Assessing Prognosis of Areas of Acute Cerebral Ischemia Using Perfusion CT

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Summary

Vascular recanalization by the vascular reconstruction method can dramatically improve ischemic symptoms in patients with acute cerebral ischemia. However, this treatment method is frequently associated with haemorrhagic complications. The indications for this therapeutic approach have been described in a number of studies in the literature. The present paper discusses the possibility of assessing the prognosis of ischemic areas using perfusion CT (PCT) by comparing the results obtained before and after thrombolytic therapy.

Twenty-six patients underwent vascular reconstruction at our hospital between July 2002 and March 2004. Of these patients, six who underwent PCT before treatment and showed adequate recanalization following vascular reconstruction were included in the present study. PCT images were obtained using the first-pass bolus-tracking method with a 16-row multislice helical CT scanner. Areas of cerebral ischemia were evaluated by CT before and after vascular reconstruction. A region of interest was placed in the area showing low density in CT images before vascular reconstruction. The mean average CBF (mL/min/100 g), CBV (mL/100 g), and MTT (s) values were calculated in areas with and without cerebral infarction after vascular reconstruction.

The %CBF, %CBV, and %MTT values relative to the normal side were evaluated with reference to the time until recanalization.

Transarterial vascular reconstruction resulted in full recanalization in four patients and partial recanalization in two. The mean time from onset to recanalization was 284.7 ± 63.27 minutes and was not longer than six hours in any patient. The patient prognosis results in terms of GOS were GR in two patients, MD in three patients, and SD in one patient. Based on comparison of the time after examination to recanalization, the %CBF showed a significant positive correlation in the salvaged area ($Y = 47.321 + 2.491 \times \%CBF$; $R^2 = 0.792$, $p < 0.05$). A significant correlation was not observed in %CBV, but %MTT showed a significant negative correlation ($Y = 269.45 - 0.356 \times \%MTT$; $R^2 = 0.794$, $p < 0.05$).

The %CBF and %MTT results obtained by PCT performed before transarterial vascular reconstruction suggest that it may be possible to estimate the time before vascular reconstruction and the relationship with prognosis. These findings are expected to help ensure the appropriate application of vascular reconstruction and to provide useful information for developing optimal therapeutic protocols, thus reducing complications. In addition, because the results are based on the time after examination, the appropriate therapeutic approach can be determined even when the time of onset of ischemia is uncertain.

Introduction

Cerebral infarction has been reported to have an incidence rate of 120 per 100,000 population per year and is one of the most common causes of stroke¹. However, most patients are managed conservatively, and treatment tends to focus on preventing expansion of the infarcted area and minimizing the risk of recurrence. On the other hand, some patients with severe symptoms undergo intravenous or intra-arterial vascular reconstruction, and such patients often show improvement in neurological deficits following therapy.

The main problem in this otherwise attractive therapeutic approach is the risk of haemorrhagic complications following recanalization. Due to such complications, the outcome may actually be worse than that for the original cerebral infarction in some patients. Furthermore, it is not uncommon for cerebral infarction to develop even after vascular recanalization.

With the aim of avoiding such complications, guidelines for the application of thrombolytic therapy in patients with acute cerebral ischemia have been discussed in a number of papers²⁻¹². However, in many mass studies, plain CT was employed to assess the indications for treatment, and accurate evaluation of the pathologic changes in acute cerebral ischemia was not possible^{4,9,12}. In addition, perfusion-weighted magnetic resonance (MR) imaging (PWI) and diffusion-weighted magnetic resonance (MR) imaging (DWI) are able to demonstrate the pathological condition of areas of acute cerebral ischemia to some extent, and PWI-DWI mismatch is generally recognized as a useful method for determining whether vascular reconstruction is indicated^{3,5,8,14}. Nevertheless, the relationships with prognosis have not yet been discussed. During transarterial vascular reconstruction procedures, the physician must judge how far treatment should be continued. At present, this decision is based on the time of onset of ischemia, the specific vessels that are occluded, and the patient's physical condition. Recently, perfusion CT (PCT), which can be performed using CT scanners commonly found in emergency rooms at many hospitals, has been used to evaluate patients with cerebral ischemia, and positive results have been reported^{5,7,12,16}.

