CLINICAL RESEARCH

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Intraoperative Perfusion Computed Tomography Received: 2015.12.30 Accepted: 2016.01.25 Published: 2016.09.22 in Carotid Endarterectomy: Initial Experience in 16 Cases BC 1 Zhe Xue Authors' Contribution: 1 Department of Neurosurgery, Chinese PLA General Hospital, Beijing, P.R. China 2 Department of Neurosurgery, Affiliated Hospital of Logistics College of Chinese Study Design A CD 1,2 Dingwei Peng People's Armed Police Forces, Tianjin, P.R. China Data Collection B ABCD 1 Zhenghui Sun Statistical Analysis C 3 Department of Radiology, Chinese PLA General Hospital, Beijing, P.R. China DE 1 Chen Wu Data Interpretation D Manuscript Preparation E EF 1 Bainan Xu Literature Search E FG 1 Fuyu Wang Funds Collection G **Dingbiao Zhou** AD 1 **Tianxiang Dong** BF 3 **Corresponding Author:** Zhenghui Sun, e-mail: szhenghui@sina.com Source of support: Departmental sources Background: This study aimed to evaluate the changes in perfusion computed tomography (PCT) parameters in carotid endarterectomy (CEA), and to discuss the use of intraoperative PCT in CEA. Material/Methods: Sixteen patients with carotid stenosis who also underwent CEA with intraoperative CT were recruited in this study. We calculated quantitative data on cerebral blood flow (CBF), cerebral blood volume (CBV), time to peak (TTP), and the relative parameter values, including relative CBF (rCBF), relative CBV (rCBV), and relative TTP (rTTP). The role of PCT was assessed and compared to conventional monitoring methods. **Results:** There were no significant differences in any of the parameters in the anterior cerebral artery (ACA) territory (P>0.05). In the middle cerebral artery (MCA) territory, the CBF and CBV increased and TTP decreased in the operated side during CEA: the rCBF and rCBV increased and the rTTP decreased significantly (P<0.05). In 16 patients, CT parameters were improved, SSEP was normal, and MDU was abnormal. In 3 patients, CBF increased by more than 70% during CEA. Relative PCT parameters are sensitive indicators for detecting early cerebral hemodynamic changes during CEA. Cerebral hemodynamics changed significantly in the MCA territory during CEA. **Conclusions:** Intraoperative PCT could be an important adjuvant monitoring method in CEA. **MeSH Keywords:** Acanthaceae • Esophageal pH Monitoring • Intraoperative Awareness Abbreviations: ACA - anterior cerebral artery; CBF - cerebral blood flow; CBV - cerebral blood volume; CEA - carotid endarterectomy; ICA - internal carotid artery; MCA - middle cerebral artery; MDU - microvascular Doppler ultrasonography; PCT - perfusion computed tomography; rCBF - relative cerebral blood flow; rCBV - relative cerebral blood volume; ROI - region of interest; rTTP - relative time to peak; SSEP - somatosensory evoked potential; TTP - time to peak Full-text PDF: http://www.medscimonit.com/abstract/index/idArt/897356 **1** 33 2 2817 2 4 **1** 🖞 🕺 1



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Background

Carotid artery stenosis is one of main risk factors for ischemic cerebrovascular diseases. Twenty to thirty percent of patients who have a transient ischemic attack or cerebral infarction have severe stenosis or occlusion of the extracranial internal carotid artery (ICA) [1,2]. Recently, 2 effective forms of carotid artery stenosis therapy were discovered. One is carotid end-arterectomy (CEA), which is considered as the first choice in most patients due to the advantage of fewer complications, lower mortality, and lower expenses. Another effective form is carotid artery stenting [2–4]. The major complications of CEA include cerebral ischemia (due to hypoperfusion and dropped embolus) and cerebral hyperperfusion, both of which can result in intracranial hemorrhage and cognitive impairment. The intracranial hemorrhage and cognitive impairment are mainly caused by cerebral hemodynamic changes [5–7].

Monitoring cerebral hemodynamics during surgery is important in CEA because cerebral hemodynamics change during CEA [8]. Some intraoperative monitoring methods for use during the CEA processes have been reported. Electroencephalogram and somatosensory evoked potential (SSEP) allow identification of already significant cerebral ischemia and can indirectly reflect the cerebral hemodynamics [9–11]. Micro-vascular Doppler ultrasonography (MDU) is the other intraoperative monitoring method for cerebral hemodynamics, which can measure the blood flow velocity directly [12].

Perfusion computed tomography (PCT) has recently become a useful tool for evaluation of cerebral perfusion. The potential of PCT to provide immediate information about cerebral perfusion during the performance of CEA means it could be a useful intraoperative monitoring method in clinical practice [13].

