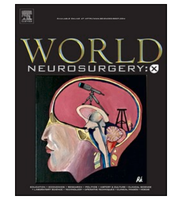
World Neurosurgery: X 24 (2024) 100398

Contents lists available at ScienceDirect

World Neurosurgery: X

journal homepage: www.journals.elsevier.com/world-neurosurgery-x



Assessment of donor-vessel after STA-MCA bypass for moyamoya disease using handheld Doppler to confirm bypass patency and predict perioperative hyperperfusion

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ARTICLE INFO

Keywords:
Moyamoya disease
Doppler
STA-MCA
TNE

ABSTRACT

The study included 12 hemispheres of 9 patients with moyamoya disease who underwent direct-indirect revascularization. The parameters (peak systolic velocity (PSV), mean flow velocity (MV), resistance index (RI), flow volume (FV)) of the superficial temporal artery (STA) on the operated side were measured using a handheld Doppler before and after surgery in all the patients. The examination was conducted in a similar manner on postoperative day (POD)1 on 9 sides of 7 patients except for 3 sides of the first 2 patients. Patency of the superficial temporal artery-middle cerebral artery (STA-MCA) bypass was confirmed by magnetic resonance angiography (MRA) performed on all 12 sides of 9 patients within the first 2 PODs. There was a statistically significant increase in the PSV ($p = 0.0201$) and the MV ($p = 0.0110$) and a decrease in the RI ($p = 0.0177$) in the STA after surgery when compared with those measured before surgery. None of the changes from the immediate postoperative period to POD1 were statistically significant. Postoperative transient neurological events (TNEs) occurred in 3 patients (25 %) in the first 2 weeks, and all of them were attributed to hyperperfusion. The FV of the three sides associated with TNEs was significantly higher than that of the nine sides that were not ($p = 0.0273$). From the early stage after moyamoya disease bypass surgery, it was clarified that the parameter of the STA changed in which the PSV and the MV increased and the RI decreased. It was clarified that the increase in the FV, which is the blood flow rate that flows through the STA in the immediate postoperative period, may be a predictor of the development of hyperperfusion during the perioperative course.

1. Introduction

The handheld Doppler, ES-100V3 (HADECO, Kawasaki, Japan), is a small (width 101 × height 141 × depth 27 mm, 225 g (main body)) portable Doppler blood flow metre. It is easily portable and used to measure the flow velocity and resistance coefficient of the blood vessel without choosing the place. It is also easy to operate, so there is an advantage that the neurosurgeon can perform the measurements himself. Although there have been reports on the assessment of blood flow parameters in the STA during the perioperative period of surgery for the treatment of moyamoya disease using conventional echography,[1,2] there have been no reports in which the handheld Doppler has been used.

In a SPECT study, the cerebral circulation greatly changed in the postoperative period[3,4] when the operative area was revascularization, including direct revascularization, was performed for the treatment of moyamoya disease. However, SPECT is difficult to perform frequently due to inadequate access to equipment and risk of radiation exposure, and CT perfusion images and ASL MRI images is also infrequently performed due risks of radiation exposure and inadequate access to equipment. Therefore, the establishment of an examination method that can estimate cerebral circulation easily, noninvasively, and repeatedly is warranted.

In this study, we conducted a retrospective analysis of clinical data to clarify the possibility of predicting the onset of TNEs, a key issue in the perioperative management of moyamoya disease, from the Doppler parameters of the STA in the early postoperative period, as well as determining the immediate postoperative Doppler STA parameters by taking advantage of the portability of the handheld Doppler and the capability of the neurosurgeon to perform by himself.