In the present study, we performed PCT in patients with acute cerebral ischemia when plain

brain CT failed to demonstrate clear signs of cerebral infarction. We compared cerebral blood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT) values in the area of cerebral ischemia against the values on the normal side and calculated the %CBF, %CBV, and %MTT values based on this comparison.

Figure 1 Time from examination to recanalization (minutes). In the salvaged area, the time from examination to recanalization shows good correlation with the %CBF and %MTT values. In areas with a %CBV less than 100%, salvage is difficult.

$p < 0.05$

Time = $47.321 + 2.491 \times \%CBF$; $R^2 = 0.792$ (salvaged area)
Time = $145.605 + 2.202 \times \%CBF$; $R^2 = 0.104$ (infarcted area)

Time = $323.292 - 1.319 \times \%CBV$; $R^2 = 0.241$ (salvaged area)
Time = $119.966 + 0.963 \times \%CBV$; $R^2 = 0.76$ (infarcted area)

Time = $269.45 - 0.356 \times \%MTT$; $R^2 = 0.794$ (salvaged area)
Time = $70.913 - 0.311 \times \%MTT$; $R^2 = 0.684$ (infarcted area)

Subsequently, transarterial vascular reconstruction was performed, and the parameters for follow-up CT demonstrating areas with or without the subsequent development of cerebral infarction were examined in relation to prognosis.

Material and Methods

Subjects

Of the 26 patients who underwent vascular reconstruction at our hospital between July 2002 and March 2004, six patients who underwent PCT before treatment and demonstrated adequate complete or partial recanalization following vascular reconstruction were selected for inclusion in this study.

The study group included three men and three women 49-82 years of age (mean age 68.3 years). The occluded vessels were identified as the right middle cerebral artery (MCA) in three patients, the left MCA in one patient, the left distal MCA in one patient, and the left anterior inferior cerebellar artery (AICA) in 1 patient (table 1).

PCT, 3D-CT angiography

PCT images were obtained using the first-pass bolus-tracking method with a multislice helical CT scanner (16-row Aquilion, Toshiba Medical Systems Corporation, Japan).

The scanning parameters employed were 8-mm slices $\times$ 4 rows, a tube voltage of 120 kV, a tube current of 70 mA, a tube rotation speed of 1 s/rot., an imaging time of 56 s, and intermittent scanning (1-s scan and 1-s interscan pause). A total of 35 mL of nonionic contrast medium (Iopamiron 370 mgI/mL, Nihon Schering, Tokyo) was injected at a rate of 5 mL/s via an antecubital vein.

Then, 16-row multislice helical CT images at the base of the skull focusing on the circle of Willis were obtained with a slice thickness of 0.5 mm, a tube voltage of 135 kV, a tube current of 260 mA, a tube rotation speed of 0.75 s/rot., and a helical pitch of 11. The contrast medium remaining after PCT was employed. A total of 65 mL was injected at a rate of 5 mL/s, and 3D-CT angiography was also performed.

The imaging conditions for PCT were selected to minimize radiation exposure in consideration of the intra-arterial vascular reconstruction procedure to be performed subsequently.

Intra-arterial vascular reconstruction

A sheath was introduced percutaneously at the groin under local anesthesia, and a microcatheter was advanced to the occluded area using a guide catheter. Recanalization was attempted by thrombolysis with urokinase and mechanical thromboclasty using a microguidewire with a basket and balloon catheter.

Analytical methods

In all patients, plain CT failed to demonstrate clear signs of acute cerebral infarction. A region of interest (ROI) was set in the area showing vascular loss in PCT and in the area of recanalization following vascular reconstruction.

Of these, the areas in which follow-up CT did not show cerebral infarction were regarded as salvaged areas, and the mean CBF, CBV, and MTT values were measured in these areas. The areas identified as showing cerebral infarction in follow-up CT were regarded as infarcted areas, and the mean CBF, CBV, and MTT values of these areas were obtained. An ROI was placed symmetrically on the normal side, and the CBF, CBV, and MTT values were obtained. In addition, the %CBF, %CBV, and %MTT values relative to the normal side were calculated and evaluated in reference to the time from the examination to the recanalization procedure.

