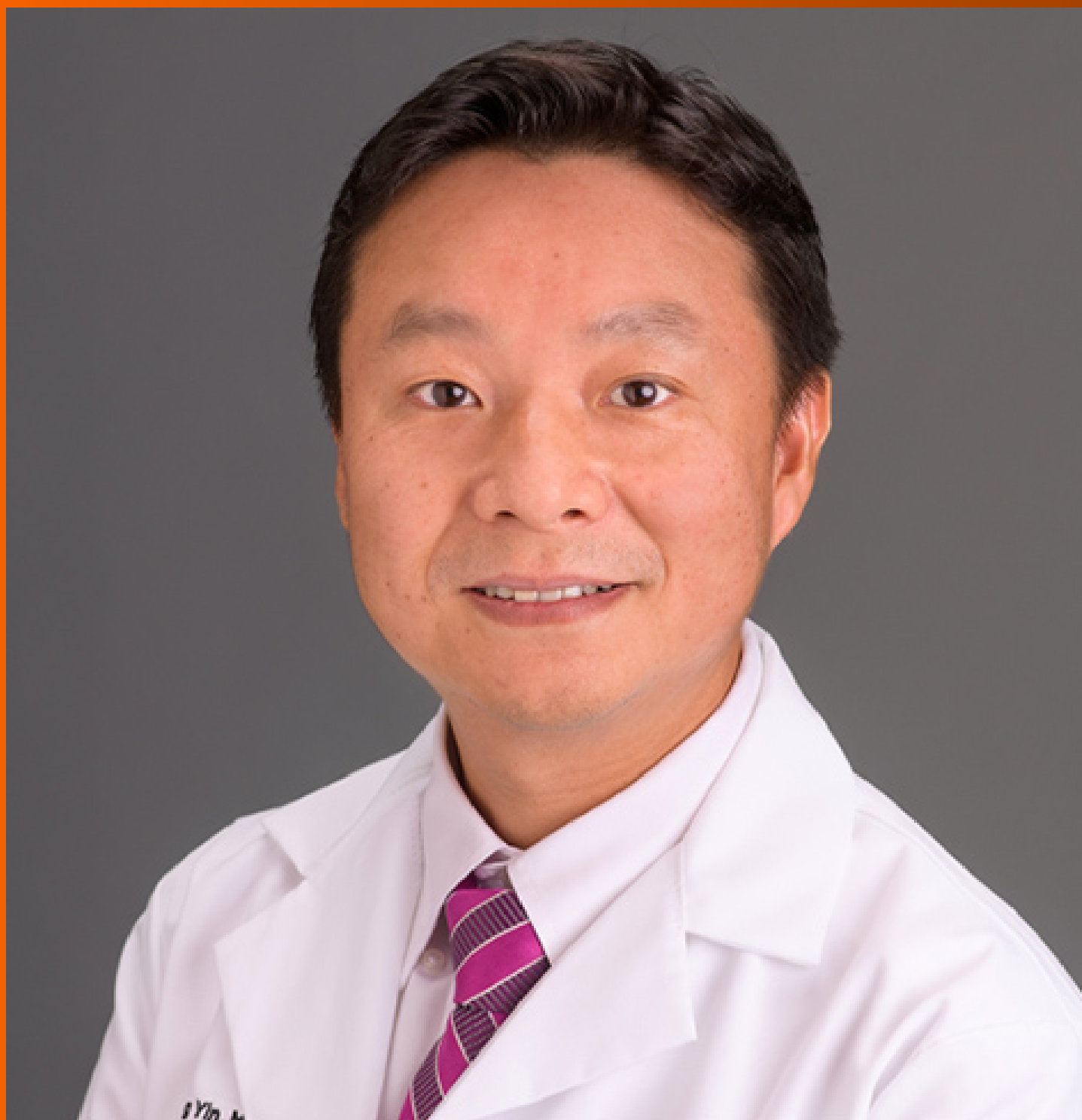


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## Relationship between treatment types and blood–brain barrier disruption in patients with acute ischemic stroke: Two case reports