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https://doi.org/10.1016/j.wnsx.2024.100398
Received 11 October 2023; Accepted 20 September 2024

2. Patients and methods

2.1. Patients

In this study, we enrolled 12 sides of 9 patients with moyamoya disease who underwent direct-indirect revascularization with the same neurosurgeon (ST) in the same procedure between the second half of 2022 and the beginning of 2023. The parameters of the STA on the operated side were measured using a handheld Doppler before and after surgery in all patients. The examination using a handheld Doppler was similarly carried out on the day after the operation in 9 sides of 7 patients except for 3 sides of the first 2 patients. The patients' radiological and clinical data were analysed under permission from the ethics committee of the site with the following permission number (20140327).

2.2. Surgery and postoperative management

At our institution, asymptomatic individuals with moyamoya disease undergo regular MRI and single photon emission computed tomography (SPECT), do not receive antiplatelet agents and are followed up on an outpatient basis. Patients with cerebral circulatory disturbances confirmed by SPECT and who have signs of ischaemia (new cerebral infarcts on imaging or repeated TIA) that are able to be explained by SPECT are operated on, and patients with haemorrhagic episodes are operated on according to JAM trial criteria[5] after informed consent forms were signed. Fluid replacement was performed preoperatively, and oral antiplatelet agents were discontinued 2–3 days before surgery (the number of days was adjusted according to the background of the patient and the kinds of antiplatelet agent) in patients who were already receiving oral antiplatelet agents and they restarted antiplatelet therapy after it was confirmed that there was no postoperative bleeding. When the patient was not on oral antiplatelet agents preoperatively, low-dose aspirin was started 2 days before surgery and continued for 3 days to 1 week after surgery after it was confirmed that there was no postoperative bleeding. All procedures are performed by direct-indirect revascularization with the addition of EDAMPS (encephalo-duro-arterio-myo- periosteal sysangiosis) at the STA-MCA. A "U-shaped" skin flap approximately 10 cm in base and 9 cm in height surrounding the parietal branch of the STA was made by separating the galea and outer layer of the temporalis fascia. The frontal branch of the STA is left in the skin to preserve blood flow to the skin. The parietal branch of the STA is detached from the back of the skin flap. After craniotomy, the dura mater is opened, the middle meningeal artery (MMA) is spared, and the STA is introduced intracranially through the hole opened at the temporalis muscle base and anastomosed to M4 of the cerebral surface. The open dura mater is folded back towards the brain surface (encephalo-duro-synangiosis: EDS), and the temporalis fascia-osteoperiosteal flap, which is adjusted in size so that the flap is not drooped into the brain surface, is sewn to the dura, the bone flap is fixed with the resorbable plate, and the skin is closed. After the surgery, based on the report by Fujimura et al, the blood pressure was controlled at 140/or less immediately after the operation in all the patients for hyperperfusion prevention,[6] and the administration of minocycline was continued for a mean of 4–7 days from the operation until it was confirmed that there was no hyperperfusion, SPECT signs or symptoms.[7]

2.3. Hand-held Doppler

The ES-100V3 (HADECO, Kawasaki, Japan) handheld Doppler was used for this study. The handheld Doppler was used by the first author (ST) in all the patients. While patients were lying down, 8 Hz probes were pressed at 60° from the plane of the skin to the area anterosuperior to the tragus, and the blood flow was measured at the point where the most blood flow could be confirmed well (sound and waveform confirmed the position where the blood flow could be confirmed well) (Fig. 1). The PSV, MV, and RI were automatically calculated using the handheld Doppler. For the FV, the vessel diameter had to be entered, and the STA vessel diameter in front of the tragus was measured using time of flight (TOF) MRA imaging immediately before surgery. The parameters measured in the current study are as follows. Parameters of flow rate: PSV (peak systolic velocity) (cm/s); MV (mean flow velocity) (cm/s); FV (flow volume) (can be calculated by $(0.5d/10)^2\pi \times MV \times 60$ (cm^3/min), d: diameter (mm)). Resistance coefficient: RI (resistance index) (calculated by (PSV-EDV)/PSV). RI is one of the indicators of vascular resistance, with larger values indicating greater resistance.