Case E is presented here as an example. This patient was a 74-year-old man who presented with left-sided paralysis and disturbance of consciousness. The time from onset to the examination was 164 minutes. Plain brain CT images obtained at that time demonstrated an old cerebral infarction in the base of the right frontal lobe (figure 2, white arrow), but did not show clear early CT signs. PCT performed at the time (figure 3) showed a decrease in CBF, a prolonged MTT, and a slight increase in CBV over a wide area in the territory of the right middle cerebral artery (figure 3, double arrow). However, a decrease in CBV was already observed in the lateral part of the right basal ganglia (figure 3, arrow). 3D-CTA (figure 4, arrow) and right internal carotid artery imaging (figure 5, arrow) revealed occlusion of right middle cerebral artery M1. Transarterial vascular reconstruction was performed, and the right middle cerebral artery was recanalized at 158 minutes after the examination (figure 5, arrowhead). Plain brain CT performed immediately

Figure 2 Case E: CT. Prethrombolysis CT demonstrates an old cerebral infarction (white arrow) in the subcortical area of the right frontal lobe, but no clear early CT signs are observed. Immediate post-recanalization CT demonstrates extravasation of contrast medium into the lateral part of the right basal ganglia (white arrowhead). CT performed three weeks after recanalization reveals that the above area of contrast medium extravasation has developed into a new area of infarction (black arrow).

after vascular reconstruction showed extravasation of contrast medium into the right basal ganglia (figure 2, white arrowhead). Plain brain CT performed three weeks later demonstrated the development of cerebral infarction in the same area (figure 2, black arrow).

Therefore, the ROI in case E was set in the territory of the right middle cerebral artery including the lateral basal ganglia (figure 3, arrow and double arrow). Then, the CBF, CBV, and MTT values in the area where cerebral infarction did not develop following recanalization (figure 6, inside the white circle) and the values relative to the normal side (%CBF, %CBV, and %MTT) were obtained (table 1). These are plotted as circles in the scatter diagram (figure 1). The values in the areas where cerebral infarction developed after recanaliza-

tion were obtained in the same manner (figure 6, inside the red circle) and are plotted as crosses in the scatter diagram (figure 1).

Results (table)

Transarterial vascular reconstruction resulted in full recanalization in four patients (cases B, D, E, and F) and partial recanalization in two patients (cases A and C). Postoperative CT showed extravasation of the contrast medium in three patients (cases B, E, and F). Cerebral infarction eventually developed in all of these areas. Patient prognosis in terms of GOS was judged good recovery (GR) in two patients (cases C and E), moderately disabled (MD) in three patients (cases A, B, and F), and severely disabled (SD) in one patient (case D).

Figure 3 Case E: PCT. In the territory of the right middle cerebral artery, a decrease in CBF over a wide area, a slight increase in CBV, and prolongation of MTT are observed (double arrow), but CBV is already reduced in the lateral part of the right basal ganglia (arrow).

The mean time from onset to recanalization was 284.7 ± 63.27 minutes, the mean time from onset to examination was 118.5 ± 42.52 minutes, and the mean time from examination to recanalization was 166.2 ± 43.19 minutes. The time from onset to recanalization was not longer than six hours in any patient.

The time from examination to recanalization was compared against the salvaged area ($p < 0.05$), with CBF: $R^2 = 0.129$, CBV ($Y = 426.932 - 97.464 \times \text{CBV}$; $R^2 = 0.543$), and MTT: $R^2 = 0.343$, not showing a significant correlation. In comparison with the infarcted area ($p < 0.05$), CBF was $R^2 = 0.505$, not showing a significant correlation. CBV was $Y = 115.808 + 49.358 \times \text{CBV}$; $R^2 = 0.939$, with a correlation opposite that in the salvaged area, which was considered to be inappropriate. MTT was $R^2 = 0.045$, not

showing a significant correlation. With regard to comparison against the normal side (%CBF, %CBV, and %MTT), when the time from examination to recanalization was compared against the salvaged area, %CBF showed a significant positive correlation ($p < 0.05$) ($Y = 47.321 + 2.491 \times \% \text{CBF}$; $R^2 = 0.792$) and %CBV did not show a significant correlation ($Y = 323.292 - 1.319 \times \% \text{CBV}$; $R^2 = 0.241$). However, it was difficult to salvage areas with CBV values lower than on the normal side (less than 100%). The %MTT showed a significant negative correlation ($Y = 269.45 - 0.356 \times \% \text{MTT}$; $R^2 = 0.794$). In the infarcted area, a significant correlation was not observed, ($p < 0.05$) %CBF: $R^2 = 0.104$. The %CBV was $Y = 119.966 + 0.963 \times \% \text{CBV}$; $R^2 = 0.76$, with a correlation opposite that in the salvaged area,

Figure 4 Case E: 3D-CT angiography. Occlusion of the right middle cerebral artery is observed (arrow).

