Original Article / Orijinal Araştırma

Arterial Spin Labelling Magnetic Resonance Perfusion Imaging for the Diagnosis of Cerebral Venous Thrombosis

Akut Serebral Venöz Tromboz Tanısında Arteriyel Spin Etiketleme Manyetik Rezonans Perfüzyon Görüntüleme

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Abstract

Aim: Early diagnosis of cerebral venous thrombosis (CVT) is crucial for a favourable prognosis as CVT can lead to severe outcomes. However, certain scenarios, such as during pregnancy, restrict the use of contrast agents, thus rendering conventional magnetic resonance imaging (MRI) methods insufficient for accurate diagnosis. In light of these challenges, our study endeavours to assess the diagnostic potential of the arterial spin labelling magnetic resonance perfusion (ASL-MRP) technique, a contrast-agent–free approach, in the context of CVT diagnosis.

Material and Method: Between 1 March 2022 and 30 May 2022, patients diagnosed with CVT via contrast-enhanced MR venography in the neurology clinic of our hospital were evaluated through ASL-MRP. Patient-specific demographics, including age, gender, presenting symptoms, underlying causes, impacted cortical sinus structures and MRI findings, were documented. Within the framework of ASL-MRP, an elevation in cerebral blood flow (CBF) detected within the affected sinus and/or neighbouring structures was deemed indicative of pathological conditions.

Results: Among the 13 patients included in our study, six were diagnosed with acute CVT, whereas seven were diagnosed with chronic CVT. The assessment of CBF using ASL-MRP revealed CBF elevation in five out of the six cases (83.3%) exhibiting acute CVT. However, no anomalous findings were observed in the ASL-MRP scans of patients presenting with chronic CVT.

Conclusion: The utilisation of ASL-MRP eliminates the need for contrast agent administration. It is a promising technique in facilitating the diagnosis of acute CVT and distinguishing it from chronic CVT cases.

Keywords: Cerebral venous thrombosis, arterial spin labelling magnetic resonance perfusion, pregnancy, diagnosis

Öz

Amaç: Serebral venöz trombozunun (SVT) erken tanısı, SVT'nin ciddi sonuçlara yol açabilmesi nedeniyle iyi prognoz için çok önemlidir. Ancak hamilelik gibi bazı durumlar, kontrast maddelerin kullanımını kısıtlar, bu nedenle de geleneksel manyetik rezonans görüntüleme (MRG) yöntemleri doğru teşhis için yetersiz kalabilir. Bu zorluklar göz önünde bulundurularak çalışmamız, kontrast madde içermeyen bir yaklaşım olan arteriyel spin etiketleme tabanlı manyetik rezonans perfüzyon (ASE-MRP) tekniğinin, SVT teşhis potansiyelini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntem: 1 Mart 2022 ile 30 Mayıs 2022 tarihleri arasında hastanemiz nöroloji kliniğinde MR venografi ile SVT tanısı konulan hastalar ASE-MRP ile değerlendirildi. Yaş, cinsiyet, başvuru semptomları, risk faktörleri, etkilenen kortikal sinüs yapıları ve MRG bulguları kaydedildi. ASE-MRP tekniğinde, etkilenen sinüs ve/veya komşu yapılardaki serebral kan akımında (SKA) artış, patolojik durumların göstergesi olarak kabul edildi.

Bulgular: Çalışmamıza dahil edilen 13 hastanın altısına akut, yedisine kronik SVT teşhisi kondu. ASE-MRP kullanarak yapılan SKA değerlendirmesinde, akut SVT tanısı alan altı olgudan beşinde (%83,3) SKA artışı saptandı. Ancak kronik SVT ile başvuran hastaların ASE-MRP taramalarında anormal bulgu gözlenmedi.

Sonuç: ASE-MRP'nin kullanılması kontrast madde uygulama ihtiyacını ortadan kaldırır. Akut SVT'nin tanısını kolaylaştırmada ve kronik SVT vakalarından ayırmada umut verici bir tekniktir.