Fig. 1. Actual STA parameter measurements using a handheld Doppler. The subject was the first author, ST. 8 Hz probes were pressed at 60° from the plane of the skin to the area anterosuperior to the tragus, and the blood flow was measured at the point where the most blood flow could be confirmed well (sound and waveform confirmed the position where the blood flow could be confirmed well).

2.4. Diagnosing TNEs

Within two weeks after the day of the operation, when numbness of the limbs and face, difficulty in mobilization, difficulty in the expression of words, aphasia and weakness were recognized, MRI was carried out as soon as possible in all cases. Symptomatic complaints on examination were objectively confirmed (all confirmed by the first author's ST) and when MRI revealed no responsible acute-phase stroke for the symptom, and those not otherwise considered to be caused were diagnosed as TNEs as described elsewhere.[3,8,9]

2.5. Statistics

A paired-samples *t* test was used to compare the parameters before and after surgery and between the postoperative and POD1, and Student's *t* test was used to compare the parameters with and without TNEs as the outcome for statistical analysis. A *p* value of 0.05 or less was considered statistically significant. PRISM software (GraphPad, CA) and JMP software version 17.0.0 (SAS Institute Inc., NC) were used for statistical analysis.

3. Result

3.1. Patients

Twelve sides of 9 patients were studied. The mean age of the patients was 42.2 ± 14.3 (mean ± SD (median 36.5, range 26–71). There were 5 females and 4 males. Six were in the right hemisphere, and 6 were in the left hemisphere. In 8 patients with symptomatic ischaemic moyamoya disease, 11 sides were studied. The remaining 1 patient was a 47-year-old woman who was referred by the previous doctor for reduced cerebral blood on SPECT, and the old cerebral haemorrhage was recognized in the vicinity of the left lateral ventricle in T2-stir weighted imaging of the enforced MRI, and the haemorrhage itself had passed asymptomatically, but the development of the choroidal channel in the moyamoya vessel was also recognized in the vicinity of the old haemorrhage and thus became a priority in the operation after consulting with the patient. Eight patients with 11 affected sides were discharged home after the operation, and there were no obvious permanent neurological sequelae at the time of discharge. In the other case, the patient suffered from aphasia due to cerebral infarction that occurred repeatedly before bypass surgery due to cerebral infarction due to moyamoya disease. The patient was transferred to the rehabilitation hospital after discharge from our institution.

3.2. Changes in STA parameters before and after surgery

MRI, including MRA, was performed by POD2 on all the patients, confirming the patency of STA-MCA bypass. In all 12 sides of 9 patients, STA blood flow was measured using handheld Doppler before and after surgery on the day of operation, and in 9 sides of 7 patients except for 3 sides of 2 patients in the early stage, handheld Doppler measurements were performed on the next day after the operation. The waveforms of a typical handheld Doppler before and after surgery are shown in Fig. 2. Fig. 3 summarizes the respective parameter changes preoperatively, postoperatively, and on POD1. The mean PSV was 18.02 ± 6.59 (mean ± SD) cm/sec in the preoperative period, 24.58 ± 10.34 (mean ± SD) cm/sec in the postoperative period, and 25.22 ± 10.65 (mean ± SD) cm/sec on POD1. When paired-samples *t* tests were performed, the increase from preoperative to postoperative was statistically significant at $p = 0.0201$, and the change from postoperative to POD1 was not statistically significant. Similarly, the mean MV of 7.75 ± 3.64 (mean ± SD) cm/sec before the operation changed to a mean of 12.76 ± 5.63 (mean ± SD) cm/sec after surgery and a mean of 14.98 ± 4.80 (mean ± SD) cm/sec on POD1. When paired-samples *t* tests were performed, the increase from preoperative to postoperative was statistically significant at $p = 0.0110$, whereas the change from postoperative to POD1 was not statistically significant. The mean RI was 0.85 ± 0.13 (mean ± SD) cm/sec preoperatively, 0.71 ± 0.11 (mean ± SD) cm/sec postoperatively and 0.66 ± 0.10 (mean ± SD) cm/sec on POD1. When paired-samples *t* tests were performed, the decrease from preoperative to postoperative was statistically significant at $p = 0.0177$, whereas the change from postoperative to POD1 was not statistically significant.