Youngbeom Seo, Jonghoon Kim, Min Cheol Chang, Hyungkyu Huh, Eun-Hee Lee

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### Abstract

#### BACKGROUND

Blood-brain barrier (BBB) disruption plays an important role in the development of neurological dysfunction in ischemic stroke. However, diagnostic modalities that can clearly diagnose the degree of BBB disruption in ischemic stroke are limited. Here, we describe two cases in which the usefulness of dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) in detecting BBB disruption was evaluated after treatment of acute ischemic stroke using two different methods.

#### CASE SUMMARY

The two patients of similar age and relatively similar cerebral infarction locations were treated conservatively or with thrombectomy, although their sex was different. As a result of analysis by performing DCE-MRI, it was confirmed that BBB disruption was significantly less severe in the patient who underwent thrombectomy ( $P = 3.3 \times 10^{-7}$ ), whereas the average  $K_{trans}$  of the contralateral hemisphere in both patients was similar ( $2.4 \times 10^{-5} \text{ min}^{-1}$  and  $2.0 \times 10^{-5} \text{ min}^{-1}$ ). If reperfusion is achieved through thrombectomy, it may indicate that the penumbra can be saved and BBB recovery can be promoted.

#### CONCLUSION

Our cases suggest that BBB disruption could be important if BBB permeability is used to guide clinical treatment.

**Key Words:** Blood–brain barrier; Ischemic stroke; Dynamic contrast-enhanced magnetic

resonance imaging; Thrombectomy; Penumbra; Case report

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**Core Tip:** We describe two cases in which the usefulness of dynamic contrast-enhanced magnetic resonance imaging in detecting blood–brain barrier (BBB) disruption was evaluated after treatment of acute ischemic stroke using two different methods. Our cases suggest that BBB disruption could be important if BBB permeability is used to guide clinical treatment.

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## INTRODUCTION

Acute ischemic stroke (AIS) is defined as a sudden dysfunction of the central nervous system due to cerebral ischemia and is associated with high mortality and disability rates[1]. Minutes after ischemic stroke, dramatic cerebral pathological changes occur at the genomic, molecular, and cellular levels. One of the major pathological changes is the disruption of the blood–brain barrier (BBB)[2]. Under pathological conditions, such as ischemic stroke, the BBB can be disrupted, followed by extravasation of blood components into the brain, thereby compromising the normal neuronal function. BBB disruption plays an important role in the development of neurological dysfunction in ischemic stroke[3]. However, diagnostic modalities that can clearly diagnose the degree of BBB disruption in ischemic stroke are limited. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is a noninvasive perfusion MRI technique that enables the evaluation of damage to the microcirculatory structure and pathological BBB dysfunction[4]. Here, we describe two cases in which the usefulness of DCE-MRI in detecting BBB disruption was evaluated after treatment of AIS using two different methods.

## CASE PRESENTATION

### Chief complaints

DCE-MRI was performed after two patients were diagnosed with AIS at the Yeungnam University Medical Center. The BBB permeability ( $K_{trans}$ ) was calculated in each patient using the Patlak model[5].

$$C_t(t) = K_{trans} \int_0^t C_p(\tau) d\tau + V_p \cdot C_p(t)$$

where,  $V_p$  and  $C_t(t)$  and  $C_p(t)$  indicate the variable of integration, plasma volume, and temporal variation of the contrast agent of the tissue and plasma, respectively.  $C_p(t)$  was measured in the internal carotid artery with the capillary hematocrit level set at 45%. The average  $K_{trans}$  values were manually segmented and compared.

**Case 1:** A 58-year-old man with a chief complaint of motor aphasia was admitted to our emergency department.

**Case 2:** A 59-year-old woman with a chief complaint of right hemiparesis and motor aphasia arrived at our emergency department.

