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Preoperative Evaluation of Computed Tomography Perfusion: Its Significance for the Risk Assessment of Cerebrovascular Complications Perioperatively¹

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Abstract

Neurological complications occur with an overall frequency of 2.8% perioperatively. Although ultrasound imaging is an excellent modality for the risk assessment of carotid arterial diseases, no comprehensive information can be obtained with respect to the intracranial cerebral blood flow. Recent advent of computed tomography perfusion (CTP) imaging has made it possible to directly measure the cerebral blood flow at any intracranial region of interest. We describe here an efficacy of CT perfusion imaging in the preoperative settings for the risk assessment of neurological complications, especially in cases with carotid arterial stenosis/occlusion.

Keywords: computed tomography perfusion, cerebral blood flow, carotid arterial stenosis

1. Introduction

Although overall mortality for patients undergoing coronary bypass graft surgery (CABG) has decreased by 23% in 1990s, the incidence of stroke perioperatively has remained unchanged [1]. Some report suggests that perioperative neurological complications occur with

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an overall frequency of 2.8%, and an incidence rate of 0.9% in patients younger than 65 years, 3.6% aged between 65 and 74 years, and 8.9% older than 75 years [2]. Additionally, the patient with a neurological complication has a ninefold increase in mortality [2]. Carotid arterial disease accounts for approximately 10% of perioperative cerebral complications [3]. Although ultrasound imaging is an excellent modality for evaluating the morphology of the carotid arteries with its excellent spatial resolution [3], intracranial cerebral blood flow dynamics cannot be assessed by the use of ultrasound. Here, we report that computed tomography perfusion (CTP) imaging is an efficacious modality for evaluating the intracranial cerebral flow.

In our facility, CTP imaging has been introduced in 2012, and 58 cases underwent its evaluation by the end of 2014. After obtaining an IRB (Institutional Review Board) approval, we have analyzed all the 58 cases, and identified 11 individuals who have been diagnosed as having carotid arterial stenosis/occlusion. We have measured cerebral blood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT) at the ipsilateral as well as at the contralateral hemisphere, and their correlation to the subsequent development of neurological events during the 2-year follow-up period was evaluated.

Of 11 patients, the decreased CBF at the ipsilateral hemisphere was noted in four individuals, and the other seven showed intact CTP findings. All the four patients who showed decreased CBF pattern and the one who showed normal CTP finding developed cerebrovascular diseases during the 2-year follow-up period. The rest of six individuals who showed normal CTP findings have remained otherwise healthy. We suggest that the decreased CBF at the ipsilateral side may predict the possible neurological complications in the patients with carotid arterial stenosis/occlusion. In patients with carotid arterial stenosis whose cerebral blood flow (CBF) has remained intact, the patients' outcome has remained favorable, and they have remained otherwise healthy. By contrast, in patients whose CBF is decreased, they have developed severe cerebrovascular complications. The findings described here potentially indicate the possibility that CT perfusion findings may predict the perioperative outcomes in patients with carotid arterial stenosis/occlusion.

2. Computed tomography perfusion

CT perfusion is a new technique which enables to evaluate both rapid qualitative and quantitative cerebral perfusion by means of generating cerebral blood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT) [4]. Thus far, several modalities such as magnetic resonance (MR) perfusion [5], xenon computed tomography (xenon CT) [6], positron emission tomography (PET) [7], and single photon emission computed tomography (SPECT) [8] have been used to evaluate cerebral perfusion. Compared to these modalities, CT perfusion can be performed easily and quickly by the use of any standard spiral CT scanner in patients where unenhanced CT is planned to exclude acute intracranial hemorrhage. The fundamental theory of this technique is the central volume principle [4]. It correlates cerebral blood flow (CBF) with cerebral blood volume (CBV) and mean transit time (MTT) in the following equation: $CBF =$

CBV/MTT. In brief, by monitoring the first pass of an iodinated contrast agent by the bolus injection through the cerebral vasculature, the linear relationship between contrast agent concentration and attenuation can be obtained in a given region of interest. After an acquisition of the raw results, data are analyzed at an imaging workstation (Advantage Windows; GE Medical Systems) equipped with commercially available software (CT perfusion; GE Medical Systems). By the use of CT perfusion, it becomes easy and quick to identify and quantify the presence and extent of a perfusion deficit in an acute stroke setting in whom an emergent thrombolytic therapy is going to be considered [9]. In addition, it is also suitable for the evaluation of cerebrovascular reserve in patients with stenotic lesions who would be the potential candidates for neuroendovascular treatment and bypass surgery.

