRI protocol since August 2010. This sequence provides good contrast opacification in the cerebral venous structures, including the dural venous sinuses (DVS), with high spatial resolution and few flow artifacts.

The purpose of this study was to compare the diagnostic accuracy of contrast-enhanced 3D THRIVE MRI sequences versus contrast-enhanced MRV for the detection of DVS thrombosis. We determined the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of contrast-enhanced 3D THRIVE compared with contrast-enhanced MRV for the detection of DVS thrombosis.

## Methods

### Patient Population

Approval for this study was obtained from the Ethics Committee, Faculty of Medicine Ramathibodi Hospital, Mahidol University, No. MURA2016/62/NP on March 22, 2016. Informed consent was not required for this retrospective review of medical records and imaging studies. We included all patient records with clinically suspected DVS thrombosis in Ramathibodi Hospital from August 2010 to November 2012 and in who underwent contrast-enhanced 3D THRIVE and contrast-enhanced MRV in addition to conventional brain MRI during a single imaging session.

We excluded patient records with following criteria: 1) patients whose MRI sequences or medical records were not available for review (n = 38); 2) follow-up sessions of previously diagnosed CVT patients (n = 13); 3) tumor invasion (n = 16) or vascular malformation (n = 3) involving the DVS; and 4) prior surgery (n = 2) or intervention (n = 1) involving the DVS.

This search of records between August 2010 and November 2012 yielded 171 patients who met the inclusion criteria. After exclusion, the remaining 98 patients who performed all required sequences with good quality were included in this study.

### MRI Technique

MRI was performed on a 3 - T magnetic resonance system (Philips, Best, Netherlands) with a 32-channel head coil. In all patients, a standard dose (0.1 mmol/kg) of gadobutrol (Gadovist, Bayer Incorporated, Canada) was injected through a standard length of IV tubing at 1.8 - 2.0 mL/s. After injection of the contrast medium and full opacification of the superior sagittal sinus, contrast-enhanced MRV sequences were performed in the coronal plane with a TR of 3 - 6 ms, TE of 1 - 2 ms, and flip angle of 30° at a slice thickness of 0.8 - 2.0 mm. Approximately 10 minutes after contrast medium injection, a 3D GRE T1-weighted imaging sequence (magnetization-prepared rapid acquisition gradient-echo) or 3D THRIVE sequence was performed in the axial plane with a TR of 5 - 7 ms, TE of 3 - 5 ms, and flip angle of 12° at a slice thickness of 1 - 2 mm.

### Evaluation of MR Images

The imaging sequences were separated into two datasets for each patient. The first dataset consisted of the contrast-enhanced 3D THRIVE with multiplanar reconstruction. The second dataset consisted of the contrast-enhanced MRV examination, including the coronal contrast-enhanced and subtracted source images, and rotating maximum intensity projection (MIP) reconstruction.

Each dataset was then reviewed independently on the same workstation by two board-certified neuroradiologists, one with 6 years and one with 5 years of experience in brain MR imaging. Both radiologists were blinded to patient information and final diagnosis as well as to associated findings on other imaging sequences.

Each dataset was scored for the presence or absence of thrombus in each of the following eight venous segments: intracranial right and left internal jugular veins, right and left sigmoid sinuses, right and left transverse sinuses, superior sagittal sinus, and straight sinus.

During evaluation of the first dataset, which consisted of contrast-enhanced 3D THRIVE with multiplanar reconstruction, the radiologists searched for abnormal filling defects that could indicate intraluminal thrombus involving the venous segments (eight segments in each patient). For the second dataset, which included coronal source and MIP images of contrast-enhanced MRV sequences, abnormal filling defects indicating intraluminal thrombus were assessed in all venous segments. Two independent blinded sessions of image interpretation were performed at least 1 week apart for each dataset to avoid recall bias. The evaluators were blinded to patient information and final diagnosis.

