Early and Noninvasive Evaluation using Superficial Temporal Artery Duplex Ultrasonography after Indirect Bypass for Adult Ischemic Moyamoya Disease

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ABSTRACT

BACKGROUND: The validity of indirect bypass for adult patients with moyamoya disease is still debatable. Some patients are poor responders to indirect bypass, and additive intervention is occasionally required in these cases. Therefore, it is necessary to evaluate the development of collateral circulation as early as possible postoperatively.
METHODS: Fifteen adult patients (>17 years old) with moyamoya disease (22 affected sides) who underwent encephalo-duro-arterio-synangiosis (EDAS) at Fukuoka University Hospital from April 2008 to August 2014 were included. All patients had ischemic symptoms of at least one hemisphere. Superficial temporal artery duplex ultrasonography (STDU) was performed before and 3, 6, and 12 months postoperatively. Digital subtraction angiography was performed 1 year after the operation to evaluate the development of collateral circulation. Hemispheres exhibiting collateral formation of more than one-third of the MCA distribution were defined as good responders, and those with less than one-third were defined as poor responders.
RESULTS: EDAS induced the formation of well-developed collaterals in 17 of 22 affected sides (77.3%) of adult patients with ischemic moyamoya disease. Regardless of the degree of collateral formation, the ischemic event subsided eventually with time in all patients. In good responders, the pulsatility index obtained by STDU showed a drastic decrease 3 months after the operation, while it did not change significantly in poor responders. Absence of this decrease in the pulsatility index along with no change in the flow velocity reliably indicated poor responders.
CONCLUSIONS: Neovascularization after EDAS can be evaluated noninvasively in early phase using STDU.

Keywords: moyamoya disease, indirect bypass, encephalo-duro-arterio-synangiosis, superficial temporal artery, duplex ultrasonography

Running Title: EARLY EVALUATION AFTER INDIRECT BYPASS

INTRODUCTION

The efficacy of indirect bypass for pediatric moyamoya disease is widely accepted. In contrast, indirect bypass for adult patients with moyamoya disease has long been considered inferior to direct bypass despite the fact that no randomized trials have been performed to compare them[19]. The biggest advantage of direct bypass is that it can establish bypass flow immediately after the operation[3]. However, because of the drastic change in the cerebral blood flow, direct bypass can cause hyperperfusion syndrome[8] including intracerebral hemorrhage[7, 9]. The incidence of these complications brought on by excessive perfusion is significantly higher in adult patients than in children[20]. Recently, the efficacy of indirect bypass also for adult patients with moyamoya disease has been shown in several studies[1, 2, 5, 6, 10, 12, 14, 17]. Some of them emphasized that indirect bypass can be performed with a lower incidence of complications than direct bypass[5, 12]. However, there do exist patients exibiting a poor response to indirect method, and some require additive revascularization surgery[1, 14, 16, 23]. Therefore, it is necessary to evaluate the development of collateral circulation as early as possible postoperatively. Whether and when neovascularization can be expected, however, remains unclear. The authors retrospectively examined the superficial temporal artery duplex ultrasonography (STDU) on the adult patients with moyamoya disease who had undergone indirect bypass surgery and analyzed the serial changes in various parameters retrospectively.

METHODS

Fifteen adult patients (>17 years old) with moyamoya disease (22 affected sides) who underwent indirect bypass surgery at Fukuoka University Hospital from April 2008 to August 2014 were included. All patients had ischemic symptoms of at least one hemisphere. Encephalo-duro-arterio-synangiosis (EDAS) using both the frontal and parietal branches of the superficial temporal artery was basically adopted for indirect bypass. Each donor artery was harvested with an abundant galeal flap (approximately 3–4 cm in width) and sutured to the dural edge (Fig. 1). STDU was performed before and 3, 6, and 12 months after the operation. The HI VISION Ascendus (Hitachi Aloka Medical, Ltd., Tokyo, Japan) with an 18- to 5-MHz linear array transducer was used. Digital subtraction angiography (DSA) was performed 1 year after the operation to evaluate the development of collateral circulation. The grade of developed collaterals was classified in accordance with the method proposed by Matsushima et al[15] (A: collateral formation of more than two-thirds of the MCA distribution; B: between two-thirds and one-third; C: less than one-third), and an absolute nonresponder with grade C collaterals was further categorized as having grade D collaterals. A good responder was defined as having grade A and B collaterals, while a poor responder was defined as having grade C and D collaterals.