Although other multi-modalities such as SPECT/CT and PET/CT system also provide good comprehensive information with respect to the combination of anatomical and functional data, they usually require the specific equipment which sometimes makes it difficult to their global diffusion into the clinical practice [7, 8]. For instance, for SPECT/CT, a dual-detector gamma camera and a low-dose four-slice CT mounted on the same rotate platform are required (Infinia Hawkeye 4, GE Medical Systems). By contrast, CT perfusion can be performed easily and quickly using a standard spiral CT scanner and does not require specific equipment except for an imaging workstation, which makes it suitable for the global use in the evaluation of cerebral blood flow.

3. CT perfusion may predict patients' outcome in patients with carotid arterial stenosis

Except for a history of hypertension, an otherwise healthy 72-year-old male was planned for an elective surgery for his cervical disc hernia. His preoperative evaluation of carotid ultrasonography revealed total occlusion of the left internal carotid artery (**Figure 1A**). Since we have experienced a similar case in which stroke has developed shortly after the diagnosis of total occlusion of the left internal carotid artery (**Figure 1B**), we planned to evaluate the potential risks of developing neurological complications perioperatively by CT perfusion. In the latter case in which stroke has been confirmed soon after the diagnosis of total left internal carotid artery occlusion, simultaneous evaluation of CT perfusion revealed clear laterality of cerebral blood flow imaging, suggesting that the left intracranial hypoperfusion was apparent owing to the total occlusion of the left internal carotid artery (**Figure 1C**). By contrast, in the former case, no laterality of the intracranial cerebral flow was observed, suggesting that the collateral circulation may have compensated the total occlusion of the left internal carotid artery (**Figure 1D**). To further confirm that there is no laterality of cerebral blood flow between the right and the left hemispheres, we calculated the cerebral blood flow (CBF), mean transit time (MTT), and the cerebral blood volume (CBV) in his both hemispheres. The right cerebral blood flow was 34.4 mL/100 g/min and the left CBF was 34.5 mL/100 g/min. The cerebral blood volume (CBV) of his right hemisphere was 2.7 mL/100 g and the CBV of his left hemisphere was 2.9 mL/100 g. The mean transit time (MTT) of his right hemisphere was 4.9 s and the left was 5.3

s. The results clearly showed that there was no difference between his right and left hemispheres with respect to the dynamics of cerebral blood flow, although prolonged MTT was equally observed in both hemispheres to some degree. Based on the results of CT perfusion, the patient was given the consent that if his neurological symptoms relating to his cervical disc hernia would further worsen, he is going to be scheduled for an elective surgery. During the 2-year follow-up period, he has not developed any cerebrovascular complications and has remained otherwise healthy.