This study aimed to evaluate the changes in PCT parameters in CEA, and to discuss the clinical use of intraoperative PCT in CEA.

Material and Methods

Patient population

Between March 2012 and February 2013, 16 patients with moderate or severe carotid stenosis combined with CEA in our department were recruited in the present study (Table 1). All patients were diagnosed by Doppler ultrasonography and digital subtraction angiography. All of the patients signed the informed consent form before the surgery. CT and MRI showed no fresh cerebral infarction or cerebral hemorrhage.

Patients inclusion criteria were: 1) the severity of the stenosis of the symptomatic carotid artery must be greater than 50%

Table 1. Patient characteristics.

Characteristic	Value
Patient age(yrs)	65±8 (range 49–79 years)
Male: female	10: 6
Presenting event	
Transient ischemic attack	4
Cerebral infarction	3
Dizzyiness or no symptoms	9
Stenosis degree(%)	
Greater than 70%	13
50–70%	3
Medical history	
Hypertension	13
Diabetes mellitus	5
Coronary heart disease	4

and 2) the severity of the stenosis of the asymptomatic carotid artery must be greater than 70%. Exclusion criteria were: intracranial artery occlusion, cerebral hemorrhage or fresh cerebral infarction within 2 weeks, stenosis location over the mandibular angle, presence of contraindications to contrast (e.g., renal failure, hyperthyroidism, and contrast material allergy), and patients not medically fit for surgery.

Introduction to the operating room

The CEA was performed in an operating room with special equipment. A 40-multislice CT scanner (Somatom Sensation Open Sliding Gantry, Siemens Medical Solutions, Germany) with a sliding gantry and an 82-cm bore diameter was installed on rails mounted into the floor of the operating room. A radiolucent, adjustable, flexible operating table with a carbon table plate (Trumpf, Ditzingen, Germany) where the patient's head is fixed in a radiolucent headclamp (Mayfield Integra, USA) was used to maintain the scanning position. This allowed the patient to move back automatically to the previous position when the scanning was performed again. A motor injection pump (ACIST, USA) was used for injection of contrast media for PCT.

Protocols of operation

After general anesthesia the patient was positioned on the operating table according to the surgery. A collision check between the gantry and operating table was performed, and then the height of the bed was stored in memory. After connecting the motor injector pump to a median cubital vein catheter, PCT

	CBF (ml/100 ml/min)			CBV (ml/100 ml)			TTP (0.1 s)		
	Operated side	Contralateral side	P Value	Operated side	Contralateral side	P Value	Operated side	Contralateral side	P Value
Pre-CEA	67.81±14.27	71.58±17.25	0.297	38.00±7.23	38.82±9.11	0.629	108.78±24.80	98.81±15.63 (0.027
Post-CEA	78.50±17.74	62.31±15.62	<0.001	41.96±8.19	35.25±7.24	0.002	99.11±20.96	104.59±20.23	0.031

Table 2. Comparison of pre- and post-CEA PCT parameters for operated side and contralateral side in MCA territory.

Data are shown as mean values \pm standard deviations. CBF – cerebral blood flow; CBV – cerebral blood volume; CEA – carotid endarterectomy; MCA – middle cerebral artery; PCT – perfusion computed tomography; TTP – time to peak.

scanning was performed (i.e., preoperative PCT). Connecting the electrodes to the head, the CEA was performed. The data of SSEP and MDU and time of temporary clamping were recorded before clamping the ICA and after closing the wound in the ICA. After the surgeon satisfied with the CEA, all metal instruments were removed from the scanned area, a sterile drape was placed over the patient, and PCT scanning was performed again (i.e., intraoperative PCT). Then, the additional drape was removed, and the surgical procedure was resumed.

PCT acquisition

A scout CT for planning of the scan range from the orbitomeatal line to the vertex was acquired first. This was followed by PCT scanning with 80 kV and 100 mAs at the level of the basal ganglia for a period of 40 s. There was a 5-s delay after a bolus injection of 40 ml contrast agent (Ultravist 300, 300 mg of iodine per milliliter). Then, a 40-ml saline flush was performed at 7 ml/s by using a motor injection pump, and PCT scanning was started. PCT data were transferred to a PCT workstation and were analyzed using the standard, vendor-provided software. Color-coded parameter maps of cerebral blood flow (CBF), cerebral blood volume (CBV), and time to peak (TTP) were also generated.

