Perfusion CT scanning and CT angiography in the evaluation of extracranial-intracranial bypass grafts

Clinical article

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Object. Extracranial-intracranial (EC-IC) bypass surgery remains an important treatment alternative for patients with occlusive cerebrovascular disease. The aim of the present study was to use perfusion CT and CT angiography (CTA) to evaluate cerebral hemodynamics and bypass patency in patients with occlusive cerebrovascular disease before and after EC-IC bypass surgery.

Methods. Ten patients underwent perfusion CT and CTA before and after bypass surgery. Preoperative and postoperative digital subtraction angiography served as the diagnostic gold standard. An artery bypass was established from the superficial temporal artery to a cortical branch of the middle cerebral artery. Perfusion CT scanning was performed at the level of the basal ganglia. Color-coded perfusion maps of cerebral blood volume, cerebral blood flow, and time to peak were calculated.

Results. Preoperative perfusion CT showed significant prolonged time to peak and reduced cerebral blood flow of the affected hemisphere. Postoperative neurological deterioration did not develop in any patient. Computed tomography angiography provided adequate evaluation of the anastomoses as well as the course and caliber of the bypass and confirmed bypass patency in all patients. Postoperative perfusion CT showed improved cerebral hemodynamics with a return to nearly normal perfusion parameters.

Conclusions. Computed tomography angiography is a noninvasive and reliable tool for evaluating patients with EC-IC bypass. Perfusion CT allows monitoring of hemodynamic changes after bypass surgery. The combination of both modalities enables noninvasive anatomical and functional analysis of superficial temporal artery–middle cerebral artery anastomoses using a single CT protocol. Hemodynamic evaluation of patients with occlusive cerebrovascular disease before and after surgery may improve the prediction of outcome and may help identify patients in whom a bypass procedure can be performed. (DOI: 10.3171/2010.6.JNS10117)

KEY WORDS • computed tomography • computed tomography angiography • perfusion computed tomography • superficial temporal artery–middle cerebral artery bypass

Abbreviations used in this paper: ACA = anterior cerebral artery; CBF = cerebral blood flow; CBV = cerebral blood volume; CTA = CT angiography; CVR = cerebrovascular reserve; DSA = digital subtraction angiography; EC-IC = extracranial-intracranial; ICA = internal carotid artery; MCA = middle cerebral artery; MRA = MR angiography; STA = superficial temporal artery; TTP = time to peak.

Stoke is one of the most common causes of death and a leading cause of disability among adults in the western world.19 Intracranial atherosclerotic disease remains a significant risk factor, and total carotid artery occlusion is the cause of ischemic stroke or transient ischemic attacks in approximately 10% of patients.19 In 1985, the Cooperative Study of Extracranial-Intracranial Bypass concluded that bypass revascularization did not reduce the risk of stroke in the subgroup studied.2 The results of that study led to a dramatic decrease in the number of bypass procedures performed.4 Recent publications on the natural history of high-risk stroke patients with symptomatic carotid artery occlusion have led to a reappraisal of this procedure.19

Intraarterial DSA used to be the gold standard evaluating an EC-IC bypass, but it is an invasive modality with a small but significant risk of complications.3 Therefore, it was challenged by other noninvasive imaging modalities, including MRA, duplex ultrasonography, and CTA, which have been reported to be useful for such assessment.2,3 However, at present it is difficult to predict if and how bypass flow will contribute to intracranial circulation.

The viability of cerebral parenchyma depends on CBF. Therefore, an impaired CVR in patients with symptomatic ICA occlusion is regarded as one of the possible indications for bypass surgery.20 Various modalities have been used for hemodynamic investigations.23 Of these modalities, perfusion CT scanning performs best in terms of spatial resolution.26
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The aim of our study was 2-fold: 1) to evaluate the clinical utility of CTA for preoperative vascular assessment and postoperative demonstration of bypass patency, and 2) to evaluate the use of perfusion CT for monitoring changes in cerebral perfusion after bypass surgery.