3.3. Predicting TNEs

Three cases of TNEs (25 %) occurred within 14 days of surgeries on 12 sides of 9 patients. In the first case, a 37-year-old woman was found to have difficulty moving the right upper and lower limbs (objectively only slight hemiparesis) and expressing words 6–10 days after bypassing for the left hemisphere with TIA onset, and SPECT showed increased blood flow compared with before surgery (Fig. 4 top row). In the second case, a 71-year-old woman was found to have severe restlessness and aphasia requiring sedation from the awakening of anaesthesia immediately after bypassing surgery for the left hemisphere with ischaemic onset who had repeated cerebral infarction, and hyperperfusion was observed by SPECT (Fig. 4 middle row). Severe symptoms continued until POD 8 and then gradually resolved. The third patient was a 28-year-old man who had left corner of mouth ptosis and dysarthria 5–6 days after bypassing for the right hemisphere with TIA onset; he showed increased blood flow when compared with that before surgery by SPECT (Fig. 4 bottom row). The transient neurological events observed in the three perioperative cases examined in this study were all attributed to hyperperfusion.

Fig. 5 shows the postoperative STA parameters of the above three sides compared with those of the nine sides without TNEs attributed to hyperperfusion within two weeks of surgery. Among the four parameters examined using Student's *t* test, PSV, MV, and RI were not significantly different between the two groups, but FV was significantly higher in the patients with TNEs than in the patients without TNEs.

4. Discussion

It is known that the postoperative cerebral circulation is greatly changed when revascularization, including direct bypass,[10] is performed in the surgical treatment of moyamoya disease and that it produces hyperperfusion and the watershed shift phenomena[11] and results in transient neurological events (TNEs) in the perioperative period.[8] All of these are syndromes resulting from an imbalance between preexisting cerebral blood flow and cerebral blood flow that are induced de novo intracranially via bypass, but there are two possibilities for the syndrome: overflow (hyperperfusion) and inadequate flow (watershed shift phenomenon). Their differentiation requires repeated SPECT for cerebral circulation assessment and repeated MRI and CT examinations to confirm the presence or absence of new cerebral infarcts, cerebral haemorrhage, and bypass patency. However, repeated examinations have problems with the availability of equipment and radiation exposure. In this regard, a minimally invasive and convenient technique that can estimate intracranial cerebral circulation is needed.

Here, we investigated the potential of the handheld Doppler as such an instrument. The usefulness of ultrasonographic STA assessment has