### Statistical Analysis

Contrast-enhanced MRV was used as the reference standard in this study. The sensitivity, specificity, PPV, NPV, false positive rate, false negative rate, positive likelihood ratio, negative likelihood ratio, and 95% confidence interval (CI) of contrast-enhanced 3D THRIVE compared with contrast-enhanced MRV for detecting DVS thrombosis were calculated per venous segment. A segment was considered positive for thrombosis if both readers scored it as positive. A patient was considered positive for thrombosis if at least one segment was scored as positive by both readers. Patients were considered negative if none of the segments were scored as positive by both readers. In case of disagreement, final decisions

were reached by consensus. The interrater agreement rate (kappa statistic, κ) was calculated for THRIVE. Agreement between the two readers was evaluated with the weighted kappa statistic. A kappa value of 0.81 - 1.0 was considered to represent excellent agreement; 0.61 - 0.80, substantial agreement; 0.41 - 0.6, moderate agreement; 0.21 - 0.4, fair agreement; and 0 - 0.2, slight agreement.[13, 14] A *P* value less than 0.05 was considered a statistically significant difference.

## Results

Of the 98 patients (median age, 48 years; range, 36 - 59 years) included in this study, 41 were male (mean age, 56 years; range, 33 - 64 years) and 57 were female (median age, 46 years; range, 36 - 59 years). A total of 784 venous segments were evaluated (eight venous segments per patient) (Table1). Sixteen patients (39 venous segments) had suspected venous sinus thrombosis as scored by two readers on contrast-enhanced 3D THRIVE dataset. A total of 11 patients (30 venous segments) were considered to have definite DVS thrombosis on contrast-enhanced MRV as scored by two readers.

The thrombosed segments detected on contrast-enhanced MRV were the right internal jugular vein (n = 4), left internal jugular vein (n = 3), right sigmoid sinus (n = 4), left sigmoid sinus (n = 3), right transverse sinus (n = 6), left transverse sinus (n = 3), and superior sagittal sinus (n = 7). Of the 11 patients determined to have DVS thrombosis in any segment, three had only one positive segment, two had two positive segments, two had three positive segments, three had four positive segments, and one had five positive segments (Table 2).

The sensitivity, specificity, PPV, NPV, false positive rate, false negative rate, positive likelihood ratio, and negative likelihood ratio of contrast-enhanced 3D THRIVE compared with contrast-enhanced MRV for the detection of DVS thrombosis per patient and per segment are shown in Table 3. Kappa statistics for detecting filling defects on contrast-enhanced 3D THRIVE per patient and per segment are shown in Table 4.

Representative cases of concordance and discordance between contrast-enhanced 3D THRIVE MRI sequences and contrast-enhanced MRV in patients with DVS thrombosis are shown in Figures 1 - 3.

**Table 1** Demographic Data

| Characteristic | Age, median (range), y | No. (%) |
|---|---|---|
| Total | 48 (36 - 59) | 98 (100) |
| Male | 56 (33 - 64) | 41 (41.8) |
| Female | 46 (36 - 59) | 57 (58.2) |
| DVS thrombosis | | 11 (11.2) |

Abbreviation: DVS, dural venous sinus.

**Table 2** Results in Each Dataset

| 3D THRIVE | Contrast - Enhanced MRV | | |
|---|---|---|---|
| | Positive | Negative | Total |
| Positive | 9 | 7 | 16 |
| Negative | 2 | 80 | 82 |
| Total | 11 | 87 | 98 |

Abbreviation: MRV, magnetic resonance venography; THRIVE, T1-weighted high-resolution isotropic volume excitation.