Methods

Between March 2006 and November 2008 we prospectively included 10 consecutive patients who were admitted for EC-IC bypass surgery to the department of neurosurgery at our hospital. Eligible patients had symptomatic occlusion of the ICA, and patients with concomitant vascular disease were excluded from the study.

All patients underwent intraarterial DSA as diagnostic gold standard before and after surgery. Intraarterial DSA was performed with transfemoral catheterization (Seldinger technique) in which we used a biplane intraarterial DSA unit (Integris V, Philips) after administration of a nonionic iodine-containing contrast agent (Iodoxanol 270, Visipaque, GE Healthcare Buchler). Preoperatively, 3-vessel angiograms including the common carotid artery on both sides, the ICA of the unaffected hemisphere, and the left vertebral artery were obtained in standardized anteroposterior, lateral, and bilaterally oblique projections for each catheterization. Postoperatively, only the external carotid artery of the bypass side and the contralateral ICA were catheterized and the same projections obtained.

Intraoperatively, bypass patency was confirmed using microvascular Doppler ultrasonography and intravenous fluorescence angiography. Patients underwent pre- and postoperative plain cranial CT, perfusion CT, and CTA within 1 week prior of surgery. The CT examinations were repeated 6 and 12 months after surgery. Before and 6 months after surgery, brain perfusion was scintigraphically studied with $^{99m}$Tc–ethyl cysteinate dimer SPECT with and without acetazolamide challenge, respectively. The SPECT data sets were visually interpreted for perfusion abnormalities, in the baseline or acetazolamide study, by 2 independent readers. A blunted increase or a paradoxical reduction in CBF after acetazolamide administration was defined as impaired CVR. An insufficient response to the vasodilator stimulus was identified by visually assessing the change in perfusion between both studies. To calculate intra- and interobserver reliability, visual analysis was repeated at the end of the study. In that second reading, SPECT data sets were presented in a randomized order. All CT examinations were performed on a 16-row multidetector CT scanner (Somatom Sensation 16, SIEMENS Medical Systems). Perfusion CT was performed after administration of an intravenous bolus of 60 ml of iodine-containing contrast agent (Iodoxanol, Visipaque). Perfusion CT was performed at the level of the basal ganglia. Perfusion CT data sets were analyzed using the vendor’s software (NeuroPCT, SyngoCT 2007S, Siemens Medical Systems). The arterial input function was placed—according to Wintermark et al.—in the ACA of the unaffected hemisphere. Color-coded maps of regional CBF, regional CBV, and TTP were calculated. A region of interest was placed manually around each hemisphere, and absolute and relative values for the perfusion parameters compared with the unaffected hemisphere were calculated.

Computed tomography angiograms of the craniovascular vessels and the bypass were acquired from the level of the C-6 vertebra up to the roof of the lateral ventricles. We administered 40 ml of contrast agent at a flow rate of 4 ml/second using a semiautomated bolus tracking with a threshold of 100 HU in the common carotid artery at the C-6 level. Sections were reconstructed with a thickness of 1 mm.

Computed tomography angiograms were evaluated using axial thin-slice maximum intensity projection reconstructions, thick-slab maximum intensity projection reconstruction with a slice thickness of 20 mm and a reconstruction interval of 5 mm, curved multiplanar constructions, and volume-rendering technique on a regular basis. The bypass was graded as patent or occluded. If the bypass was patent, the anastomosis was graded using a 4-point scoring system: 0, no stenosis; 1, mild stenosis less than 50% of the vessel diameter; 2, moderate stenosis greater than 50% and less than 70% of the vessel diameter; and 3, severe stenosis with vessel diameter reduction greater than 70%.

All data were evaluated by 2 experienced neuroradiologists and 1 neurosurgeon who was not involved in the bypass procedure.