Anahtar Kelimeler: Serebral venöz tromboz, arteriyel spin etiketleme manyetik rezonans perfüzyon görüntüleme, gebelik, tanı

INTRODUCTION

Cerebral venous thrombosis (CVT) constitutes a relatively uncommon cause, accounting for approximately 0.5–1% of all stroke cases.[1] Although it often exhibits a favourable prognosis, CVT can still lead to significant rates of disability and mortality.[2,3] Timely and effective treatment has been demonstrated to impact patient outcomes positively.[4] Given the diverse range of clinical presentations and characteristics associated with this condition, the role of imaging modalities in the diagnostic process is crucial.[5] However, the identification of CVT can sometimes face delays or challenges due to atypical clinical manifestations.[6]

Although computed tomography (CT) and magnetic resonance (MR) angiography are recommended diagnostic tools for detecting CVT, these methods have limitations.[7,8] They include issues such as false negatives/positives, susceptibility to motion artefacts, extended examination times and reduced sensitivity in cases where contrast agents cannot be used, particularly in non-contrast-enhanced time-of-flight (TOF) MR venography (MRV).[9,10] Among these limitations, the requirement for contrast agents is particularly significant. Furthermore, circumstances such as pregnancy (a notable risk factor for CVT), drug allergies and renal impairment can limit the use of contrast agents. In situations where contrast agents cannot be administered, the diagnostic sensitivity of the procedure diminishes, exacerbating difficulties in distinguishing between hypoplasia and thrombosis.[11] Digital subtraction angiography, often considered the gold standard for CVT diagnosis, is feasible for only a select group of patients due to its invasive nature.[12]

Arterial spin labelling (ASL) MR perfusion (MRP) has emerged as a non-invasive and reliable technique for evaluating cerebral blood flow (CBF) without the need for intravenous contrast agent administration.[13] Although the existing literature provides limited evidence of its effectiveness in diagnosing acute ischemic stroke and CVT, these studies are based on a few clinical cases.[14-16] Consequently, ASL-MRP has not been integrated into the routine imaging approach for CVT diagnosis thus far.

In the context of our investigation, our primary aim was to assess the diagnostic effectiveness of the ASL-MRP technique in CVT cases.

MATERIAL AND METHOD

Ethics Committee

The study was approved by Ankara City Hospital No: 1 Clinical Researches Ethics Committee (Date: 01.02.2022, Decision no: E1-22-2365). Informed voluntary consent was obtained from all patients included in the study. Our study was conducted in accordance with research and publication ethics following the principles in the Declaration of Helsinki.

This prospectively designed study was conducted between March 2022 and May 2022 at our hospital's neurology clinic. Within this period, patients diagnosed with CVT following MRV were subsequently evaluated using ASL-MRP. The patients' age, gender, comorbidities, risk factors, presenting symptoms, neurological examinations, MRI results, affected venous sinuses and prognoses were recorded. The exclusion criteria for the study included pregnancy, allergy to medications, history of stroke and any diagnosed neurological disorder related to the central nervous system.

MRI and Analysis Protocol

All patients were examined using a 3-T MRI unit (SIGNA™ Pioneer 3T MRI; GE Healthcare, Milwaukee). ASL-MRP imaging was conducted using a pseudocontinuous ASL pulse sequence. The ASL parameters were configured as follows: labelling pulse duration=1.5 s, post-labelling delay=1.5 s, TR=4948 ms, TE=10.9 ms, field-of-view=240 × 240 mm, number of excitations=3, number of interleaved slices=32 and slice thickness=4 mm. A quantitative map of CBF in mL/100 g tissue/min was obtained using the perfusion quantification model. An increase in CBF in the affected sinuses and/or neighbouring structures detected through ASL-MRP was considered pathological. The images were interpreted and reported by a radiology specialist with over 20 years of experience in the field of neuroradiology.

Statistical Analysis

The obtained data were analysed using a statistical software package (SPSS) (Version 17, Chicago IL, USA). Descriptive statistics (mean, standard deviation, median, minimum, maximum, count and percentage) were provided for categorical and continuous variables in the study.

RESULTS

Our study included 13 patients, with a mean age of 32.7±9.7 years and 76.9% (n=10) being female. Among the 13 patients, six were diagnosed with acute CVT, whereas seven exhibited chronic CVT. Within the acute CVT group, five (83.3%) demonstrated an increase in CBF when assessed using the ASL-MRP technique. Conversely, the ASL-MRP sequences for patients diagnosed with chronic CVT showed no pathological findings (Figure and Table).

Among the thrombosed sinuses, the transverse sinuses were the most commonly affected, accounting for 77% of the cases (46.2% and 30.8% on the right and left, respectively). The sigmoid sinuses followed closely at 46.2% (23.1% and 23.1% on the right and left, respectively), whereas the superior sagittal sinus was involved in 30.8% of the cases. In terms of clinical presentation, the most frequent complaint was headache, as reported by 69.2% of the patients. Seizures were observed in 23.1% of the cases, and altered consciousness was noted in 7.7% of the cases.