**Table 3** Performance of Contrast-Enhanced 3D THRIVE MRI Sequence Compared With Contrast-Enhanced MRV for the Detection of Filling Defects in Patients With DVS Thrombosis

| Performance Value | Filling Defect on 3D THRIVE | 95% CI |
|---|---|---|
| Perpatient (n = 98) | | |
| Sensitivity,% | 81.8 | 48.2 - 97.7 |
| Specificity,% | 92 | 84.1 - 96.7 |
| PPV,% | 56.3 | 29.9 - 80.2 |
| NPV,% | 97.6 | 91.5 - 99.7 |
| False positive,% | 43.8 | 20.8 - 69.4 |
| False negative,% | 2.43 | 0.42 - 9.35 |
| Positive likelihood ratio | 10.2 | 4.74 - 21.8 |
| Negative likelihood ratio | 0.19 | 0.05 - 0.69 |
| Persegment (n = 784) | | |
| Sensitivity,% | 90 | 73.5 - 97.9 |
| Specificity,% | 98.4 | 97.2 - 99.2 |
| PPV,% | 69.2 | 52.4 - 83 |
| NPV,% | 99.6 | 98.8 - 99.9 |
| False positive,% | 30.8 | 17.5 - 47.7 |
| False negative,% | 0.40 | 0.10 - 1.28 |
| Positive likelihood ratio | 56.5 | 31.9 - 100 |
| Negative likelihood ratio | 0.10 | 0.03 - 0.29 |

Abbreviation: CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value; THRIVE, T1-weighted high-resolution isotropic volume excitation.

**Table 4** Interrater Concordance Rates for Detecting Filling Defects Indicating DVS Thrombosis on Contrast-Enhanced 3D THRIVE MRI Sequences

| Data | Agreement, % | Κ |
|---|---|---|
| Per patient (n = 98) | 89.8 | 0.68 |
| Per segment (n = 784) | 96.9 | 0.71 |

Abbreviation: Κ, kappa statistic.

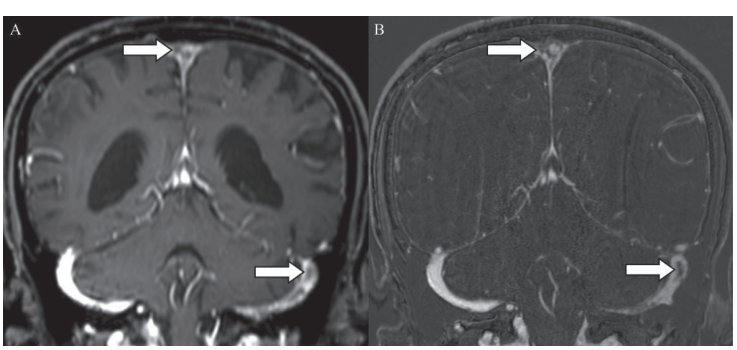


***Figure 1*** *A 78-Year-Old Man Who Presented With Altered Consciousness*

A, Coronal contrast-enhanced 3D THRIVE MR image shows filling defects (arrows) in the left sigmoid sinus and the superior sagittal sinus. B, Coronal contrast-enhanced MRV subtracted image confirms that filling defects (arrows) are consistent with venous thrombosis.