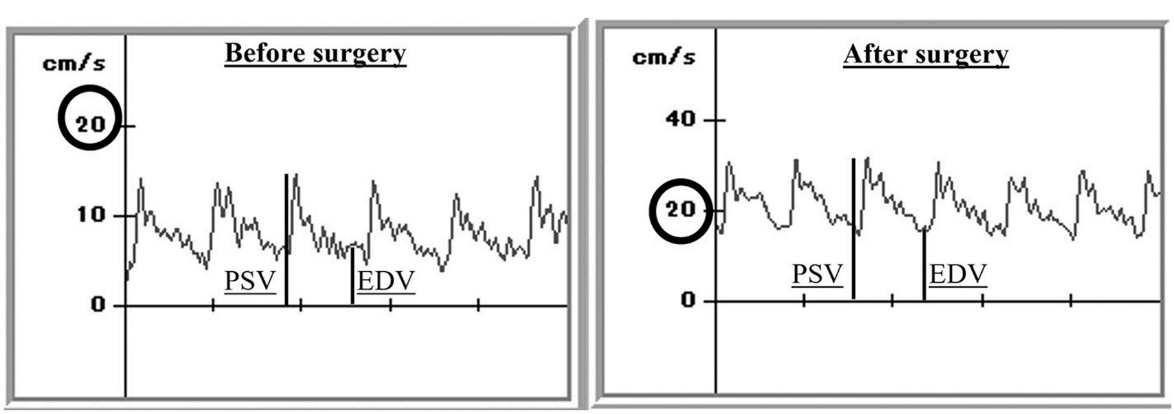

Fig. 2. Waveforms of typical handheld Doppler before and after surgery. The preoperative waveform (left) was a waveform of the external carotid artery type with an EDV close to 0, whereas the waveform after bypass surgery (right) changed to a waveform of the internal carotid artery type with an elevated EDV and an elevated PSV (MV, a mean blood flow velocity, is also elevated by increasing EDV and PSV). Note the different scale of the *y*-axis showing flow velocities in the left and right waveforms.