### History of present illness

**Case 1:** The patient developed symptoms 9 h before arrival at the hospital.

**Case 2:** The patient developed symptoms 10 h before arrival at the hospital.

### History of past illness

**Case 1:** The only notable medical history was hypertension.

**Case 2:** There was no specific medical history.

**Physical examination**

**Case 1:** His National Institute of Health Stroke Scale (NIHSS) score was 3.

**Case 2:** The NIHSS score was 4.

**Imaging examinations**

**Case 1:** Diffusion-weighted imaging (DWI) and perfusion-weighted imaging (PWI) showed acute infarctions in the left temporal and insular lobes with no significant DWI-PWI mismatch in the left middle cerebral artery (MCA) territory (Figure 1A and B).

**Case 2:** DWI and PWI showed acute infarctions in the left parietal and insular lobes with significant DWI-PWI mismatch in the left MCA territory (Figure 1D and E).

**FINAL DIAGNOSIS****Case 1**

Magnetic resonance angiography confirmed occlusion of the M2 inferior trunk of the MCA (Figure 1C).

**Case 2**

Digital subtraction angiography confirmed the occlusion of the M2 inferior trunk (Figure 2F).

**TREATMENT****Case 1**

Since there was no definite DWI-PWI mismatch, we decided to perform treatment with dual antiplatelet medication without endovascular treatment (EVT). The patient was discharged 1 wk later with no new acute infarction and slight improvement in motor aphasia.

**Case 2**

**EVT:** Considering definite DWI-PWI mismatch, we decided to perform EVT. EVT was performed under local anesthesia. A balloon guide catheter (Optimo, Tokai Medical) was placed in the proximal internal carotid artery through the femoral artery. The balloon of the balloon guide catheter was inflated, and the target vessel was navigated using a 0.014-inch micro-guidewire (Asahi Chikai 10, Asahi Intecc) through the occlusion. A microcatheter (Rebar 18, Medtronic) was then advanced over the wire distal to the occlusion. Selective microcatheter angiography was performed to confirm the occlusion site and distal blood flow. The microcatheter was exchanged for a Solitaire FR (4 × 40). Further, stent-retriever thrombectomy using a Solitaire FR was performed. Finally, reperfusion and good antegrade blood flow were confirmed (Figure 1G). The patient was discharged 1 wk later with no definite neurologic deficits, except mild dysarthria.