Figure 5 Case E: Right internal carotid artery angiography, AP view. Pre-recanalization examination shows occlusion of the horizontal peripheral branches of the right middle cerebral artery (arrow). Post-recanalization examination shows residual stenosis at the above occlusion site, but recanalization is confirmed (arrowhead).

Figure 6 Case E: Before analysis. Of the ischemic areas before recanalization, those that did not develop cerebral infarction after recanalization are shown in a white circle, and the CBF, CBV, and MTT values are obtained. These values are plotted (circles) in the scatter diagram, with the time from examination to recanalization shown on the x-axis. In a similar manner, areas that developed cerebral infarction after recanalization are shown in a red circle, and the CBF, CBV, and MTT values are obtained. These values are plotted (crosses) in the scatter diagram, with the time from examination to recanalization shown on the x-axis.

which was considered to be inappropriate. The %MTT was $R^2 = 0.684$, not showing a significant correlation.

Discussion

In the present study, the %CBF and %MTT values showed significant correlations with the time from examination to the development of irreversible cerebral infarction. This means that in patients with a greater reduction in vascular flow compared with the normal side and a substantially prolonged MTT, salvage is possible if recanalization is performed as early as possible. On the other hand, in patients with a slight reduction in vascular flow and a mildly

prolonged MTT, the results suggest that salvage is possible even if there is a substantial delay before recanalization. In addition, it is suggested that even when the time of onset of ischemia is uncertain, the prognosis can be assessed on the basis the time up to the start of examination.

Furthermore, salvage by intravascular reconstruction is considered to be difficult in areas where the CBV value is lower than that on the normal side.

In infarcted areas, the time from examination to recanalization was correlated with the CBV and %CBV values in only three patients. This correlation was opposite that in the salvaged area and was considered to be inap-

Case	age	sex	occluded artery	onset to (min.) recanalization	examination to (min.) recanaliz.	onset to (min.) examination	ml/min./100g		sec.	CBF%		CBV%	MTT%	result	contralateral		
							ml/min./100g	CBV		MTT	CBF	CBV	MTT		CBF	CBV	MTT
A	49	F	Rt. MCA	179	125	54	20.78	3.021	11.61	30.282716	139.66713	516.919	516.919	salvaged	68.62	2.163	2.246
							20.51	2.99	9.954	27.719962	127.17992	410.305	410.305	salvaged	73.99	2.351	2.426
							16.75	3.006	13.44	31.990069	149.32936	382.3613	382.3613	salvaged	52.36	2.013	3.515
							19.38	3.078	10.64	38.705812	146.85115	351.8519	351.8519	salvaged	50.07	2.096	3.024
B	60	M	Rt. MCA	238	111	127	22.67	2.986	10.27	42.588766	119.15403	319.8381	319.8381	salvaged	53.23	2.506	3.211
							17.69	2.588	12.43	33.986551	113.95861	400.5801	400.5801	salvaged	52.05	2.271	3.103
C	70	F	Lt. AICA	309	192	117	10.75	2.427	14.23					salvaged			
							13.92	3.018	13.6					salvaged			
D	75	F	Lt. MCA	313	225	88	13.7	2.161	12.11	30.437681	107.19246	372.1573	372.1573	infarcted	45.01	2.016	3.254
							21.07	2.292	7.741	57.67862	121.26984	207.1448	207.1448	salvaged	36.53	1.89	3.737
							12.45	2.197	13.13	27.106466	115.99789	452.743	452.743	infarcted	45.93	1.894	2.9
							26.97	2.606	6.032	71.805112	128.43765	157.8644	157.8644	salvaged	37.56	2.029	3.821
							12.75	2.254	13.11	21.86964	105.22876	531.6302	531.6302	infarcted	58.3	2.142	2.466
							29.57	2.142	4.625	79.639106	106.99301	125.3388	125.3388	salvaged	37.13	2.002	3.69
							9.836	1.983	14.08	14.833358	72.372263	484.6816	484.6816	infarcted	66.31	2.74	2.905
							26.15	2.123	5.124	62.936221	88.569045	139.0879	139.0879	salvaged	41.55	2.397	3.684
E	74	M	Rt. MCA	322	158	164	6.701	0.6453	11.67	20.256953	34.489578	280.4614	280.4614	infarcted	33.08	1.871	4.161
							16.79	2.879	13.44	43.452381	136.0586	324.5593	324.5593	salvaged	38.64	2.116	4.141
							7.55	0.9837	12.91	19.094588	48.746283	340.1845	340.1845	infarcted	39.54	2.018	3.795
							14.06	2.432	14.24	33.936761	105.78512	332.4772	332.4772	salvaged	41.43	2.299	4.283
							6.594	0.9227	13.78	21.121076	55.053699	306.8359	306.8359	infarcted	31.22	1.676	4.491
							14.72	2.673	12.49	39.794539	113.50318	279.606	279.606	salvaged	36.99	2.355	4.467
F	82	M	Lt. dist MCA	347	186	161	15.03	1.689	10.27	24.724461	84.365634	421.2469	421.2469	infarcted	60.79	2.002	2.438
MCA = middle cerebral artery AICA = anterior inferior cerebellar artery																	