Statistical analysis was performed between parameters of any two points in time for both good and poor responders. The Wilcoxon signed rank test was used after these parameters were confirmed to be normally distributed. A p value of <0.05 was considered statistically significant. Receiver operating characteristic analyses were performed to ascertain the pulsatility index (PI) as the cutoff point for the prediction of neovascularization. Data were analyzed using SPSS for Windows version 21.0 (SPSS; IBM Co., Armonk, NY, USA).

RESULTS

At 1 year postoperatively, the development of collateral circulation was classified as grade A in 10 sides (45.5%) (Fig. 2), grade B in 7 sides (31.8%), grade C in 3 sides (13.6%), and grade D in 2 sides (9.1%). Consequently, there were 17 (77.3%) good responders.

With respect to perioperative complications, a minor infarction of the operated side without a

permanent deficit occurred on the second postoperative day in one patient. An ipsilateral chronic subdural hematoma was seen on one operated side, but spontaneously resolved with time. This side was eventually classified as grade A by postoperative DSA. Delayed wound healing was observed on two sides but healed with conservative treatment in both. No hyperperfusion syndrome or intracerebral hemorrhage was seen. The ischemic attack on the operated side diminished within 1 year after the operation on all sides regardless of the DSA results (Table 1).

Serial changes in each STDU parameter are shown in Figure 3. The diameter of the superficial temporal artery (STA) showed only a temporary increase 3 months after the operation in good responders. In poor responders, it tended to become smaller with time. The peak systolic velocity (PSV), end-diastolic velocity (EDV), and mean flow velocity (MFV) increased with time in good responders, but did not change in poor responders. The PI [(PSV − EDV) / MFV] showed a significant decrease 3 months after the operation and did not change thereafter in good responders. In contrast, it did not show a significant change in poor responders. In the analyses of the receiver operating characteristic curves (Fig. 4), a PI of 1.335 was determined as the most reliable cutoff value for predicting good responders at 3 months postoperatively (95% confidence interval, 0.854–1.000). Based on this cutoff, the sensitivity and specificity were 86.7% and 100.0%, respectively. The positive and negative predictive values were 100.0% and 66.7%, respectively.

DISCUSSION

Studies of postoperative serial changes measured by STDU for moyamoya disease have been reported for direct bypass[7, 13, 22] and combined bypass[21]. However, the present study is the first to evaluate purely indirect bypass. The PSV, EDV, and MFV gradually increased until 6 to 12 months after the operation in good responders. This indicates that collateral vessels may still develop beyond 6 months postoperatively. On the other hand, the PI, which reflects the peripheral resistance of the measured vessel, showed a drastic decrease at 3 months postoperatively and no significant change thereafter. The drastic decrease at this time point may indicate that basic collateral network has been established. In fact, Gonzalez et al.[10] reported the cases with well-developed collaterals proved by DSA at 1 and 2 months after the operation, respectively.