To quantify changes in perfusion parameters before and during CEA, the slab closest to the level of the basal ganglia on the pretreatment perfusion CT scan was matched to the corresponding slab at the same level after treatment. When regions of interest (ROIs), including middle cerebral artery (MCA) territory and anterior communicating artery (ACA) territory in the hemisphere were manually drawn on each slab, the mirrored ROIs in contralateral hemisphere were automatically selected. Bone, vessels, and cerebrospinal fluid were automatically removed.

Statistical analyses

From each ROI, the absolute PCT parameter values, including CBF (expressed in milliliters per 100 milliliters of tissue per minute), CBV (expressed in milliliters per 100 milliliters of tissue), and TTP (expressed in milliliters per 100 milliliters of tissue) in the operated side and contralateral, side were calculated. Relative PCT parameters, including relative CBF (rCBF), relative CBV (rCBV), and relative TTP (rTTP), were calculated. The two-tailed paired t test was used to compare the absolute PCT parameter values in the operated side with those in the contralateral side separately, before and during CEA. Then we compared the relative and absolute PCT parameter values before CEA with those during CEA. All statistical analyses were performed using SPSS software (version 13.0). P<0.05 was considered as statistical significance.

The sensitivity of PCT, SSEP, and MDU for evaluation of the cerebral perfusion was compared. The criteria for SSEP changes included the amplitude decreasing by more than 50% or latent period delaying more than 10% compared with baseline, which was confirmed before temporary ICA clamping [11]. The criterion for MDU changes was the blood flow increasing or decreasing more than 10% compared with that before temporary ICA clamping [12].

All PCT scanning was performed by the same experienced radiology technologist, the PCT data processing was done by a neuro-radiology technologist and a neurosurgeon, and the SSEP and MDU were performed by an experienced electrophysiology technologist.

Results

Absolute PCT parameters

Compared to the absolute PCT parameters in the operated side and contralateral side, the TTP in the operated side was increased significantly (P<0.05), whereas no difference in the CBF and CBV was found (P>0.05) before CEA in the MCA territory. During CEA, the increases in CBF and CBV and the decreases in TTP in the operated side were significant (P<0.05, Table 2).

In the ACA territory, all the absolute PCT parameters had no significant changes (P>0.05, Table 3).

	CBF (ml/100 ml/min)			CBV (ml/100 ml)			TTP (0.1 s)		
	Operated side	Contralateral side	P Value	Operated side	Contralateral side	P Value	Operated side	Contralateral side	P Value
Pre-CEA	61.76±16.34	61.40±13.11	0.929	34.88± 7.97	34.31±7.76	0.789	105.86±23.03	3101.38±16.77	0.175
Post-CEA	61.38±16.59	53.91±18.69	0.079	33.20±6.15	30.36±9.32	0.128	105.24±20.8	1105.73±21.93	0.889

Table 3. Comparison of pre- and post-CEA PCT parameters for operated side and contralateral side in ACA territory.

Data are shown as mean values \pm standard deviations. ACA – anterior cerebral artery; CBF – cerebral blood flow; CBV – cerebral blood volume; CEA – carotid endarterectomy; PCT – perfusion computed tomography; TTP – time to peak.

Table 4. Comparison of relative PCT parameters for pre- and post-CEA in ACA territory and MCA territory.

	rCBF			rCBV			rTTP		
	Pre-CEA	Post-CEA	P Value	Pre-CEA	Post-CEA	P Value	Pre-CEA	Post-CEA	P Value
MCA territory	0.97±0.20	1.29±0.25	< 0.001	1.00±0.17	1.22±0.24	0.002	1.10±0.15	0.95±0.09	<0.001
ACA territory	1.04±0.32	1.22±0.36	0.080	1.06±0.31	1.16±0.30	0.250	1.04±0.12	1.00±0.12	0.412

Data are shown as mean values \pm standard deviations. ACA – anterior cerebral artery; CBF – cerebral blood flow; CBV – cerebral blood volume; CEA – carotid endarterectomy; PCT – perfusion computed tomography; TTP – time to peak.

Relative PCT parameters

Comparison of relative PCT parameters before CEA with those during CEA revealed that the rCBF and rCBV were significantly increased and the rTTP was significantly decreased in the MCA territory (P<0.05), but no significant difference was detected in the ACA territory (P>0.05, Table 4).

Comparison of PCT with SSEP and MDU

In all 16 patients, PCT parameters were improved, SSEP was normal, and MDU was abnormal. In 3 patients, CBF increased by more than 70% after CEA (Figure 1).

Routine CT and time of temporary clamping

Intraoperative routine CT scan showed no cerebral hemorrhage. The mean time of temporal clamping was (27.56±5.26) min (range, 16–41 min).