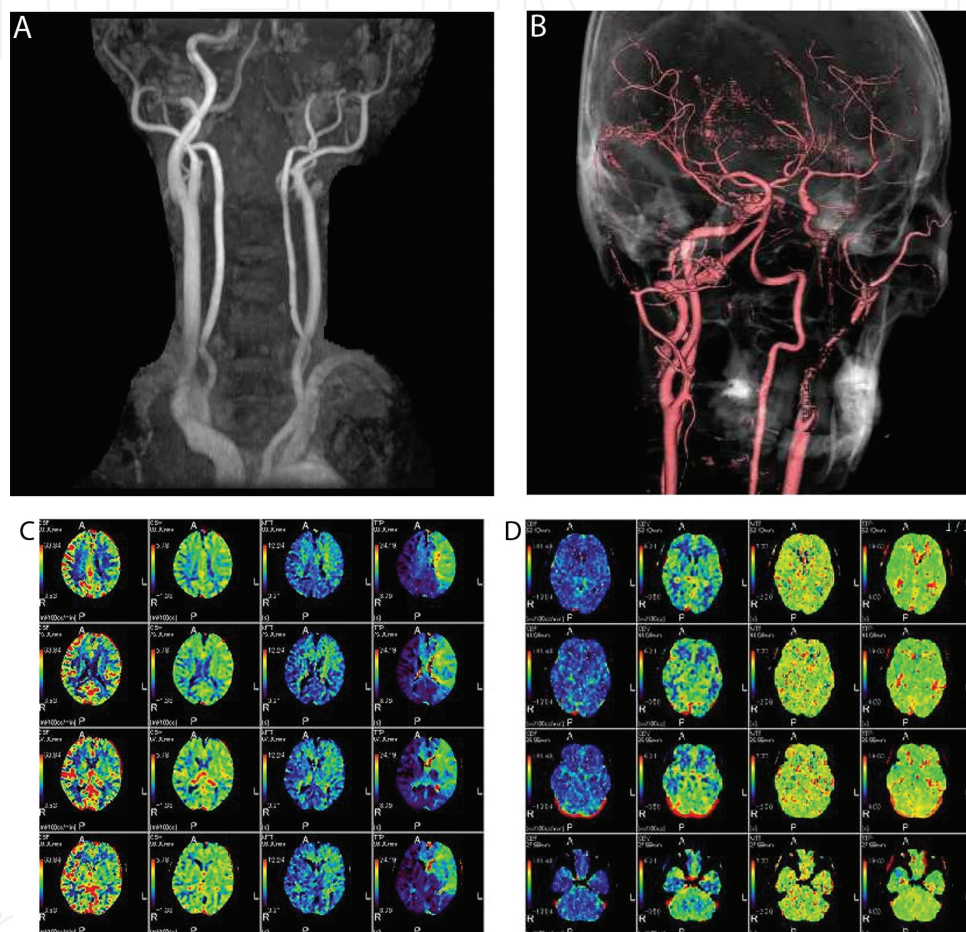


Figure 1. (A) A 72-year-old male presented to our hospital complaining the pain in the left upper extremity. He was diagnosed as having cervical disc hernia. Simultaneous evaluation of cervical MR angiography together with ultrasound imaging revealed total occlusion of the left internal carotid artery. (B) A 65-year-old male presented to our hospital because of transient gait instability and dysarthria. CT angiography together with ultrasound imaging revealed total occlusion of the left internal carotid artery. (C) CT perfusion imaging revealed an apparent decrease of CBF and prolonged MTT in his left hemisphere. (D) CT perfusion imaging of the 72-year-old male revealed no apparent laterality of CBF, CBV, and MTT between the right and the left hemispheres.

After obtaining Institutional Review Board's approval, we have further surveyed all the medical charts of 58 patients who have been examined by CT perfusion in our facility between 2012 and 2014. Among the 58 cases, we have identified 11 individuals who have been diagnosed as having carotid arterial stenosis by ultrasonography. Among 11 patients with carotid arterial stenosis, 7 patients had no apparent CBF laterality or CBV laterality. Except for one

case in whom bilateral carotid arterial stenosis (77% stenosis in the right internal carotid artery and 85% stenosis in the left carotid artery) was noted by ultrasonography who subsequently was found dead at his home, all the six cases have remained otherwise healthy without any cerebrovascular complications during the 2-year follow-up period, which suggests that the intact CT perfusion findings may predict favorable outcome in patients with carotid arterial stenosis (**Table 1**). By contrast, the rest of four patients with an apparent CBF decrease either with maintained CBV or with decreased CBV developed irreversible cerebrovascular complications either at the time of evaluation of CT perfusion or during the 2-year follow-up period (**Table 1**). The incidence of development of cerebrovascular complication was significantly higher in whom an abnormal CT perfusion finding was observed ($p = 0.006$, chi-squared test).