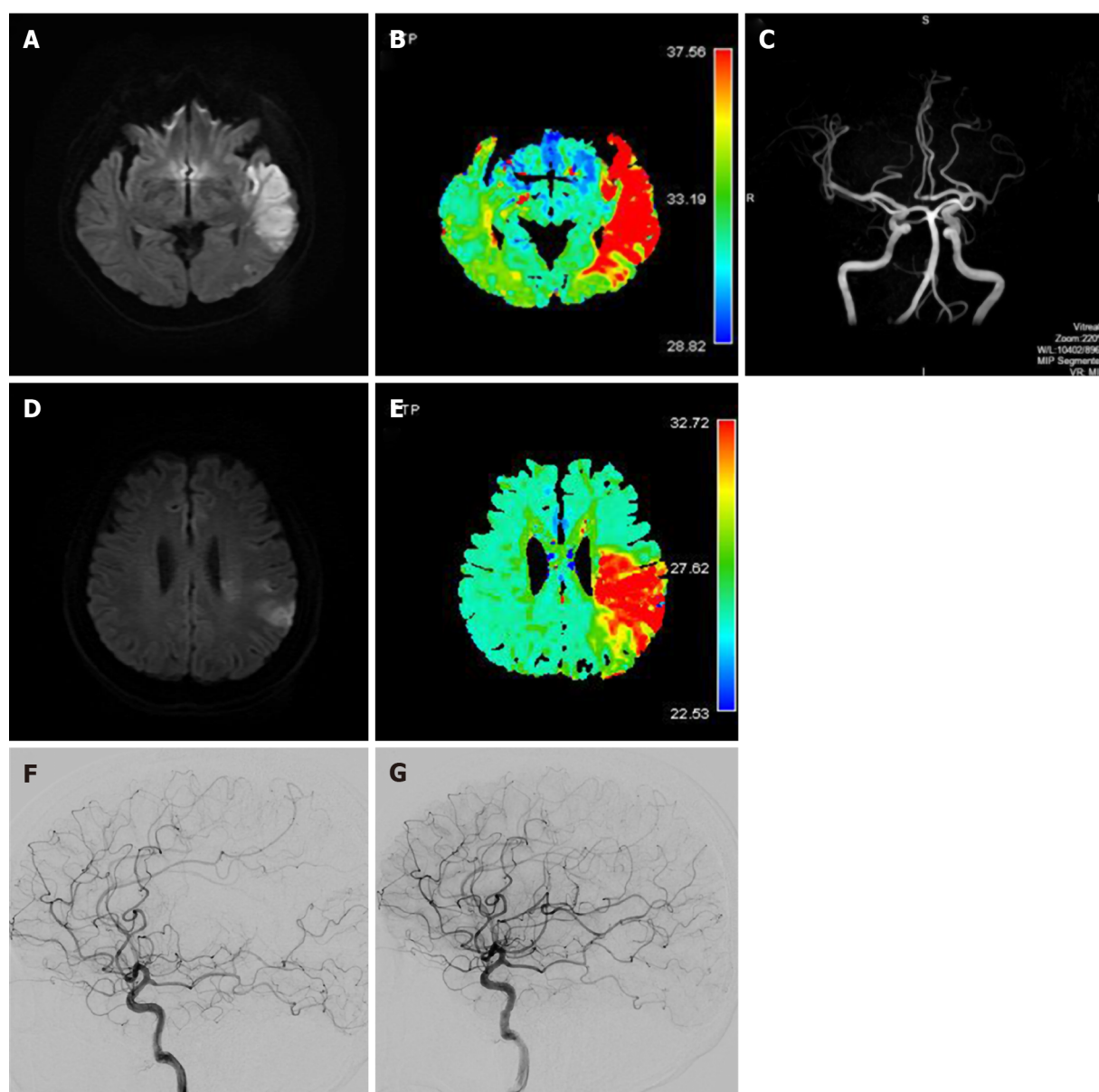
**OUTCOME AND FOLLOW-UP****Case 1 and Case 2**

**BBB disruption:** DCE-MRI was performed after 1 week, the average  $K_{trans}$  of the entire ischemic region after the treatment was  $0.067 \pm 0.026 \text{ min}^{-1}$ , whereas that of the contralateral hemisphere was  $2.4 \times 10^{-5} \text{ min}^{-1}$  (Figure 2A). DCE-MRI was performed after 1 wk, the average  $K_{trans}$  of the entire ischemic region after the treatment was  $0.0097 \pm 0.0024 \text{ min}^{-1}$ , and that of the contralateral hemisphere was  $2.0 \times 10^{-5} \text{ min}^{-1}$  (Figure 2B).

**DISCUSSION**

BBB disruption begins at the onset of ischemic stroke and increases with sustained hypoperfusion. Maintenance of the BBB immediately after stroke onset might be expected to stop the downstream progression of ischemic brain injury and improve clinical outcomes[2].

BBB disruption is an important component of the pathological progression of AIS and is a potential therapeutic target. Thrombectomy is an interventional means to dislodge and remove the blood clot, and the recent American Heart Association recommendations approve its use up to 24 h after symptoms appear[6,7]. The two patients of similar age and relatively similar cerebral infarction locations were