Clinical outcome

None of the 16 patients had complications related to CEA or the iodine contrast agent.

Discussion

PCT was performed at the selected level with the help of a bolus injection of contrast agent, and the PCT parameters obtained from time-density curve analysis were used to evaluate the brain perfusion. Compared to the other methods of perfusion imaging, such as positron emission tomography, singlephoton emission computed tomography, xenon CT, and perfusion-weighted imaging [5,14,15], PCT was shown to have advantages of simplicity, short acquisition time, and providing a high-quality image. Therefore, PCT is widely used to diagnose acute cerebral ischemic stroke [16], to access delayed ischemia in patients with subarachnoid hemorrhage [17], to measure reserve capacity in patients with carotid occlusive disease using acetazolamide [18], to evaluate the effect of endovascular treatment and extracranial-intracranial bypass surgery [19,20], to predict hyperperfusion after surgery [21], and to diagnose and classify brain tumors [22].

PCT can provide quantitative information about brain perfusion status according to the CBF, CBV, and TTP. However, the absolute PCT parameters are easily subject to high intersubject variation and influenced by physiologic parameters, and frequently do not reflect true brain perfusion. Several measures were used to deal with this problem in the present study. First, all the PCT maps and ROIs were generated by the same experienced neuroradiologic technologist and neurosurgeon to minimize interoperator variability. Second, the transverse



Figure 1. Preoperative DSA revealing a 90% stenosis of the left internal carotid artery (A). PCT before CEA demonstrates a slightly decreased CBF (B), decreased CBV (C), and increased TTP (D) in the left hemisphere. Intraoperative SSEP in the left side indicated no changes (E). During CEA, PCT demonstrated increased CBF (F) and CBV (G), and decreased TTP (H). Compared relative PCT parameters before and during CEA. The rCBF increased from 0.78 to 1.23, the rCBV increased from 0.84 to 1.16, and the rTTP decreased from 1.25 to 0.90. CBF – cerebral blood flow; CBV – cerebral blood volume; CEA – carotid endarterectomy; DSA – digital subtraction angiography; PCT – perfusion computed tomography; rCBF – relative CBF rCBV – relative CBV; rTTP – relative TTP; TTP – time to peak.

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section was chosen through the level of the basal ganglia because this level contains representative territories supplied by the anterior, middle, and posterior cerebral arteries; therefore, the ROIs were easy to select. Third, hand-drawn ROIs over the cortical gray matter of the expected territory of MCA and ACA were created, with care not to involve substantial parts of the cerebral white matter. Fourth, the ROIs should be as big as possible [23]. Fifth, relative PCT parameters were used to avoid influence of intraoperative anesthesia and blood pressure fluctuation [24,25].

In the present study, 2 ROIs – ACA territory and MCA territory – were chosen. None of the absolute or relative PCT parameters changed significantly before or during CEA in the ACA territory. This is different from the results reported by Duan et al. [19]. There are 2 possible reasons for this difference. First, the ACA territory in the basal ganglia was so small that variation would easily be generated. Waaijer et al. reported that the MCA territory showed the least measurement variability compared with the ACA territory [25]. Secondly, unilateral carotid stenosis was well compensated from the anterior communicating artery.

In the MCA territory, statistical analysis showed that only the TTP in the operated side increased significantly, compared to the absolute PCT parameters in the operated side and contralateral side before CEA, as in the results reported by Kämena [26]. When carotid stenosis develops, the cerebral hemodynamics change and result in a prolonged TTP at first. The CBF and CBV do not change until the cerebral autoregulation is decompensated. Therefore, the TTP is a sensitive parameter for detection of cerebral hypoperfusion. During the CEA, all the PCT parameters, including CBF, CBV, and TTP, in the operated side changed significantly compared with the contralateral side. This is not completely in concordance with the literature [19,27]. When plaques are removed during CEA, blood flow in the carotid artery are restored quickly, and the cerebral hemodynamics noticeably change in a short time. However, other studies comparing PCT parameters were done at 1 week or even longer after surgery. In the present study, the significant change found in rCBF, rCBV, and rTTP during CEA, in comparison with before CEA, agrees with the study by Waaijer et al. [27]. However, Duan et al. reported that the rCBF and rTTP changed significantly but the rCBV had no significant changes at 1 week after carotid stenting of unilateral symptomatic carotid artery [19]. Various reasons may explain these differing results. First, the sample was too small and might easily produce errors. Second, the time points of investigation of brain perfusion were different; our study investigates brain perfusion at 1 h after surgery, but other studies used later time points. Third, CBV, which reflects the vascular volume of arterial, capillary, and venous compartments in ROIs, is a complex physiological parameter and the vasodilatory response of these different vessels is variable.