appropriate. Further data must be gathered with regard to infarcted areas.

Vascular reconstruction is thought to be indicated for patients in whom conventional CT and MRI demonstrate no abnormalities (with the exception of PCT and PWI) and should be performed intravenously within three to six hours after onset^{3,4,9,13} or intra-arterially within 6 hours after onset^{7,17}. It is also known that the posterior circulation has a longer therapeutic window^{2,18,19}. Nevertheless, even when therapeutic intervention is performed in accordance with the above guidelines, it is not uncommon for patients to develop cerebral infarction or to have a poor prognosis due to haemorrhagic complications.

In the present study, areas with and without the development of cerebral infarction were observed in all patients even when successful recanalization was achieved within six hours. In addition, cerebral infarction developed in all areas that showed extravasation of contrast medium. It is considered that the blood-brain barrier (BBB) was damaged and irreversible ischemic changes developed.

The reserve capacity in ischemic areas differs depending on the degree of development of the collateral circulation and also varies significantly from patient to patient. Moreover, even when recanalization was performed in the same patient at the same time, some areas developed cerebral infarction and others did not, indicating that the reserve capacity and resistance to ischemic injury differ from area to area. Therefore, it is considered that the values relative to the normal side should show higher correlations than the absolute CBF and MTT values.

In cases D and E, in which a mixture of areas with and without the development of cerebral infarction were observed following recanalization, either a greater decrease in CBF and CBV or a greater prolongation of MTT was observed than in areas without the development of cerebral infarction. In addition, even though recanalization was performed a relatively long

time after examination, some areas did not develop cerebral infarction. In these areas, the CBF and CBV values were well maintained and prolongation of the MTT was less than in other patients.

It is known that in early cerebral ischemia, the CBV falls, and if ischemia is not alleviated, the CBV falls further, eventually leading to irreversible infarction. Therefore, even though plain CT showed no abnormalities, our results indicate that it is difficult to avoid cerebral infarction following recanalization in areas with CBV values lower than those on the normal side at the time of examination.

3D-CT angiography performed after PCT permits occluded blood vessels to be visually identified (figure 4). Their relationships with other normal blood vessels can also be clearly understood. This is thought to be useful in that the number of additional examinations in transarterial vascular reconstruction follow-up can be reduced and the treatment time can be minimized.

Conclusions

The results of the present study indicate that patient prognosis can be assessed based on the %CBF and %MTT values obtained by PCT before transarterial vascular reconstruction as well as the time until vascular reconstruction. These factors are considered to provide useful information before vascular reconstruction, resulting in greater accuracy in selecting suitable candidates for the reconstruction procedure. In addition, analysis of these factors should prove useful in developing optimal therapeutic protocols and minimizing the risk of complications.

In conclusion, the method described here permits the prognosis to be assessed based on the time from the examination and is therefore considered to provide useful information for determining the optimal therapeutic approach even in patients in whom the time of onset of ischemia is uncertain.

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