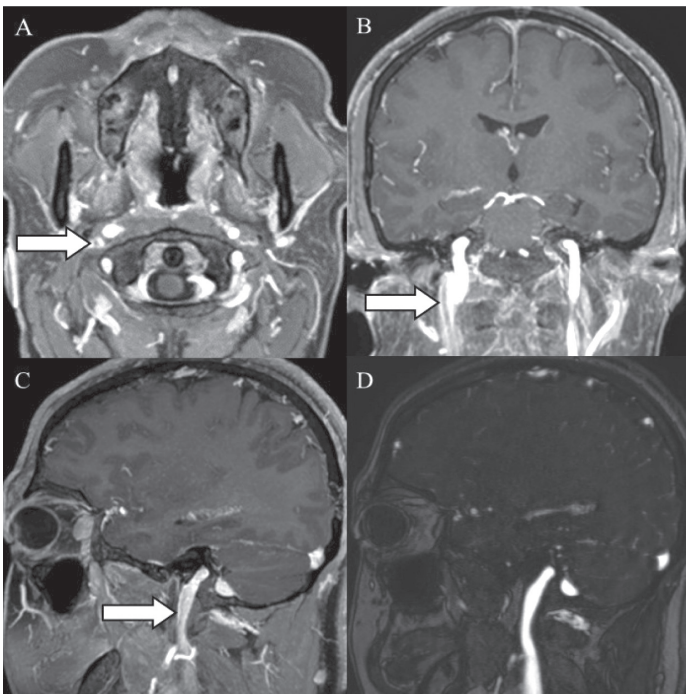


***Figure 2*** *A 26-Year-Old Woman Who Presented With Behavioral Changes*

A, B, and C, Axial, coronal, and sagittal coronal contrast-enhanced 3D THRIVE MR images show a long filling defect (arrows) in the right internal jugular vein. D, Sagittal contrast-enhanced MRV image was read as negative for thrombosis and indicated that the filling defect on contrast-enhanced 3D THRIVE MR images was a false positive from flow artifact high flow velocity in the right internal jugular vein.

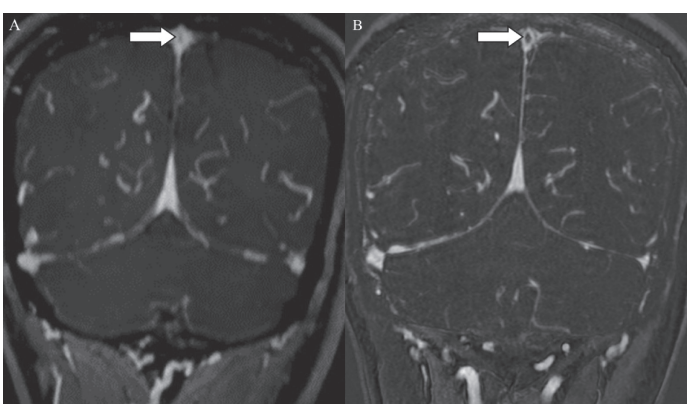


***Figure 3*** *A 41-Year-Old Woman Who Presented With Redness of the Right Eye of 2 Years' Duration Was Evaluated to Rule Out Dural Venous sinus (DVS) Thrombosis*

A, Coronal contrast-enhanced 3D THRIVE MR image shows thin filling defects (arrows) in the superior sagittal sinus, which were interpreted as dural sinus septum or flow-related artifact and were scored as negative for venous sinus thrombosis. B, Coronal contrast-enhanced MRV subtracted image shows that the filling defect (arrows) was thrombosis. The false negative resulted from partial enhancement of the thrombus.

## Discussion

Angiography remains the gold standard for diagnosing DVS thrombosis. However, because of the invasiveness of angiography, various MRI sequences, including contrast-enhanced MRV, are currently preferred for making the diagnosis.[7] In patients with venous sinus thrombosis, the clinical presentation, including headache or altered consciousness, is often nonspecific.[1, 2] For that reason, routine brain MRI may be performed instead of contrast-enhanced MRV.

At our institution, contrast-enhanced 3D THRIVE has been included in the brain MRI protocol since August 2010. It is important to understand the performance, pitfalls, and reliability of this MRI technique for the diagnosis of DVS thrombosis. In this study, we used contrast-enhanced MRV as the reference standard because of its accuracy and superiority in comparison with phase contrast or time-of-flight MRV techniques.[12]

Saindane et al[6] studied the accuracy of spin-echo and gradient-echo T1-weighted imaging for the detection of DVS thrombosis. Compared with contrast-enhanced MRV, 3D GRE T1-weighted imaging had a per-patient sensitivity and specificity of 67% and 100%, respectively, and a per-patient PPV and NPV of 100% and 97.6%, respectively, in detecting DVS thrombosis in that study. However, they found a high false-negative rate of 33%, which they attributed to the fact that the acquisition timing for 3D GRE T1-weighted imaging sequences was approximately 5 minutes after contrast injection, which resulted in thrombus enhancement, thus limiting the evaluation of filling defects.