DSA, which is an invasive method, remains the gold standard with which to confirm newly developed collaterals. In the present study, we carried out DSA at 1 year postoperatively. However, there is no consensus on the best time at which to perform postoperative DSA to confirm neovascularization. Various researchers have waited at least 3 months[18], 6 months[4], at least 6 months[5, 11], 2 to 16 months[12], or 10 to 12 months[14]. In the present study, no additional intervention was performed because the ischemic symptoms subsided after the operation in all patients regardless of the amount of neovascularization. However, cases do exist that require direct bypass[14, 16, 23] or other types of indirect bypass[1, 16] additionally, and the timing may be as early as 3 months[16]. Hence, patients who need additional treatment should be identified as soon as possible. The present analysis of serial changes in STDU findings indicates that the absence of a drastic decrease in the PI in combination with no increase in the PSV, EDV, or MFV at 3 months postoperatively indicates a high probability of a poor response to the indirect bypass procedure. For patients suspected to be poor responders by STDU at this time point and who do not show clinical stabilization, to perform DSA may be required for confirmation. If the bypass flow is not established, additional intervention should be considered as soon as possible, instead of waiting more. Further investigation should be carried out if a judgment based on STDU findings can be made even earlier than 3 months postoperatively.

CONCLUSION

Neovascularization after EDAS can be evaluated noninvasively in early phase using STDU. Early identification of poor responders using STDU will reinforce the safety of this intervention.

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Disclosure
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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Figure legends

Fig 1. Encephalo-duro-arterio-synangiosis with abundant galeal flaps

Fig 2. Postoperative digital subtraction angiography of 10 sides of patients with grade A collateral circulation (collateral formation of more than two-thirds of the middle cerebral artery distribution)

#1L, left side of Case 1; R, right

Fig 3. Serial changes in parameters obtained by superficial temporal artery duplex ultrasonography (STDU). A: Diameter, B: peak systolic velocity, C: end-diastolic velocity, D: mean flow velocity, E: pulsatility index, F: STDU measurement

Boxes represent the interquartile range. Horizontal lines in boxes indicate the medians. The range of whiskers does not include outliers. *P < 0.05

Fig 4. Receiver operating characteristic curve analyses indicated that a pulsatility index of 1.335 was the most reliable cutoff value for predicting good responders.

AUC: area under the curve

Table 1. Patients' characteristics, classification based on digital subtraction angiography (DSA), changes in symptoms, and perioperative complications

Asy: asymptomatic, CSDH: chronic subdural hematoma, Hem: hemorrhage, Inf: infarction, Isc: ischemia, less freq: less frequent, POD: postoperative day, TIA: transient ischemic attack, WH: wound healing