Table : Characteristics of the Cases and ASL-MRP Results							
No	Age	Gender	Presenting symptoms	Possible underlying causes	Impacted cortical sinus	Timeliness	ASL-MRP (+/-)*
1	25	Male	Headache	Drug abuse	Right TS and SS	Acute	+
2	29	Female	Headache	Postpartum period	Right TS and SS	Acute	+
3	57	Female	Altered Consciousness	-	SSS	Acute	+
4	21	Female	Seizure	Steroid use	Right TS and SSS	Acute	-
5	29	Female	Headache	Postpartum period	Right TS and SSs	Acute	+
6	28	Female	Seizure	-	Left TS and SS	Acute	+
7	25	Female	Headache	Postpartum period	Right TS	Acute	-
8	40	Male	Seizure	Thrombophilia	Right TS and SS	Cronic	-
9	32	Male	Headache	-	Bilateral TS	Cronic	-
10	38	Female	Headache	Migraine	SSS	Cronic	-
11	42	Female	Headache	-	Left TS and SS	Cronic	-
12	35	Female	Headache	-	Left TS	Cronic	-
13	28	Female	Headache	-	Right TS	Cronic	-

SS; sigmoid sinus; FAQ; superior sagittal sinus, TS; transverse sinus *In this table ASL-MRP results (+/-) are presented.
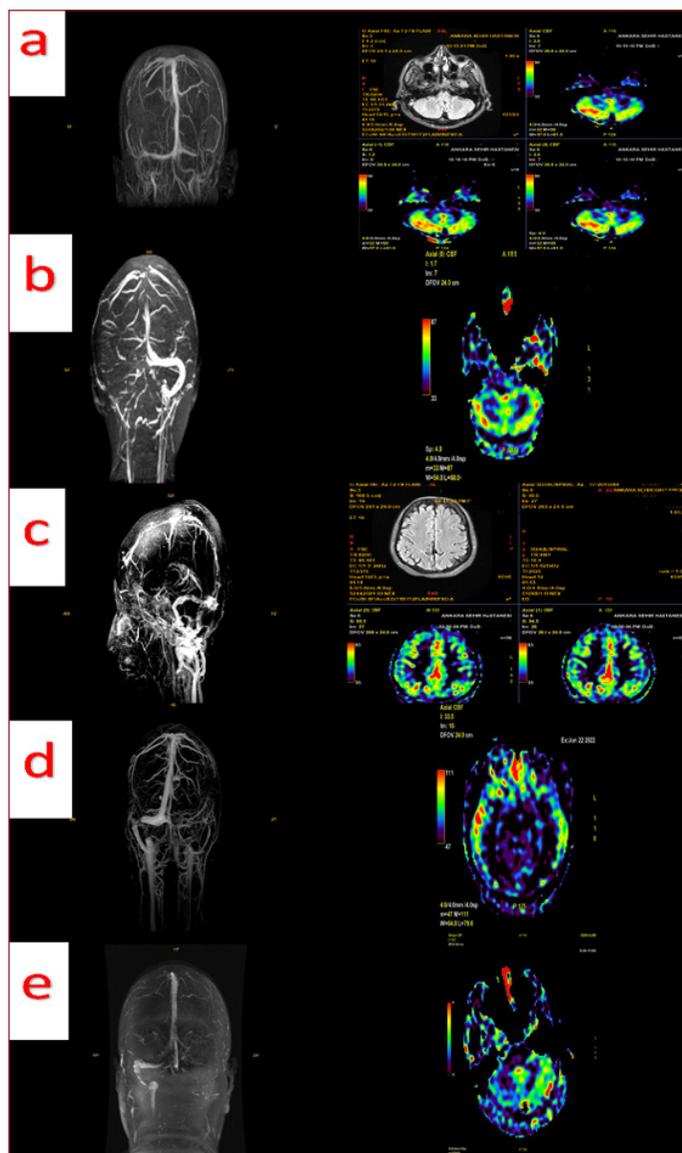

Figure: In cases 1 and 2 with right TS and SS thrombosis (right image), CBF increase in adjacent structures in ASL-MRP images (image on the right, red color) [a and b]. In case 3 with CNS thrombosis (right image), CBF increase in adjacent structures in ASL-MRP images (left image, red color). In case 5, TS and CNS thrombosis on the right, TS hypoplasia on the left (right image), increased CBF in adjacent structures on ASL-MRP images (left image, red color) [d]. CBF increase in adjacent structures in ASL-MRP images in case 6 (right image) with left TS and SS thrombosis (image in left, red color).