We performed all statistical analysis using Version 17 of the Statistical Packages for the Social Sciences. Differences in the evaluation of bypass patency between CTA and intraarterial DSA studies were analyzed using the chi-square test. Intraobserver and interobserver variability was evaluated with Cohen kappa test. Differences in each perfusion CT parameter between pre- and postoperative measurements as well as between 6- and 12-month follow-up were calculated using the modified Wilcoxon rank sum test. A p value $< 0.05$ was considered significant.

We obtained approval from our institutional review board before initiating the study.

Results

Of CTA, perfusion CT, or intraarterial DSA, none was degraded by motion artifacts or technical failure in any patient. The readers’ ratings agreed in all cases with a kappa value of 1 (substantial reproducibility). Preoperatively, the STA was visualized in all patients. In 2 patients (20%) frontal and parietal branches were of equal caliber; in 5 patients (50%) the parietal branch was dominant; and in 3 cases (30%) it was atretic. The mean donor vessel diameter was $2.53 \pm 0.26$ mm. These results were in agreement with the angiographic findings.

Preoperative cranial CT scanning showed lacunar infarction in 1 patient (10%) and territorial infarcts in 3 patients (30%). These were located in the territory of the MCA in 2 cases and in the ACA and MCA, respectively, in 1 patient each.

There was occlusion of both ICAs in 1 patient (10%). However, only 1 hemisphere was affected clinically due to absence of the anterior communicating artery and
good collateralization of the contralateral hemisphere by a wide posterior communicating artery. The other patients had unilateral ICA occlusion.

Preoperative acetazolamide ethyl cysteinate dimer SPECT revealed impaired cerebrovascular reserve in all patients (κ = 0.97). Preoperative perfusion CT (Fig. 1) showed TTP prolongation of the affected hemisphere (mean 12.3 ± 3.36 seconds) with a relative increase of 16.03% compared with the unaffected hemisphere (mean 10.6 ± 3.28 seconds). Cerebral blood flow showed a relative increase in the affected hemisphere (mean 57.82 ± 11.11 ml/100 g/min) compared with the unaffected hemisphere (mean 55.33 ± 7.54 ml/100 g/min) (p = 0.514). Cerebral blood volume of the affected hemisphere was significantly increased (mean 34.39 ± 3.03 ml/100 g) (p = 0.028).

Follow-up examinations were performed within 6 months (mean 6.2 months) and 12 months (mean 11.77 months) of surgery. After bypass surgery, the course of the bypass and anastomosis could be identified in all patients by all readers. The bypass was rated “patent” in all patients and using both imaging modalities. The ratings agreed in all patients with a kappa value of 1 (substantial reproducibility). This was in agreement with the clinical findings. In 1 patient a preexisting motor aphasia resolved immediately after surgery. During follow-up, clinical signs of recurrent stroke or transient ischemic attack did not develop in any patient.

Follow-up CTA 12 months after surgery revealed bypass patency in all patients. In 1 case all readers still rated the anastomosis moderately stenosed. There was no significant change in vessel diameter of the bypass or intracranial vessels between 6-month follow-up CTA (2.56 ± 0.27 mm) and 12-month follow-up CTA (2.57 ± 0.26 mm).

Postoperative perfusion CT (Fig. 3) showed a significant decrease in TTP of the affected hemisphere (mean 9.53 ± 1.21 second) compared with preoperative values (p = 0.02). The difference in TTP between both hemispheres was not significant. The decrease in CBV (mean 31.49 ± 3.26 ml/100 g [−9.2%]) of the affected hemisphere was statistically significant (p = 0.008), whereas the difference in CBV between both hemispheres was no longer significant (p = 0.977).

There was a decrease in CBF of 10.8% in the affected hemisphere surgery (mean 51.58 ± 6.93 ml/100 g/min; p = 0.101) and again the difference after in CBF between the hemispheres was not significant (p = 0.799). Follow-up acetazolamide ethyl cysteinate dimer SPECT was available in 9 patients and confirmed the improvement of the cerebral hemodynamic situation indicated by perfusion CT in all cases (κ = 0.98).

