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ORIGINAL ARTICLE

The Role of Dynamic Susceptibility Contrast Perfusion Magnetic Resonance Imaging in the Evaluation of Active and Inactive Demyelinating Plaques in Multiple Sclerosis

Multipl Sklerozda Aktif ve İnaktif Demiyelinizan Plakların Değerlendirilmesinde Dinamik Duyarlılık Kontrastlı Perfüzyon Manyetik Rezonans Görüntülemenin Rolü

[1]Seyit Erol, [1]Hakan Cebeci

[1]Department of Radiology, Selcuk University, Faculty of Medicine, Konya, Türkiye

Correspondence

Seyit Erol, MD, Assist. Prof., Department of Radiology, Selcuk University, Faculty of Medicine, Konya, Türkiye

E-Mail: seyiterol42@gmail.com,

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ABSTRACT

Aim: Our goal in this study was to find out if active plaques that exhibiting enhancement and inactive plaques that do not differing in dynamic-susceptibility-contrast perfusion-weighted-imaging (DSC-PWI)DSC-PWI measures in multiple sclerosis (MS) patients.
Material and Methods: In our study, DSC-PWI mDynamic susceptibility contrast perfusion-weighted agnetic resonance imagingMRI (DSC-PI) (MRI) examinations of 30 patients diagnosed with Multiple Sclerosis were retrospectively analyzed. A region of interest (ROI) was manually drawn on DSC-PWI between active plaques that showing ed enhancement on conventional MRI sequences and inactive plaques that did not showing enhancement. Cerebral blood volume (CBV), cerebral blood flow (CBF), mean transit time (MTT), and time to peak (TTP) in this ROI were also recorded. These measurements were also normalized to apparently unaffected contralateral white matter hemisphere measurements. These normalized values were named relative (rCBV), rCBF, rMTT, and rTTP.
Results: Both rCBV and rCBF were significantly higher in active demyelinating plaques compared to chronic demyelinating plaques ($p<0.001$). Mean rCBV and rCBF values in active plaques were 1.61 ± 0.66 and 1.44 ± 0.59, respectively. In chronic plaques, the mean rCBV was 0.91 ± 0.32 and the mean rCBF was 0.81 ± 0.26. The mean rMTT was 0.98 ± 0.53 in active demyelinating plaques and 1.30 ± 0.44 in chronic demyelinating plaques and there was a significant difference between the two groups ($p=0.004$). Mean rTTP was also significantly prolonged in active demyelinating plaques compared to chronic plaques ($p<0.001$). Mean rTTP was 0.93 ± 0.14 and 1.06 ± 0.21 in active and chronic demyelinating plaques, respectively.
Conclusions: In conclusion, the DSC-PWI examination may provide reliable information in the evaluation ofactive and inactive demyelinating plaques in MS.

Keywords: Demyelinating disease, Multiple Sclerosis, magnetic resonance ımaging, multiple sclerosis