	Decreased CBF at the ipsilateral hemisphere	Intact CT perfusion findings
The number of patients who developed irreversible cerebrovascular complications	4	1*
The number of patients who remained otherwise healthy without neurological symptoms	0	6**

Among 11 patients who were diagnosed as having carotid arterial stenosis by ultrasonography, 4 patients showed an apparent decreased CBF at the ipsilateral hemisphere, and 7 patients showed normal CT perfusion findings. All the four patients developed irreversible cerebrovascular complications either at the time when CT perfusion was evaluated or during the 2-year follow-up period.

*Bilateral carotid arterial stenosis (77% stenosis in the right internal carotid artery and 85% stenosis in the left carotid artery) was noted by ultrasonography, and the patient was subsequently found dead at his home.

**Although the sample power is not strong enough, the likelihood of the patients with carotid arterial stenosis to remain healthy appeared to have correlated with their intact CT perfusion findings ($p = 0.006$, chi-squared test).

Table 1. The outcome of the patients with carotid arterial stenosis (with 2-year follow-up) and its correlation to their findings of CT perfusion.

4. Delayed hypocerebral perfusion following aneurysmal clipping surgery: A new clinical entity

Among 58 cases, we found five individuals who had undergone neurosurgical clipping for subarachnoid hemorrhage either at our facility or in the other hospital. Notably, two out of five cases were found to have hypoperfusion of cerebral blood flow at the distal regions of artery where clipping was performed. A 72-year-old female underwent neurosurgical clipping of the right mid-cerebral artery due to the ruptured aneurysm at the age of 58 at the other hospital (**Figure 2A**). Eleven years after surgery, she presented at our hospital, complaining of right tinnitus, vertigo, and headache. She was eventually evaluated by CT angiography together with CT perfusion, which revealed an apparent hypoperfusion of the right mid-cerebral artery (**Figure 2B**). Her cerebral blood flow corresponding to the region where the right mid-cerebral artery perfuses is 16.4 mL/100 g/min, whereas the cerebral blood flow of the contralateral hemisphere was 32.7 mL/100 g/min. The CBV corresponding to the right mid-cerebral artery is 1.0 mL/100 g and the CBV of the contralateral hemisphere was 1.1 mL/100 g.