Another study by Sari et al[8] aimed to lessen the influence of thrombus enhancement by using immediate post-contrast 3D GRE T1-weighted imaging to detect DVS thrombosis. That study included only patients clinically suspected of having DVS and/or cortical venous thromboses. The contrast-enhanced 3D GRE T1-weighted sequence was found to have high sensitivity, specificity, PPV, and NPV values of 92.5%, 100%, 97.9%, and 98.3%, respectively. However, a limitation of that study was the heterogeneity of the reference standard, which included contrast-enhanced MRV, angiography, CT venography, and follow-up imaging. The immediate acquisition of contrast-enhanced 3D GRE T1-weighted sequences was meant to avoid the late enhancement of thrombi and was good for detecting potentially obscured filling defects. However, immediate acquisition might have prevented detection of other enhancing lesions in non-thrombotic patients with similar clinical presentations.

In our study, the contrast-enhanced 3D THRIVE sequences had the potential advantages of high-resolution (1-mm isotropic) volumetric acquisition with fewer flow-related venous artifacts. This sequence was highly sensitive (90%) and specific (98.4%) in detecting DVS thrombotic segments. Furthermore, the high NPV of 97.6% was beneficial to exclude DVS thrombosis in clinically suspicious cases. However, false-positive cases slightly diminished the PPV of the 3D THRIVE sequence. Both readers scored these cases positive for thrombotic segments on 3D THRIVE sequences; however, the contrast-enhanced MRV demonstrated no abnormal filling defects. These false positives were flow-related venous artifacts at the transverse sinuses, sigmoid sinuses, and internal jugular veins, as well as inhomogeneous contrast opacification with flow artifacts in the superior sagittal sinuses. We found only two false-negative patients in our study. Both of these patients had superior sagittal sinus thromboses which were misinterpreted as venous sinus septum or flow artifacts. A potential explanation for this misinterpretation is delayed enhancement of the intravascular thrombus, impeding detection of the filling defect in 3D THRIVE, which was acquired approximately 10 minutes after contrast injection in our protocol. This pitfall was also reported by Saindane et al.[6] The interrater agreement for 3D THRIVE of 96.94% per venous segment was good (kappa coefficient = 0.71). Among those segments that the two readers scored differently, there were cases with hypoplastic transverse/sigmoid sinuses (which one reader

interpreted as abnormal filling defects), cases with inhomogeneous contrast opacification or arachnoid granulations in the superior sagittal sinuses (which were scored as thrombotic segments), as well as cases with venous flow artifacts at the transverse sinuses, sigmoid sinuses, and internal jugular veins. These pitfalls are important and should be considered before reporting abnormal filling defects when using the 3D THRIVE technique to detect DVS thrombosis.

As for the limitations of this study, we included all patients who underwent contrast-enhanced MRV and 3D THRIVE in the same imaging session with the exclusion criteria described earlier to represent the true prevalence of DVS thrombosis at our institution over more than a 2-year period. This minimized reader bias for positive cases and decreased bias in randomization technique as well as selection bias. However, this approach resulted in a small ratio of positive-to-negative cases because of the low prevalence of venous sinus thrombosis.

Another limitation is that readers limited their interpretation to only the 3D THRIVE sequence because the main purpose of this study was to evaluate the diagnostic accuracy of this technique. However, routine current MRI protocol commonly includes conventional sequences, such as unenhanced and contrast-enhanced spin echo-based T1-weighted images, T2-weighted images, and susceptibility weighted images, which help in evaluating suspicious filling defects seen on 3D THRIVE sequences in the diagnosis of venous thrombosis.[6, 9]

## Conclusions

Our results indicate that contrast-enhanced 3D THRIVE has high sensitivity (90%) and specificity (98.4%) for detection of DVS thrombotic segments, using contrast-enhanced MRV as the reference standard. Its high NPV (97.6%) also makes 3D THRIVE useful for excluding DVS thrombosis in clinically suspicious patients.