Fig 1

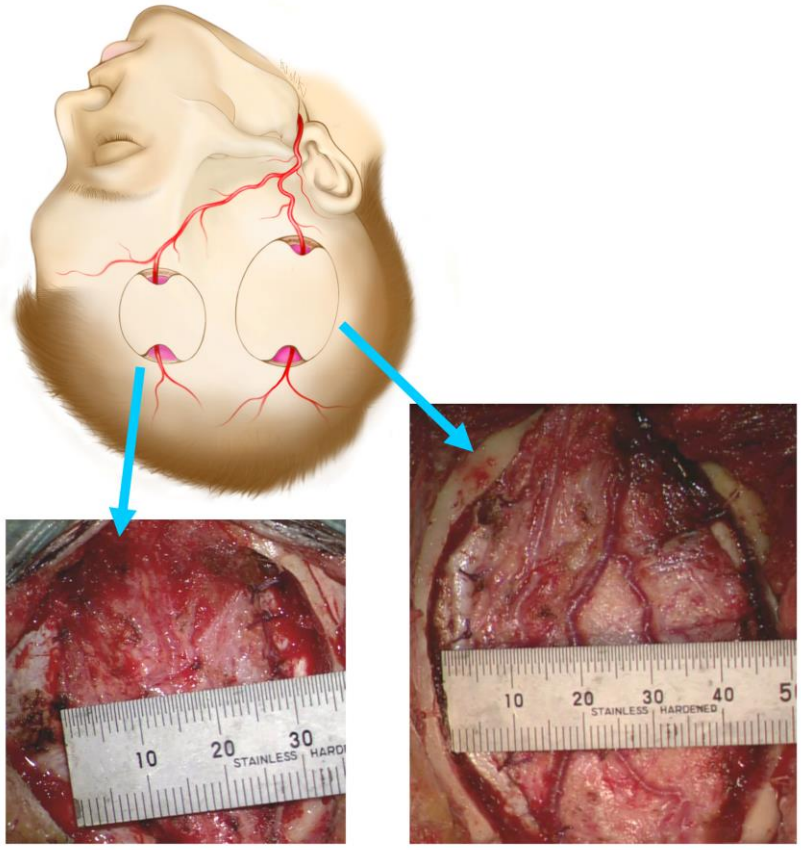

Fig 2

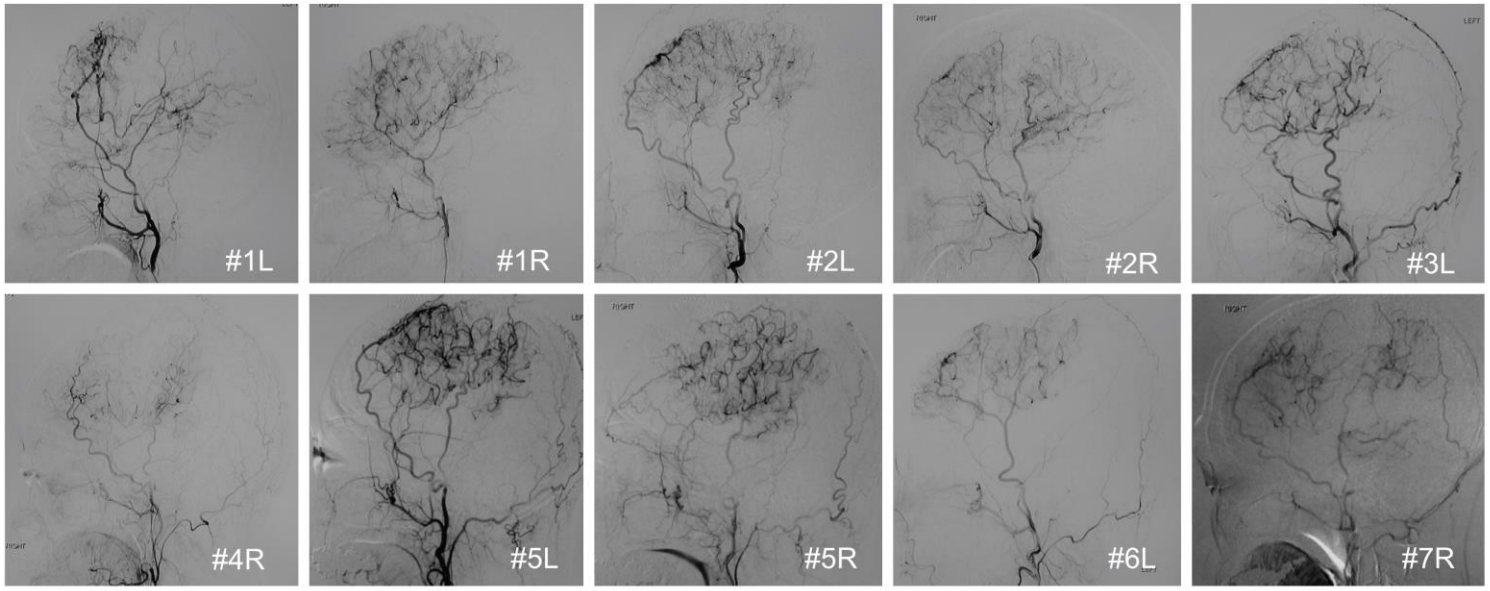

Fig 3

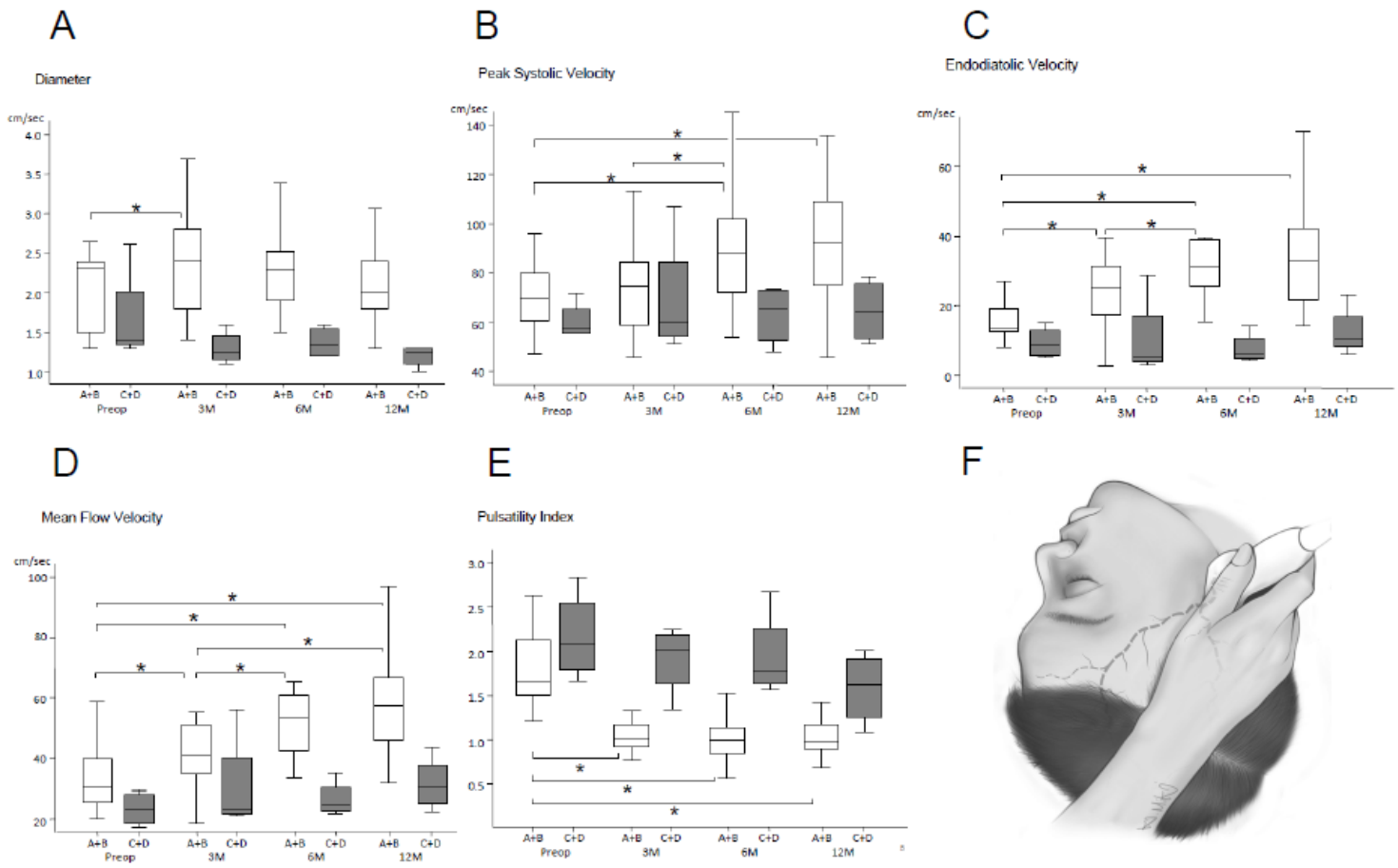
A
Diameter
cm/sec
4.0
3.5
3.0
2.5
2.0
1.5
1.0
A+B C+D A+B C+D A+B C+D A+B C+D
Preop 3M 6M 12M
B
Peak Systolic Velocity
cm/sec
140
120
100
80
60
40
A+B C+D A+B C+D A+B C+D A+B C+D
Preop 3M 6M 12M
C
Endodiatolic Velocity
cm/sec
60
40
20
0
A+B C+D A+B C+D A+B C+D A+B C+D
Preop 3M 6M 12M
D
Mean Flow Velocity
cm/sec
100
80
60
40
20
A+B C+D A+B C+D A+B C+D A+B C+D
Preop 3M 6M 12M
E
Pulsatility Index
3.0
2.5
2.0
1.5
1.0
0.5
A+B C+D A+B C+D A+B C+D A+B C+D
Preop 3M 6M 12M
F