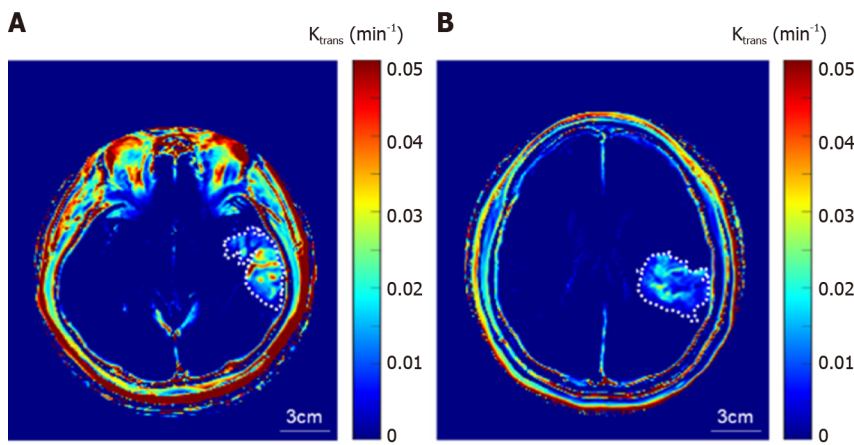


**Figure 1 Diffusion-weighted imaging.** Case 1, A and B: Diffusion-weighted imaging and perfusion-weighted imaging show acute infarctions in the left temporal and insular lobes with no significant diffusion-weighted imaging-perfusion-weighted imaging mismatch; C: Magnetic resonance angiography shows occlusion of the M2 inferior trunk. Case 2, D and E: Diffusion-weighted imaging and perfusion-weighted imaging show acute infarctions in the left parietal and insular lobes with significant DWI-PWI mismatch; F: Digital subtraction angiography confirmed the occlusion of the M2 inferior trunk; G: After thrombectomy, reperfusion and good antegrade blood flow was confirmed.

treated conservatively or with thrombectomy, although their sex was different. As a result of analysis by performing DCE-MRI, it was confirmed that BBB disruption was significantly less severe in the patient who underwent thrombectomy ( $P = 3.3 \times 10^{-7}$ ), whereas the average  $K_{trans}$  of the contralateral hemisphere in both patients was similar ( $2.4 \times 10^{-5} \text{ min}^{-1}$  and  $2.0 \times 10^{-5} \text{ min}^{-1}$ ). If reperfusion is achieved through thrombectomy, it may indicate that the penumbra can be saved and BBB recovery can be promoted. The reversible BBB disruption may be associated with rapid reperfusion, which is associated with shorter periods of cerebral ischemia.

However, it should be noted that studies have found BBB hyperpermeability 3-4 weeks after ischemia onset, indicating that there can be long-term derangement in barrier function[8]. Indeed, in patients with stroke, there is evidence that there may be low-level BBB dysfunction at 1 mo[9]. Rapid reperfusion after mechanical thrombectomy can result in brain tissue injury[10]. Efforts to decrease the duration of BBB disruption could improve clinical outcomes in patients with successful reperfusion.

The impact of BBB disruption after EVT and outcomes in patients with AIS should be investigated in a larger prospective study. For patients with AIS, BBB protective agents could play an important role and should be investigated in the future. The examination of BBB disruption in the management of AIS is an emerging field of research. With the advancement of DCE-MRI, future research on the BBB is likely to reveal potential therapeutic targets for protecting the BBB and improving outcomes in patients with



**Figure 2 Dynamic contrast-enhanced magnetic resonance imaging.** A representative blood-brain barrier permeability ( $K_{trans}$ ) map of the patients without (A) and with (B) thrombectomy. The dashed line indicates the manually segmented stroke region with enhanced  $K_{trans}$ .

AIS.

## CONCLUSION

Our cases suggest that BBB disruption could be important if BBB permeability is used to guide clinical treatment.

## FOOTNOTES

**Author contributions:** Kim J contributed to conception and design of the study; Huh H and Lee EH organized the database; Kim J and Seo Y wrote the first draft of the manuscript; Huh H, Kim J, Chang MC, and Seo J wrote sections of the manuscript; all authors contributed to manuscript revision, read, and approved the submitted version.

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