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Original Article/นิพนธ์ต้นฉบับ

# การศึกษาเปรียบเทียบระหว่างภาพเอ็มอาร์ไอของสมองด้วยเทคนิคไทรฟ์หลังจากการฉีดสารประกอบแกโดลิเนียมและภาพเอ็มอาร์วีร่วมกับการฉีดสารประกอบแกโดลิเนียมในการวินิจฉัยภาวะหลอดเลือดดำในสมองอุดตัน

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## บทคัดย่อ

**บทนำ:** ภาวะหลอดเลือดดำในสมองอุดตัน (Cerebral venous thrombosis, CVT) มีอาการทางคลินิกที่หลากหลายและไม่จำเพาะ ปัจจุบันการตรวจวินิจฉัยด้วยภาพเอ็มอาร์ไอ (Magnetic resonance imaging, MRI) ของสมองและภาพเอ็มอาร์วี (Magnetic resonance venography, MRV) มีบทบาทมากขึ้นเนื่องจากเป็นวิธีตรวจที่ไม่ต้องสอดใส่อุปกรณ์เข้าไปในร่างกายร่วมกับภาพวินิจฉัยมีความละเอียดสูง

**วัตถุประสงค์:** เพื่อศึกษาความแม่นยำของภาพเอ็มอาร์ไอของสมองด้วยเทคนิคไทรฟ์ (T1-weighted high-resolution isotropic volume excitation, THRIVE) หลังจากการฉีดสารประกอบแกโดลิเนียม (Gadolinium) ในการวินิจฉัยภาวะหลอดเลือดดำในสมองอุดตัน

**วิธีการศึกษา:** การศึกษาแบบพรรณนาย้อนหลัง เปรียบเทียบภาพเอ็มอาร์ไอของสมองด้วยเทคนิคไทรฟ์หลังจากการฉีดสารประกอบแกโดลิเนียมและภาพเอ็มอาร์วีร่วมกับการฉีดสารประกอบแกโดลิเนียม ในกลุ่มตัวอย่างผู้ป่วย จำนวน 98 คน ตั้งแต่เดือนสิงหาคม พ.ศ. 2553 ถึงเดือนพฤศจิกายน พ.ศ. 2555 เพื่อวินิจฉัยภาวะหลอดเลือดดำในสมองอุดตัน

**ผลการศึกษา:** จากกลุ่มตัวอย่างพบผู้ป่วย จำนวน 11 คน มีภาวะหลอดเลือดดำในสมองอุดตันจากการวินิจฉัยด้วยภาพเอ็มอาร์วีร่วมกับการฉีดสารประกอบแกโดลิเนียม โดยพบว่า ภาพเอ็มอาร์ไอของสมองด้วยเทคนิคไทรฟ์หลังจากการฉีดสารประกอบแกโดลิเนียมมีค่าความไวและความจำเพาะต่อหนึ่งผู้ป่วยคิดเป็นร้อยละ 81.8 และ 92 ตามลำดับ และมีค่าความไวและความจำเพาะต่อหนึ่งส่วนของหลอดเลือดดำคิดเป็นร้อยละ 90 และ 98.4 ตามลำดับ

**สรุป:** ภาพเอ็มอาร์ไอของสมองโดยเทคนิคไทรฟ์หลังจากการฉีดสารประกอบแกโดลิเนียมมีความแม่นยำสูงในการวินิจฉัยภาวะหลอดเลือดดำในสมองอุดตัน

**คำสำคัญ:** เอ็มอาร์ไอ ไทรฟ์ หลอดเลือดดำในสมองอุดตัน

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