Fig 4

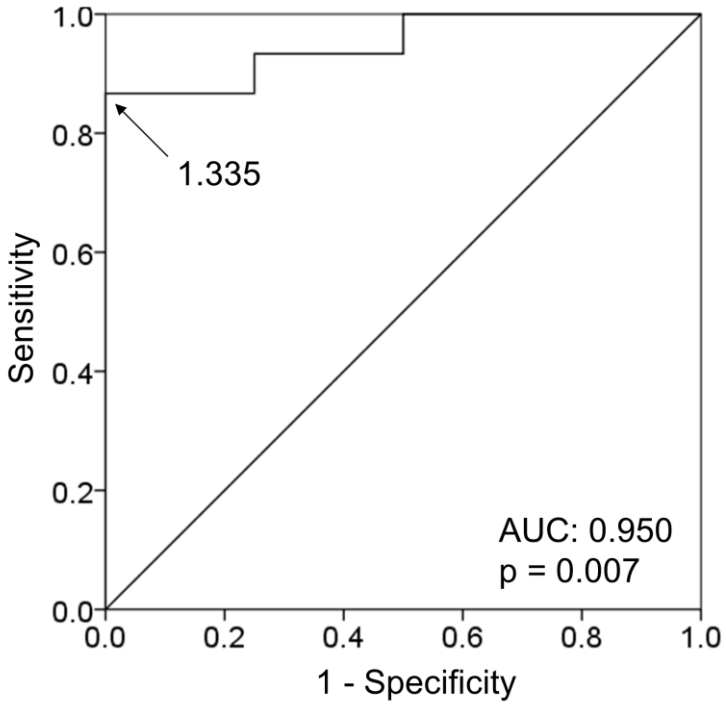
1.0
0.8
0.6
0.4
0.2
0.0
Sensitivity
1.335
AUC: 0.950
p = 0.007
0.0
0.2
0.4
0.6
0.8
1.0
1 - Specificity

Table 1

Case No.	Sex	Side	Age(yrs) at Operation	DSA	Preoperative Presentation	Changes of Symptoms				Perioperative Complication
						Preop	3M	6M	12M	
1	F	L	18	A	Isc	TIA	-	-	-	-
		R	18	A	Isc	TIA	-	-	-	-
2	F	L	40	A	Asy	-	-	-	-	-
		R	40	A	Isc	TIA	-	-	-	-
3	F	L	33	A	Isc	Inf / TIA	TIA	-	-	-
		R	33	B	Asy	-	TIA	-	-	-
4	F	L	38	B	Isc	TIA	-	-	-	-
		R	39	A	Isc	TIA	-	-	-	Inf (POD2)
5	F	L	48	A	Isc	Inf / TIA	Seizure	-	-	CSDH / delayed WH
		R	48	A	Asy	-	Seizure	-	-	-
6	F	L	28	A	Asy	-	-	-	-	-
		R	28	B	Isc	TIA	-	-	-	-
7	F	R	55	A	Isc	TIA	TIA (less freq)	TIA (less freq)	TIA (less freq)	delayed WH
8	F	R	64	B	Isc	TIA	-	-	-	-
9	F	L	51	B	Isc	TIA	-	-	-	-
10	F	R	38	B	Isc	TIA	-	-	-	-
11	F	R	26	B	Hem / Isc	TIA	-	-	-	-
12	F	L	25	D	Isc	TIA	-	-	TIA (less freq)	-
		R	25	C	Isc	TIA	TIA	-	TIA (less freq)	-
13	F	L	60	C	Isc	Inf / TIA	TIA	TIA	-	-
14	M	R	45	C	Isc	TIA	TIA	-	-	-
15	M	R	55	D	Isc	Inf	-	-	-	-