ÖZ

Amaç: Bu çalışmadaki amacımız, MS hastalarında kontrastlanma gösteren aktif plakların ve göstermeyen inaktif plakların DSC-PWI ölçümlerinde farklılık olup olmadığını bulmaktı.
Gereç ve Yöntemler: Çalışmamızda, Multipl Skleroz tanısı konmuş 30 hastanın Dinamik susceptibilite kontrastlı perfüzyon ağırlıklı MRG incelemeleri retrospektif olarak analiz edildi. Konvansiyonel MRG sekanslarında kontrastlanma gösteren aktif plaklar ile kontrastlanma göstermeyen inaktif plaklar arasında DSC-PI üzerinde manuel olarak bir ilgi bölgesi (ROI) çizildi. Bu ROI'deki serebral kan hacmi (CBV), serebral kan akışı (CBF), ortalama geçiş süresi (MTT) ve zirveye ulaşma süresi (TTP) de kaydedildi. Bu ölçümler ayrıca görünüşte etkilenmemiş kontralateral beyaz cevher hemisfer ölçümleri ile normalize edildi. Bu normalize edilen değerler rCBV, rCBF, rMTT ve rTTP olarak adlandırıldı.
Bulgular: Hem rCBV hem de rCBF, aktif demiyelinizan plaklarda kronik demiyelinizan plaklara kıyasla anlamlı derecede yüksekti ($p<0.001$). Aktif plaklarda ortalama rCBV ve rCBF değerleri sırasıyla 1.61 ± 0.66 ve 1.44 ± 0.59 idi. Kronik plaklarda ortalama rCBV 0.91 ± 0.32 ve ortalama rCBF 0.81 ± 0.26 idi. Ortalama rMTT aktif demiyelinizan plaklarda 0.98 ± 0.53 ve kronik demiyelinizan plaklarda 1.30 ± 0.44 idi ve iki grup arasında anlamlı bir fark vardı ($p=0.004$). Ortalama rTTP de aktif demiyelinizan plaklarda kronik plaklara kıyasla anlamlı derecede uzamıştır ($p<0.001$). Ortalama rTTP aktif ve kronik demiyelinizan plaklarda sırasıyla 0.93 ± 0.14 ve 1.06 ± 0.21 idi
Sonuçlar: Sonuç olarak, DSC-PI incelemesi MS'de aktif ve inaktif demiyelinizan plakların değerlendirilmesinde güvenilir bilgi sağlayabilir.

Anahtar Kelimeler: Demyelinizan hastalık, manyetik rezonans görüntüleme, mMultipl sSkleroz

Introduction

Multiple sclerosis (MS) is an inflammatory and demyelinating disease affecting the central nervous system and is one of the most common neurological disorders in young adults worldwide (1). The pathophysiology of multiple sclerosis is characterized by the immune system targeting the myelin sheath, leading to demyelination and impairment of nerve conduction (2). Understanding the nature of demyelinating plaques displaying this inflammatory activity is crucial for prognosis and treatment strategies, as active plaques are often associated with clinical flares and disease progression (3).

An essential diagnostic and follow-up technique for MS patients is magnetic resonance imaging (MRI) (4). Further, although advanced MRI has demonstrated encouraging outcomes in MS disease monitoring and prognosis determination, it remains understudied

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Complaints: geneltip@selcuk.edu.tr

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and requires additional MRI indicators (5). Dynamic susceptibility contrast perfusion-weighted imaging (DSC-PWI), one of the advanced MRI techniques, measures the degree of tumor vascularity and capillary permeability. In DSC-PWI, intravenous gadolinium causes rapid loss of MRI signal on T2*-weighted images; the amount of this signal loss is related to tumor angiogenesis. DSC-PWI takes advantage of the signal loss brought on by local susceptibility in T2-weighted images by paramagnetic contrast agents, such as the widely used gadolinium-based compounds (6). Although both T2 (such as spin echo) and T2* (such as gradient-echo echo-planar) sequences can be utilized with this technique, T2* approaches are more frequently employed because the former requires greater contrast dosages (7). DSC-PWI is a perfusion MRI method that allows the measurement of cerebral blood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT) in brain tissue (8). DSC-PWI allows the assessment of cerebral blood flow and vascular permeability and provides insights into the inflammatory processes underlying MS plaques. It can also be used to assess active and inactive MS plaques. Since neoangiogenesis and blood-brain barrier (BBB) disruption are present in active plaques, they usually exhibit higher perfusion, whereas inactive plaques may have lower perfusion properties (9,10). Clinicians can use this difference to learn about the disease's present status and potential treatment options. Studies have shown that the use of DSC-PWI can effectively identify these differences, enhancing the diagnostic accuracy for active versus inactive lesions (10).

In our study, we aimed to investigate whether there are differences in DSC-PWI measurements between active plaques showing enhancement and inactive plaques not showing enhancement in patients with MS.