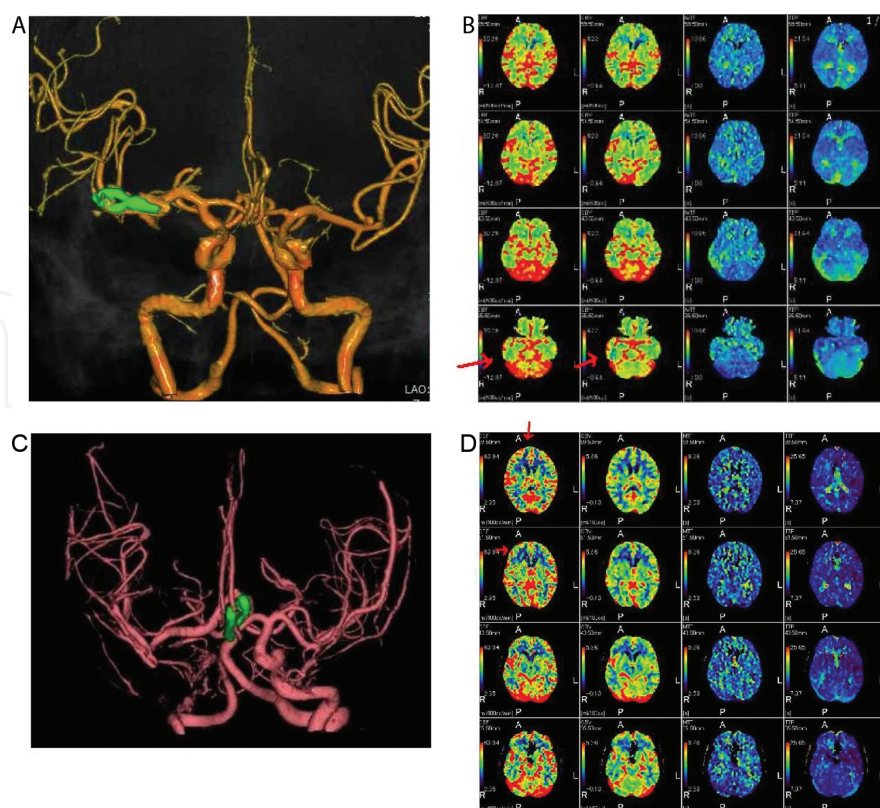


Figure 2. (A) A 72-year-old female underwent neurosurgical clipping of the right mid-cerebral artery due to the ruptured aneurysm at the age of 58 at the other hospital. Her CT angiography is shown in the figure. (B) CT perfusion findings revealed an apparent decrease of cerebral blood flow perfused by the right mid-cerebral artery (indicated by the arrows). (C) A 63-year-old woman underwent emergent neuroclipping surgery for the ruptured anterior-communicating artery aneurysm. Her CT angiography is shown in the figure. The surgery is successfully carried out. (D) Six months postoperatively, a physiotherapist noticed her slight memory defect, and CT perfusion was evaluated, which revealed an apparent hypoperfusion of both frontal lobes (indicated by the arrows).

The right MTT was 4.6 s and the left MTT was 4.6 s, confirming the results that the cerebral blood flow of the right mid-cerebral artery just distal of the clipped region is actually decreasing. Similarly, a 63-year-old woman underwent emergent clipping surgery for the ruptured anterior-communicating artery aneurysm (**Figure 2C**). During the follow-up period, she had a slight defect of memory, and the CT perfusion was evaluated, which clearly revealed the impairment of cerebral blood flow in both the frontal lobes (**Figure 2D**). The quantification of the cerebral blood flow actually confirmed the decrease of the cerebral blood flow in both the frontal lobes as compared to the regions where mid-cerebral artery perfuses (CBF; right frontal: 17.1 mL/100 g/min, left frontal: 14.1 mL/100 g/min; right temporal: 43.5 mL/100 g/min, left temporal: 48.4 mL/100 g/min). The significance of the findings is that although anesthesiologists usually consider the patients who had successfully undergone neuroclipping surgery as the standard risk group, we found here that they still may pose a risk for neurological complications perioperatively even after the successful surgery. The finding may encompass not only to the perioperative risks of patients who had undergone aneurysmal clipping surgery but also to its delayed neurological manifestations associated with the hypoperfusion of parental artery, a possible new diagnostic clinical entity.

5. Computed tomography perfusion as the means to noninvasively measure tumor malignancy

Tumors usually exhibit increased angiogenic activity and neovascularization, which result in increased blood volume. Accordingly, previous studies suggested that CBV and CBF were elevated in tumors, and they may be efficacious in the assessment of tumor angiogenic activity.

A 59-year-old male visited our hospital complaining of dizziness and nausea. His T2-weighted magnetic resonance image showed an overt edematous left temporal lobe (**Figure 3A**). Based on the images obtained, the presence of limbic encephalitis was suspected. He was coincidentally seropositive for human T-cell leukemia virus-1 (HTLV-1). Accordingly, the other differential diagnosis such as non-Hodgkin lymphoma, limbic encephalitis associated with autoimmunity, paraneoplastic syndrome (PNLE; paraneoplastic limbic encephalitis), herpes encephalitis, and astrocytoma could also be possible. In an attempt to obtain further clues for the diagnosis of his disease, especially to determine whether or not directly to obtain histopathological findings by craniotomy, CT perfusion study was performed. The CT perfusion findings indicated a moderate increase of CBV in the corresponding region (**Figure 3B**), an apparent increase of TTP (time to peak) (**Figure 3B**), a slight increase of MTT, and an intact CBF (**Figure 3B**), which indicates the potential possibility of the presence of the primary tumor surrounded by the edematous normal brain tissue. Based on the findings, he underwent computer-navigated craniotomy. The postoperative histopathological findings confirmed the presence of astrocytoma grade 2.