Cerebral blood volume and CBF in the surgically treated hemisphere were not below the values of the unaffected hemisphere, and there were no alterations of CBF and CBV indicating cerebral ischemia. Cranial CT also revealed no new ischemic lesions. One patient had persistent TTP prolongation in the anterior border zone, which did not persist at the 12-month follow-up. There was no significant difference for the other perfusion CT parameters between the 6-month and the 12-month follow-up. Plain cranial CT revealed no new ischemic lesion at 6 months and 1 year.

Discussion

Although there is controversy regarding its effectiveness,6 low-flow EC-IC arterial bypass surgery can be used to increase cerebral circulation in patients with ischemic cerebrovascular disease and impaired cerebrovascular reserve, thereby preventing extension of the affected areas and reducing the risk of further strokes.6,15 Postoperatively, the EC-IC bypass is required not only to be patent but also to provide sufficient blood flow to hypoperfused areas.

To our knowledge, this report for the first time de-
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Fig. 2. Postoperative CT angiograms acquired after EC-IC bypass surgery on the right side. A: Volume-rendering reconstruction clearly depicts the extracranial course of the bypass. B: Volume-rendering reconstruction of the intracranial course of the bypass. C: Thin-slice curved multiplanar image of the intracranial anastomosis, which was rated as moderately stenotic by all readers.

Fig. 3. Postoperative perfusion CT scans obtained in the same patient represented in Fig. 1 after EC-IC bypass surgery on the left side. A: Time to progression shows normalization in the left hemisphere with mild prolongation in the territory of the posterior cerebral artery. B: Markedly elevated CBV with no mismatch between the 2 hemispheres. C: Cerebral blood flow is also elevated with no mismatch between CBF and CBV.

scribes the prospective evaluation of both the course and patency of the EC-IC bypass and of the hemodynamic changes after bypass surgery using CTA and perfusion CT.

Intraarterial DSA used to be the diagnostic modality of choice for the follow-up of such patients. However, intraarterial DSA has recently been challenged by other noninvasive imaging modalities such as duplex ultrasonography, MRA, and CTA.

One of the major disadvantages of CTA, compared with intraarterial DSA and MRA is the lack of information about the flow direction in the vascular system. Recent publications have shown that flow rates in bypass vessels correlate with bypass function and patency. Magnetic resonance angiography can provide this information using either phase contrast MRA or time-of-flight MRA. In an early study of 3D phase contrast MRA, Kodoma et al. found phase contrast MRA to be of superior diagnostic value when evaluating EC-IC bypass grafts compared with time-of-flight MRA. This study is limited by the fact that the authors did not correlate their findings with intraarterial DSA or CTA. Praharaj et al. evaluated postoperative bypass patency in 6 patients using 3D time-of-flight MRA. They performed MRA using presaturation pulses to obtain additional information on the flow direction in the bypass. Although DSA was superior in demonstrating small vessels, they found a good correlation between DSA and time-of-flight MRA regarding bypass patency. In a recent study, Tsuchiya and coworkers evaluated 13 patients with STA-MCA bypass using time-resolved contrast-enhanced MRA. They were able to visualize flow in distal M2 segments distal to the anastomosis. The major limitation of their study again is that they did not correlate their results to DSA.

However, in all these studies the spatial resolution of the MRA techniques investigated was inferior to that of CTA. Because of the small caliber of the target vessels and the slow flow within them, we think that MRA is limited in depicting the bypass and bypass blood flow.

One of the major advantages of CTA in comparison with MRA is the fast scanning time, the relatively high spatial resolution, and the visualization of the relation-
ship of the course of the bypass to adjacent bone. This assumption is supported by our results: we did not find CTA to be degraded by motion artifacts and the entire bypass including the anastomoses could be evaluated in all patients. Tsujiya et al.\textsuperscript{23} and Teksam and coworkers\textsuperscript{22} retrospectively investigated the use of CTA for EC-IC bypass evaluation. They showed a good correlation between CTA and intraarterial DSA. These findings are in agreement with the results of our study. However, in our study even a moderate stenosis was identified on CTA with high interobserver agreement and confirmed by DSA.