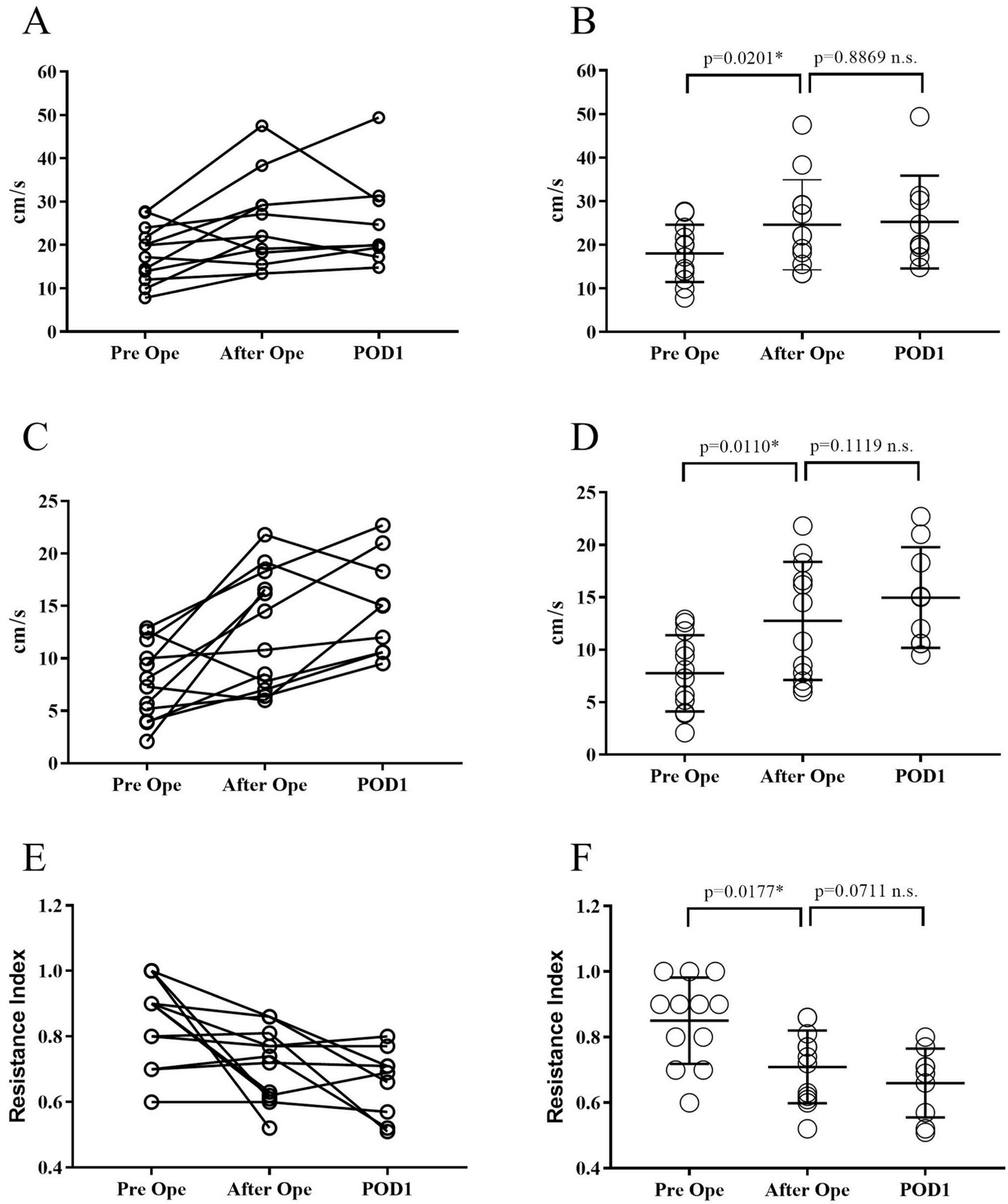

Fig. 3. Chronological changes in the parameters preoperatively, postoperatively, and at POD1 A, B: PSV. C, D: MV. E, F: RI. A, C, and E show the change for each case with a line.

been previously reported and has been evaluated in relation to patency,[1,2] functional assessment of bypass,[12] and TNEs.[1,2] Ultrasound echo instruments can also be used, but the device body is large and difficult to manoeuvre, so it cannot be said that it is convenient to use anytime or anywhere. In comparison, handheld Doppler is also an instrument for measuring blood flow using ultrasound, but it is easy to carry because it is small and light (width 101 × height 141 × depth 27 mm, 225 g (main body)), and, despite its limited function, it has the advantage of having a simple operation. Considerations using this type of Doppler have not yet been reported in the existing literature. In contrast, the disadvantage of handheld Doppler compared to conventional ultrasound is that ① the use of 8 Hz probes for blood vessels running superficial to the skin, such as STA, ensures an error of no more than 10 % only at a flow rate of 3 cm/sec - 60 cm/sec (from the product instructions) and may not capture a higher blood flow ② because blood vessels cannot be visualized on images, and vascular diameters must be measured on other images to calculate the FV (flow volume) ③ The third point is that the absolute value of the flow rate tends to be calculated lower than the conventional echo because the blood vessel cannot be depicted as on an image, and it will be searched for the position of the fastest flow rate depending on the sound. This time, the handheld Doppler was evaluated, and its advantages and