Since CEA began to be used for treatment for carotid stenosis in 1950s, the effectiveness had been confirmed through more than 50 years of development and testing. However, neurologic complications of CEA due to cerebral hemodynamic changes during and after surgery occur in up to 5% of patients. Therefore, it was very important to get accurate and immediate information about brain perfusion during CEA. SSEP and MDU are the most commonly used monitoring methods during CEA. SSEP is sensitive to the cerebral ischemia, but it may show false-negative results and influence by anesthetics [10]. MDU, which had been widely used in cerebral aneurysm surgerv. can obtain the blood floor velocity and detect vascular stenoses as early as possible. However, it had some inherent limitations, including inability to evaluate the distal collateral flow and provide information about cerebral circulatory [28]. In addition, intraoperative MR imaging can provide information about perfusion status of brain, but it is not widely used in clinical practice due to high expense and time required.

To the best of our knowledge, our study is the first to describe use of intraoperative PCT in CEA. Intraoperative PCT had some advantages in comparison with commonly used monitoring methods during CEA.

First, intraoperative PCT can provide immediate information about brain perfusion to help guide surgical therapy. Sanford et al. described using of PCT to evaluate the effectiveness of ICA stent placement in a patient with symptomatic transient ischemic attacks caused by tandem stenoses of ICA and MCA. Intraoperative PCT revealed a marked improvement in mean transit time and CBF in the operated hemisphere after treating the proximal supraclinoid ICA stenosis. Considering the increased risks associated with MCA stent implantation, and the improvements in cerebral perfusion, the surgeon decided to terminate treatment of the MCA stenosis. The patient had a clinically significant improvement in symptoms [29]. In the present study, the time of intraoperative PCT scanning procedure was approximately 10 min, including 2 to 3 min for preparation, 5 min for analysis of PCT data, and 2 to 3 min for resuming surgery. Therefore, the surgical strategy could be quickly changed if cerebral hemodynamic abnormalities were observed.

Secondly, intraoperative PCT can provide accurate information on brain perfusion. PCT directly reflects capillary bed perfusion status [30]. Compared quantitative perfusion parameters in operated side with those in contralateral side, and compared those before and during CEA, cerebral hemodynamic changes would be identified. PCT showed brain perfusion improved in all 16 patients. SSEP indicated no changes and could not estimate brain perfusion improvement. MDU indicated blood flow changed obviously. Therefore, the accuracy of PCT was superior to SSEP and MDU in evaluation of brain perfusion.

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Thirdly, intraoperative PCT could predict cerebral hyperperfusion during CEA, which was defined as CBF increase of more than 100% compared with preoperative values in the operated side [31]. Although none of the patients had cerebral hyperperfusion in the present study, the incidences of cerebral hyperperfusion after CEA and cerebral hemorrhage caused by cerebral hyperperfusion were 12.5% and 0.37%, respectively, according to the literature [32]. Several studies on using PCT for cerebral hyperperfusion have been published. Chang et al. reported that CBV index and TTP index were effective tools for screening cerebral hyperperfusion [33]. Tseng et al. suggested that patients with a prolonged dMTT of more than 3 s should be closely monitored for evidence of hyperperfusion after undergoing carotid stenting [21]. Therefore, the sensitivity and specificity of PCT were much better than SSEP. In the present study, 3 patients had a CBF increase of more than 70% as measured by PCT. Fortunately, controlling blood hypertension during CEA avoided cerebral hyperperfusion.

Fourth, intraoperative routine CT scan, performed before the PCT scan, revealed no cerebral hemorrhage.

This study was limited in a number of ways that need to be addressed in future research. First, the study sample was small, consisting of only 16 patients. Second, the level of twice the

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PCT scan was relatively fixed. In addition, the selection of ROI was related to operators. Third, when the ROI was selected, compensation of anterior communicating artery and posterior communicating artery was not taken into account. Fourth, PCT scanning was performed only at the level of the basal ganglia, not the total brain. Fifth, this study analyzed brain perfusion during surgery and lacked long-term follow-up data. Finally, data analysis may be affected by the incomplete symmetry of space due to posture requirements during CEA, such as head spins and cervical extension.

Conclusions

Relative PCT parameters, including rCBF, rCBV, and rTTP, are sensitive indicators for detecting early cerebral hemodynamic changes during CEA. Cerebral hemodynamics obviously changed in the territory of the MCA during CEA. Intraoperative PCT could be an important adjuvant monitoring method in CEA.

Statement

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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