Materials and Methods

The images were evaluated after receiving approval from the Ethics Committee of Selcuk University Faculty of Medicine (Decision No: 2024/634). The study was conducted under the principles of the Declaration of Helsinki.

Patients

In this study, MRI examinations of patients diagnosed with MS according to the 2017 McDonald criteria (4) undergoing conventional cranial MRI and DSC-PWI between April 2018 and December 2020 were analyzed retrospectively. The inclusion criteria for the study were more than 8 weeks since the last relapse or steroid treatment and no recent known trauma history. Exclusion criteria are those not of MRI examinations with insufficient diagnostic quality, or having metallic artifacts. The database search found 30 MS patients with active plaques enhancing contrast. The largest enhancing active plaque and the largest non-enhancing inactive plaque from each patient were evaluated.

MRI protocol, post-processing, and image analysis

Conventional cranial MRI and DSC-PWI were performed in the supine position by using a 1.5 T (Aera, Siemens Healthcare, Erlangen, Germany) MRI scanner with an 18-channel head coil and a 3T (Skyra, Siemens Healthcare) MRI scanner with a 32-channel head coil. Our routine conventional MRI protocol for MS includes conventional cranial MRI without contrast agent, axial and sagittal T1A, axial T2A, axial and sagittal FLAIR after administration of a gadolinium-based contrast agent (0.1 mmol/kg, injection rate: 3–5 mL/s, acquisition time: 102 s) T1A axial, coronal MRI and DSC-PWI. To perform DSC-PWI, a T2*-weighted gradient-echo echo-planar imaging sequence was used. After the evaluation of conventional MRI sequences, perfusion data were transferred to a dedicated workstation running MRI neurology software for DSC-PWI data processing (syngo.via version VB30A, Siemens Healthcare). In conventional MRI sequences, a region of interest (ROI) was manually drawn on DSC-PWI to cover the entire lesion among the active plaques enhancing contrast and the inactive plaques not enhancing contrast. Cerebral blood volume (CBV) and cerebral blood flow (CBF) in this ROI were normalized by the CBV and CBF of the unaffected contralateral white matter hemisphere, termed rCBV and rCBF. Mean transit time (MTT) and time to peak (TTP) were also noted. They also were normalized by the MTT and TTP of the unaffected contralateral white matter and termed rMTT and rTTP.

Statistical analysis

The Statistical Package for Social Sciences software was used for all procedures (IBM SPSS Statistics 22.0, IBM Corporation, Armonk, NY, USA). The Kolmogorov-Smirnov, Shapiro-Wilk test, histogram, and Q-Q plots were used to determine the normal distribution of scale variables. For continuous numerical variables, descriptive statistics are presented as mean ± standard deviation. Categorical variables are represented by the number of cases and percent. The chi-square test was used to compare categorical variables.

A dependent samples t-test was used for data comparisons between active and inactive plaques. Unless otherwise specified, the results were deemed statistically significant at $p< 0.05$.

Results

A total of 30 active and an equal number of chronic lesions in 30 patients with relapsing-remitting MS were included, mostly located in the periventricular areas. In our study, there were 8 (26.7%) males and 22 (73.3%) females, with a mean age of 31.03±10.74 years.

Both rCBV and rCBF were significantly higher in active demyelinating plaques compared to chronic demyelinating plaques ($p<0.001$). Mean rCBV and rCBF values in active plaques were 1.61±0.66 and 1.44±0.59, respectively. In chronic plaques, the mean rCBV was 0.91±0.32 and the mean rCBF was 0.81±0.26 (Table 1).