DISCUSSION

Diagnosing CVT can be exceptionally challenging due to variability in clinical presentations and imaging findings. When conventional cranial MRI and head CT yield inconclusive results, the possibility of CVT cannot be definitively ruled out, necessitating further assessment through MRV.[6,17] In cases where contrast agents cannot be administered, MRV's sensitivity and specificity diminish, potentially leading to false-negative or false-positive outcomes.[10] In our study aimed at evaluating the impact of the ASL-MRP technique on CVT diagnosis, we observed an increase in CBF in five out of six patients with acute CVT. However, no abnormal CBF findings were detected in the ASL-MRP scans of the seven chronic CVT cases.

Although the annual incidence of CVT is reported to be 1–2 million cases, recent advances in neuroradiology suggest higher rates.[18,19] CVT, commonly observed in young females with a favourable prognosis,[20,21] can result in mortality rates of up to 5%[2] and long-term neurological sequelae of up to 15%.[3] Given that effective treatment can improve prognosis in CVT cases, early diagnosis is crucial.[4] Similar to our findings, multiple venous sinuses are often affected, with the superior sagittal sinus, transverse sinuses and sigmoid sinuses being the most commonly involved.[17] The female gender-specific pregnancy risk factor constituted approximately three-quarters of our study population and may impose limitations on imaging techniques.

The complexity of diagnosing CVT is influenced by various factors. For instance, the use of ionising radiation in CT is contraindicated during pregnancy.[22] Additionally, conditions such as pregnancy, renal insufficiency and drug allergies limit the use of contrast agents, resulting in reduced sensitivity of TOF-MRV images.[9] Moreover, clinical symptoms, particularly changes in consciousness, can lead to motion artefacts during imaging procedures, potentially compromising the accuracy of CVT diagnosis. These complexities underscore the need for a comprehensive approach to CVT diagnosis, considering the limitations of various imaging modalities and the dynamic nature of

disease presentation. Therefore, the sensitivity of different MR techniques in diagnosing CVT has been investigated in the literature. They include FLAIR, echo-planar T2*-weighted susceptibility-weighted imaging and diffusion-weighted images.[23-25]

The ASL-MRP technique operates on the principles of subtracting a 'tag' image acquired through magnetic labelling of blood from a 'control' or 'reference' image obtained without labelling. This approach involves labelling the magnetisation of water protons in the blood using methods such as inversion at the major feeding arteries. In ASL-MRP, an elevation in blood flow within the affected vascular structures is considered indicative of pathology.[26] Previous studies have demonstrated the effectiveness of ASL-MRP in diagnosing acute stroke resulting from arterial occlusion.[14,15] For instance, Knag et al. conducted a study involving 13 CVT patients using ASL-MRP and identifying the bright sinus appearance image in all patients. They also observed hypoperfusion in 77% of the cases. The authors emphasised the potential utility of bright sinus appearance as a diagnostic marker within ASL-MRP assessments.[16] Similarly, our study also evaluated CBF through ASL-MRP, detecting abnormalities in 83.3% of acute cases. This finding suggests that ASL-MRP may offer benefits in diagnosing acute CVT, akin to its utility in acute arterial stroke cases. The ability of ASL-MRP to assess CBF non-invasively presents a promising avenue for enhancing the accuracy and timeliness of acute CVT diagnosis, which could potentially influence treatment decisions and patient outcomes.

Furthermore, the variability in the presentation and progression of CVT cases underscores the need for a multimodal diagnostic approach. Combining ASL-MRP with other imaging techniques, such as conventional MRV and dynamic contrast-enhanced imaging, could enhance diagnostic accuracy and offer a more comprehensive assessment of cerebral haemodynamics.

CONCLUSION

Our study contributes to the growing body of literature providing evidence on the potential of ASL-MRP as a valuable tool for diagnosing CVT, particularly in the acute phase. Assessing CBF non-invasively through ASL-MRP offers a unique advantage in cases where contrast agents cannot be used. However, further research involving larger cohorts and longitudinal follow-up is necessary to validate and refine the diagnostic utility of ASL-MRP in different stages of CVT. As our understanding of neuroimaging techniques continues to evolve, integrating advanced methods such as ASL-MRP into clinical practice holds the promise of improving the accuracy and timeliness of CVT diagnosis, leading to more informed treatment decisions and ultimately better patient outcomes.

ETHICAL DECLARATIONS

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