Superficial temporary artery-to-MCA bypasses can take several days to mature and may not demonstrate exuberant blood flow immediately after surgery.\textsuperscript{23} Therefore postoperative CTA and perfusion CT were performed 6 and 12 months after surgery.

Various imaging modalities have been used for postoperative hemodynamic evaluation after EC-IC bypass surgery including SPECT, PET, and perfusion MR imaging.\textsuperscript{23}

Single-photon emission CT and PET provide less morphological information than CT or MR imaging. The feasibility of perfusion CT in the evaluation of patients with chronic cerebral ischemia has been investigated in several studies.\textsuperscript{17, 27} Thresholds have been defined to identify normal tissue, severely hypoperfused tissue, and infarction. Moreover, perfusion CT has higher spatial resolution than perfusion MR imaging and can be easily integrated into a CT protocol for morphological evaluation of patients with an EC-IC bypass. All patients in our study had increased CBV and CBF as well as TTP prolongation in the affected hemisphere. This can be attributed to tissue under hemodynamic stress resulting in a compensatory vasodilatory response of precapillary resistance vessels to reduced cerebral perfusion pressure; therefore, an increase in CBV may be an early indicator of a fall in cerebral perfusion pressure and reduction of CVR. This mechanism aims to maintain a blood supply adequate to metabolic response and has also been observed in carotid artery stenosis.\textsuperscript{3} It is thus a good indicator of the hemodynamic relevance of the underlying vascular lesion. After bypass surgery, cerebral hemodynamics improved on the surgically treated side in all cases. The normalization of CBV and CBF of the affected in comparison with the unaffected hemisphere with no statistically significant difference between the 2 hemispheres clearly demonstrates the hemodynamic benefit from the EC-IC bypass. These results were confirmed by acetazolamide ethyl cysteinate dimer SPECT. The normalization of TTP after bypass surgery as indicator of hemodynamic improvement is supported by the study of Lythgoe and coworkers.\textsuperscript{12}

There are a few limitations that deserve mention. First, the study cohort is small, consisting of only 10 patients. This limitation is shared by other studies because the entity under investigation is uncommon.\textsuperscript{11, 14, 24} Second, the sensitivity and specificity of CTA compared with intraarterial DSA were 100% each. This might be biased by the low number of patients, but comparable results have been reported by Teksam et al.\textsuperscript{22} Therefore, we think, especially in consideration of the technical improvement of multidetector CT, that noninvasive CTA will be equal to invasive intraarterial DSA in evaluating patency and course of an EC-IC bypass. Third, CTA does not depict flow in bypass vessels. However, changes in perfusion CT parameters were in agreement with the results of acetazolamide SPECT. It has been shown that the hemodynamic parameters that can be determined using perfusion CT may enable more accurate assessment than qualitative techniques such as SPECT.\textsuperscript{8, 25} However, the aim of this study was only to evaluate the clinical use of perfusion CT to monitor hemodynamic changes after EC-IC bypass surgery.

Conclusions

Computed tomography angiography is a noninvasive, quick, and reliable tool for evaluating patients with an EC-IC bypass. Perfusion CT allows monitoring of hemodynamic changes after bypass surgery. The combination of both examinations enables noninvasive anatomical and functional analysis of STA-MCA anastomoses using a single CT protocol. Hemodynamic evaluation of these patients before and after surgery may improve the prediction of outcome and may help identify patients in whom this procedure can be performed and allow noninvasive long-term patient monitoring.

Disclosure

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

Author contributions to the study and manuscript preparation include the following. Conception and design: Langner. Acquisition of data: Langner, Schroeder, Seipel, Kirsch. Analysis and interpretation of data: Langner, Fleck, Kirsch. Drafting the article: Langner, Fleck. Critically revising the article: all authors. Reviewed final version of the manuscript and approved it for submission: all authors. Statistical analysis: Langner, Fleck. Administrative/technical/material support: Langner, Hosten, Kirsch. Study supervision: Langner, Hosten.

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