Table 1. Dynamic susceptibility contrast perfusion MRI parameters in active and chronic demyelinating plaques (n=30)

	Plaque	Value±SD	p
rCBV(mL/100g)	Active	1.61±0.66	<0.001
	Chronic	0.91±0.32	
rCBF(mL/100g/min)	Active	1.44±0.59	<0.001
	Chronic	0.81±0.26	
rMTT	Active	0.98±0.53	0.004
	Chronic	1.30±0.44	
rTTP	Active	0.93±0.14	<0.001
	Chronic	1.06±0.21	

rCBV: Relative cerebral blood volume, rCBF: Relative cerebral blood flow, rMTT: Relative mean transit time, rTTP: Relative time to peak

The mean rMTT was 0.98±0.53 in active demyelinating plaques and 1.30±0.44 in chronic demyelinating plaques, and there was a significant difference between the two groups ($p=0.004$). rMTT was significantly prolonged in active demyelinating plaques (Table 1).

The mean rTTP was also significantly prolonged in active demyelinating plaques compared to chronic plaques ($p<0.001$). Mean rTTP was 0.93 ± 0.14 and 1.06±0.21 in active and chronic demyelinating plaques, respectively (Table 1).

Discussion

In this study, we measured perfusion parameters such as rCBV, rCBF, rMTT, and rTTP in active plaques with gadolinium contrast enhancement and in inactive plaques without contrast enhancement using the DSC-PWI method (Figures 1 and 2). We wished to investigate the effects of BBB permeability disruption and inflammatory activation on perfusion MRI in MS patients. Our results show MRI evidence of BBB disruption and secondary perfusion enhancement in active demyelinating plaques. Our study found increased rCBV, rCBF, prolonged rMTT, and rTTP in active plaques compared to chronic plaques, consistent with increased perfusion.

Regarding the vascular alterations frequently linked to MS lesions, not much has been written. MS lesions typically occur in perivenular areas (5). There is still controversy about the mechanisms of demyelination (6, 7). Studies report that histopathological changes in MS are quite heterogeneous (6,8). Perivascular T cell infiltration and microglia activation are common in MS. Scattered parenchymal T cell infiltration has also been reported in chronic MS (9). Additionally, Adams et al. reported macrophage infiltration, lesion hypercellularity, and lymphocytic perivascular infiltration in MS lesions (10). According to Lassmann et al., certain individuals may experience demyelination due to localized edema in inflammatory lesions, an inflammatory response of the arterial wall resulting in microvascular thrombosis, or microcirculatory problems brought on by T lymphocyte-induced endothelial damage (9). Increased density of microvascularity has also been reported (11). Perfusion parameters in MS patients may be impacted by each of these factors.

There are studies showing abnormalities in the BBB in MS lesions in different regions of the brain (12,13,14). Post-contrast T1W images should be examined to evaluate BBB disruption in MS plaques. Additionally, dynamic contrast-enhanced MRI can measure the permeability of the BBB, and there are studies reporting that dynamic examination is more specific compared to other methods (15). In a study by Ingrisch et al., rCBV and rCBF values were found to be significantly higher in active plaques with contrast enhancement in Dynamic Contrast-Enhanced Perfusion MRI (DCE-PI) (16). Some studies have measured parameters such as the transfer rate constant between plasma and extracellular space to show changes in the BBB in MS patients. Increases in measured parameters were found in plaques in MS patients compared to normal white matter (12,17). According to Ortiz et al., BBB dysfunction in plaques in white matter is based on pathological changes in immunity and inflammatory cytokines (18).