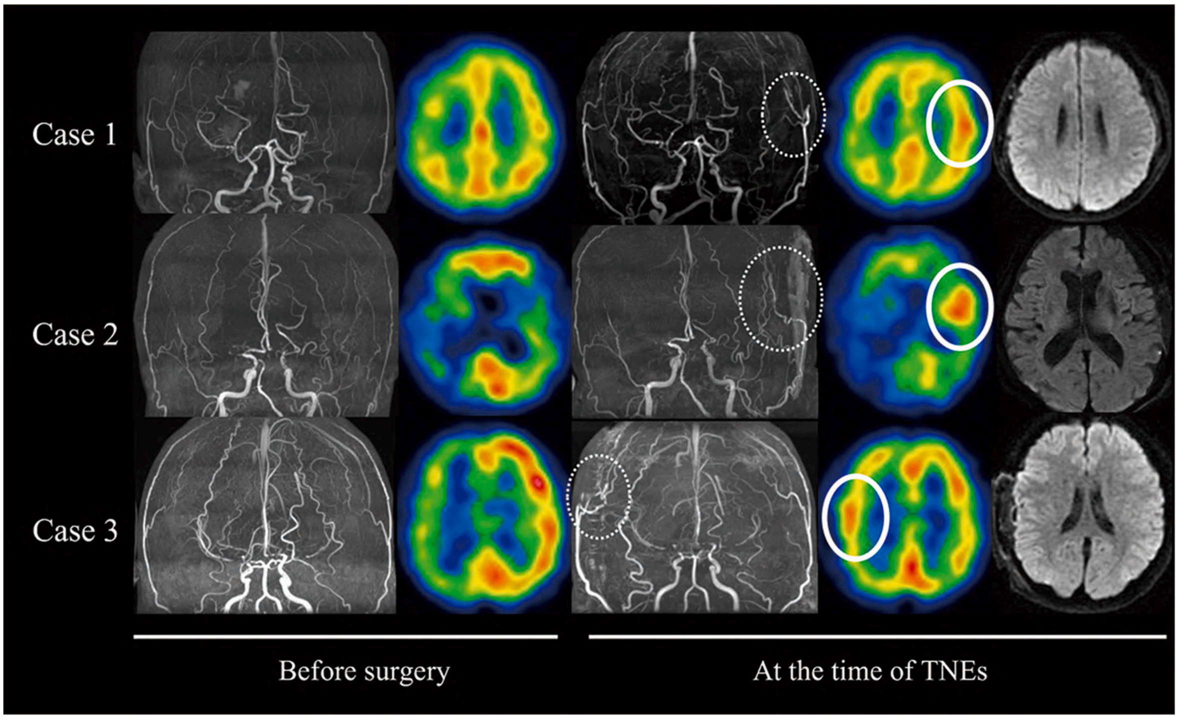

Fig. 4. Images of the three cases resulting in TNEs. The top row shows Case 1, the middle row shows Case 2, and the bottom row shows Case 3. The same slices of pre- and postoperative SPECTs and diffusion-weighted MR images are shown.

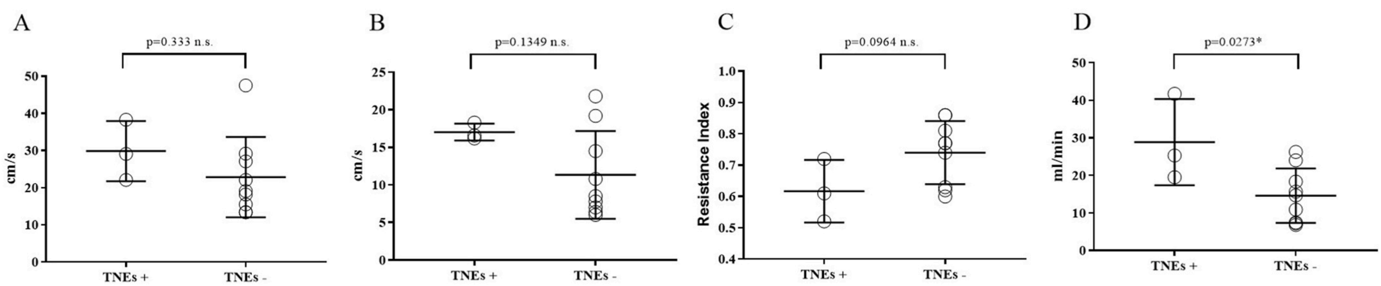

Fig. 5. Changes in parameters categorized according to the presence of TNEs during the perioperative period. A: PSV, B: MV, C: RI, D: FV.

disadvantages were examined.

Previous reports have shown that increased PSV and MV of the STA and decreased RI indicate patency of the bypass compared with the gold standard cerebral angiography in assessing bypass patency,[1,2] and their findings are consistent with our current results. Since the 1980s, it has been reported that STA anastomosed with intracranial vessels by STA-MCA bypass changed from the waveform of the external carotid artery to the waveform of the internal carotid artery.[13] In this study, it was confirmed that the patency of the bypass was confirmed by MRA rather than cerebral angiography as in the previous report, but PSV and MV increased immediately after the operation and RI decreased compared with that before the operation, and it changed from the waveform of the external carotid artery to the waveform of the internal carotid artery. Therefore, it was confirmed that bypass patency can also be confirmed by handheld Doppler. This study also confirmed that this study was the first to examine changes in the PSV, MV, and RI, a characteristic of the STA with intracranial communication, on the day of surgery and immediately after surgery and that these changes arose during the immediate postoperative period.