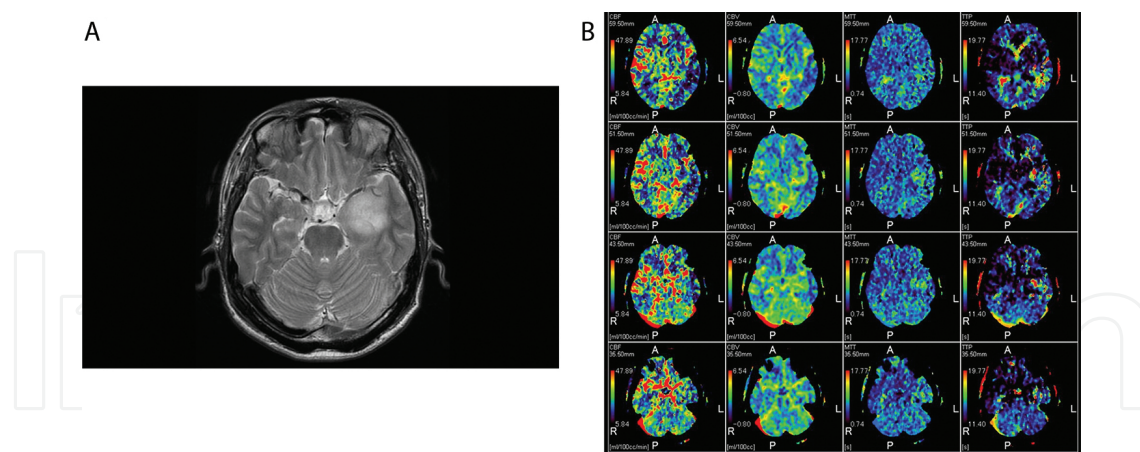


Figure 3. (A) T2-weighted magnetic resonance image of a 59-year-old male who presented to our hospital because of dizziness and nausea. An edematous region of the temporal lobe is apparent, suggesting the presence of limbic encephalitis. (B) A CT perfusion imaging of the same patient. From left to the right, CBF, CBV, MTT, and TTP are visualized. The corresponding region where limbic encephalitis is suspected, an apparent increase of CBV and TTP is observed. CBF remained intact and a slight increase of MTT is also observed.

Since an increase of CBV and TTP reflects angiogenic activity and neovascularization of the tumor, our findings may indicate that CT perfusion findings may potentially be predictive of pathologic grade of the tumor and correlate with tumor mitotic activity. Because the diagnosis

of limbic encephalitis is extremely difficult and the laboratory investigations often only provide inconclusive evidence, we suggest that CT perfusion is potentially an important modality that may provide clues to the correct diagnosis.

6. Implications of the study results

We have shown here that the CT perfusion is an efficacious modality to evaluate the intracranial cerebral blood flow dynamics and may predict the favorable outcome in the cases with carotid arterial stenosis whose CT perfusion findings have remained intact. Using the standard 16-section multidetector scanners, CT perfusion together with CT angiography can be rapidly performed in less than 2 min. CT perfusion can measure virtually every brain tissue blood perfusion, and the commonly used parameters in CT perfusion are as follows: CBF: cerebral blood flow, CBV: cerebral blood volume, and MTT: mean transit time. CBF is defined as the flowing blood volume moving through a given volume (usually 100 g) of brain in a specific amount of time. CBV is defined as the flowing blood volume in the given volume of brain. MTT is defined as the average amount of time the blood takes to transit through the given volume of brain.

CT perfusion has come to its clinical use in the mid-2000s and it has now a growing role in the evaluation of intracranial hemodynamics [9–11]. The tissue that shows decreased CBF with maintained CBV indicates those with severe hypoperfusion. The tissue that shows decreased CBF with decreased CBV and increased MTT suggests those with irreversible ischemic change. Although the number of patients we were able to evaluate was limited, it appears likely that those with intact CT perfusion findings have apparent good prognosis irrespective of the presence of carotid stenosis.

In conclusion, by using CT perfusion, it appears feasible to evaluate the intracranial cerebral flow dynamics which is difficult to assess by the use of ultrasound, and it may predict the favorable outcome if the CT perfusion findings have remained intact. The findings described here would further contribute to the preoperative evaluation of the risk assessment of potential devastating neurological complications, especially for those undergoing cardiac surgeries. We also suggest that in patients with carotid arterial stenosis, the evaluation of CT perfusion in the preoperative settings would be the prerequisite for the avoidance of possible development of cerebrovascular complications perioperatively.

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