According to some studies, positron emission

tomography showed that patients with MS had significantly lower CBF in their normal-appearing white matter (NAWM) as compared to healthy control groups (19,20). Furthermore, a DSC-PWI analysis revealed that MS patients' cerebral perfusion was much lower than that of healthy controls (21,22). In a study by Ge et al., mean CBV and CBF values in enhancing lesions were found to be significantly higher in the non-enhancing group and in the group whose perfusion was not similar to the perfusion of enhancing lesions. Mean CBV and CBF values were 1.4±0.3 and 21.5±5.1 in enhancing lesions, respectively, and 0.8±0.2 and 10.2±1.8 in the non-enhancing group, respectively (23). Sowa et al. found that CBF was significantly lower in MS plaques compared with normal white matter ($p<0.001$). The mean CBF in MS plaques was 101.97±28.99, while the mean CBF in normal white matter was 130.32 ± 41.91. In addition, in the same study, the mean MTT values were significantly prolonged in plaques, with the mean MTT in MS plaques being 4.34±0.86 and in normal white matter being 3.45±0.73 ($p<0.001$) (13). Sowa et al. found that in patients with newly diagnosed MS, lower MTT was linked with higher disease severity and the existence of disease activity one year later (11). However, there are studies suggesting normal perfusion in normal white matter compared with MS plaques and healthy controls (24). In our study, we found an increase in rCBV and rCBF (Figures 3, 4, 5, and 6), as well as prolongation in rMTT and rTTP in active plaques, consistent with the literature.

We are aware that the study has limitations. Our study was retrospective, and the number of patients was small. We used supratentorial healthy white matter as a reference to normalize perfusion parameters across lesions, but there are studies reporting that these parameters vary regionally in the WM (21,25). However, our results showed that abnormalities in active plaques were consistent with the literature. However, large-scale prospective studies are needed to confirm our results and better elucidate its effect on active disease status and progression.

In conclusion, our study demonstrated that perfusion properties of active and chronic MS lesions can be quantitatively measured via DSC-PWI. Perfusion parameters of active lesions are consistent with BBB disruption and are significantly higher than chronic lesions. This study shows that MR perfusion parameters can be promising for assessing disease activity in MS.

Conflicts of interest

The authors declare no conflicts of interest.

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References

1.Compston A, Coles A. Multiple sclerosis. Lancet. 2008;372(9648):1502-17.

2.Lublin FD, Reingold SC, Cohen JA, Cutter GR, Sørensen PS, Thompson AJ, et al. Defining the clinical course of multiple sclerosis: the 2013 revisions. Neurology. 2014;83(3):278-86.

3.Soheila R, Arezoo B, Galavani H, Saber R. Comments on "Genetic characterization and phylogenetic analysis of Fasciola species based on ITS2 gene sequence, with first molecular evidence of intermediate Fasciola from water buffaloes in Aswan, Egypt". Ann Parasitol. 2021;67(2):351-2.

4.Thompson AJ, Banwell BL, Barkhof F, Carroll WM, Coetzee T, Comi G, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol. 2018;17(2):162-73.

5.Ge Y, Zohrabian VM, Grossman RI. Seven-Tesla magnetic resonance imaging: A new vision of microvascular abnormalities in multiple sclerosis. Arch Neurol. 2008;65(6):812-6.

6.Stadelmann C, Wegner C, Brück W. Inflammation, demyelination, and degeneration - recent insights from MS pathology. Biochim Biophys Acta. 2011;1812(2):275-82.

7.Kutzelnigg A, Lucchinetti CF, Stadelmann C, Brück W, Rauschka H, Bergmann M, et al. Cortical demyelination and diffuse white matter injury in multiple sclerosis. Brain. 2005;128(Pt 11):2705-12.

8.Popescu BF, Pirko I, Lucchinetti CF. Pathology of multiple sclerosis: where do we stand? Continuum (Minneap Minn). 2013;19(4 Multiple Sclerosis):901-21.

9.Lassmann H. Hypoxia-like tissue injury as a component of multiple sclerosis lesions. J Neurol Sci. 2003;206(2):187-91.

10.Adams CW, Poston RN, Buk SJ. Pathology, histochemistry and immunocytochemistry of lesions in acute multiple sclerosis. J Neurol Sci. 1989;92(2-3):291-306.

11.Sowa P, Nygaard GO, Bjørnerud A, Celius EG, Harbo HF, Beyer MK. Magnetic resonance imaging perfusion

is associated with disease severity and activity in multiple sclerosis. Neuroradiology. 2017;59(7):655-64.