There have been two previous reports on predicting TNEs from STA parameters. Chen reported that postoperative PSV was lower in patients with TNEs than in controls.[1] In contrast, Dong et al reported that the PSV of patients with TNEs was higher than that of patients without TNEs.[2] In our study, only FV levels were significantly higher in patients with TNEs than in those without TNEs. Since FV is calculated by multiplying the cross-sectional area of the blood vessel by MV and then by the flow rate per minute, the high PSV value is regarded as almost the same as the high FV value. In this regard, our results were supportive of the results of Dong et al.[2] However, when the values for each patient were examined individually, the postoperative FV of the cases with marked hyperperfusion was 25.33 ml/min, and it was much lower than that of the patient with mild TNEs at 5–6 days (41.72 ml/min). Moreover, there were several cases in which postoperative FV exceeded 20 ml/min even in the cases in which TNEs did not occur. Thus, although there were statistically significant differences, it is considered that high postoperative FV levels may be a prerequisite for TNEs attributed to hyperperfusion but not a sufficient condition. Other considerations are in the context of the cerebral parenchyma receiving blood flow from bypass, which may be influenced, for example, by cerebrovascular reserve capacity. In summary, from the present findings, it is considered feasible to predict the occurrence of TNEs attributed to hyperperfusion from the FV measured and calculated immediately after bypass surgery.

The limitation of this study is that the sample size is small. The present study involved a study population of 12 hemispheres and a study period of approximately 6 months. We believe that the presence or absence of changes from the immediate postoperative period to POD1 can be more closely assessed by increasing the sample size in the future. Although the present examination was only the parameter in the immediate postoperative stage, it seems to be a future theme to analyse the relation between parameter change and cerebral circulation in the longer term. In this study, there were only three cases of TNEs attributed to hyperperfusion, and although the small sample size limits our analysis, patient backgrounds indicating the degree of arteriosclerosis—such as diabetes, hypertension, and hyperlipidemia—should be further investigated as potential confounding factors for the presence or absence of hyperperfusion in an expanded cohort.

5. Conclusions

In the examination using a handheld Doppler, it was clarified that the parameter of the STA changed from the parameter of the external carotid artery type to the parameter of the internal carotid artery type, in which the PSV and the MV increased and the RI decreased from the immediate postoperative period after treatment for moyamoya disease with direct revascularization. FV, which was the blood flow rate that flowed through the STA in the immediate postoperative period, was a predictor of the development of hyperperfusion in the later perioperative stage. Since a handheld Doppler does not require radiation exposure and is not an expensive piece of equipment, we believe that it may be helpful for cerebral circulation assessment after moyamoya disease bypass.

Funding

This work was supported in part by a grant from Nakatani Foundation for Advancement of Measuring Technologies in Biomedical Engineering for Satoshi Takahashi.

Availability of data and materials

Nothing else.

CRediT authorship contribution statement

Satoshi Takahashi: Writing – review & editing, Writing – original draft, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Masahiro Toda:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We would like to thank AJE (www.aje.com) for English language editing.

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Abbreviations

STA: superficial temporal artery
MCA: middle cerebral artery
TNE: transient neurological events
PSV: peak systolic velocity
MV: mean flow velocity
RI: resistance index
FV: flow volume
MRA: magnetic resonance angiography
POD: postoperative day
SPECT: single photon emission computed tomography
CT: computed tomography
ASL:: arterial spin labeling
MRI: magnetic resonance imaging
EPAMPS: encephalo-duro-arterio-myo- periosteal sysangiosis
MMA: middle meningeal artery
EDS: encephalo-duro sysangiosis
TOF: time of flight
TIA: transient ischemic attack