12.Cramer SP, Simonsen H, Frederiksen JL, Rostrup E, Larsson HB. Abnormal blood-brain barrier permeability in normal appearing white matter in multiple sclerosis investigated by MRI. Neuroimage Clin. 2014;4:182-9.

13.Sowa P, Bjørnerud A, Nygaard GO, Damangir S, Spulber G, Celius EG, et al. Reduced perfusion in white matter lesions in multiple sclerosis. Eur J Radiol. 2015;84(12):2605-12.

14.Bae J, Zhang J, Wadghiri YZ, Minhas AS, Poptani H, Ge Y, et al. Measurement of blood-brain barrier permeability using dynamic contrast-enhanced magnetic resonance imaging with reduced scan time. Magn Reson Med. 2018;80(4):1686-96.

15.Oghabian MA, Fatemidokht A, Haririchian MH. Quantification of Blood-Brain-Barrier Permeability Dysregulation and Inflammatory Activity in MS Lesions by Dynamic-Contrast Enhanced MR Imaging. Basic Clin Neurosci. 2022;13(1):117-28.

16.Ingrisch M, Sourbron S, Morhard D, Ertl-Wagner B, Kümpfel T, Hohlfeld R, et al. Quantification of perfusion and permeability in multiple sclerosis: dynamic contrast-enhanced MRI in 3D at 3T. Invest Radiol. 2012;47(4):252-8.

17.Taheri S, Rosenberg GA, Ford C. Quantification of blood-to-brain transfer rate in multiple sclerosis. Mult Scler Relat Disord. 2013;2(2):124-32.

18.Ortiz GG, Pacheco-Moisés FP, Macías-Islas M, Flores-Alvarado LJ, Mireles-Ramírez MA, González-Renovato ED, et al. Role of the blood-brain barrier in multiple sclerosis. Arch Med Res. 2014;45(8):687-97.

19.Lycke J, Wikkelsö C, Bergh AC, Jacobsson L, Andersen O. Regional cerebral blood flow in multiple sclerosis measured by single photon emission tomography with technetium-99m hexamethylpropyleneamine oxime. Eur Neurol. 1993;33(2):163-7.

20.Sun X, Tanaka M, Kondo S, Okamoto K, Hirai S. Clinical significance of reduced cerebral metabolism in multiple sclerosis: a combined PET and MRI study. Ann Nucl Med. 1998;12(2):89-94.

21.Law M, Saindane AM, Ge Y, Babb JS, Johnson G, Mannon LJ, et al. Microvascular abnormality in relapsing-remitting multiple sclerosis: perfusion MR imaging findings in normal-appearing white matter. Radiology. 2004;231(3):645-52.

22.Inglese M, Adhya S, Johnson G, Babb JS, Miles L, Jaggi H, et al. Perfusion magnetic resonance imaging correlates with neuropsychological impairment in multiple sclerosis. J Cereb Blood Flow Metab. 2008;28(1):164-71.

23.Ge Y, Law M, Johnson G, Herbert J, Babb JS, Mannon LJ, et al. Dynamic susceptibility contrast perfusion MR imaging of multiple sclerosis lesions: characterizing hemodynamic impairment and inflammatory activity. AJNR Am J Neuroradiol. 2005;26(6):1539-47.

24.Ingrisch M, Sourbron S, Herberich S, Schneider MJ, Kümpfel T, Hohlfeld R, et al. Dynamic Contrast-Enhanced Magnetic Resonance Imaging Suggests Normal Perfusion in Normal-Appearing White Matter in Multiple Sclerosis. Invest Radiol. 2017;52(3):135-41.

25.Ciccarelli O, Werring DJ, Barker GJ, Griffin CM, Wheeler-Kingshott CA, Miller DH, et al. A study of the mechanisms of normal-appearing white matter damage in multiple sclerosis using diffusion tensor imaging--evidence of Wallerian degeneration. J Neurol. 2003;250(3):287-92.