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Modified encephalo-duro-periosteal-synangiosis (EDPS) for the revascularization of anterior cerebral artery territory in moyamoya disease: A single-center experience

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ABSTRACT

Objectives: Anterior cerebral artery (ACA) territory, a crucial area of intellectual development in children, is frequently involved in the progress of moyamoya disease (MMD). However, revascularization surgeries for this area are not as established as surgeries for middle cerebral artery (MCA) territory. This study aimed to describe our experience and study the effect of revascularizing ACA territory with periocranium and dural leaflets, which is referred to as 'encephalo-duro-periosteal-synangiosis (EDPS)'.

Patients and method: Fourteen hemispheres of 9 MMD patients who had undergone EDPS from November 2015 till July 2017 in our hospital were retrospectively included. Clinical characteristics and procedure-related information were recorded. Cerebral perfusion was evaluated by computed tomography perfusion (CTP). Absolute and relative (r) CTP parameters of ROIs in ACA territory at the level of centrum semiovale and middle basal ganglia were calculated. Preoperative and postoperative parameters were compared.

Results: All EDPS procedures were technically successful with no postoperative complications. The mean operating time was 75.00 ± 22.53 min per hemisphere. Postoperative absolute cerebral blood flow (CBF), rCBF were significantly increased and absolute time to peak (TTP), rTTP, absolute mean transit time (MTT) were significantly reduced in ACA territory at centrum semiovale level ($P = 0.002$, 0.045, 0.007, 0.005 and 0.039 respectively). Improved outcomes were achieved in five patients, stabilization in three and one patient had deterioration out of intracerebral hemorrhage during follow-up.

Conclusion: EDPS is a simple but effective technique to revascularize ACA territory for MMD. EDPS significantly improved cerebral blood perfusion of frontal lobe in the majority of patients without increasing procedure-related risks.

1. Introduction

Anterior cerebral artery (ACA) territory, an important area of brain intellectual and cognitive functioning [1], is frequently involved along with the progressive stenosis and occlusion of internal carotid artery (ICA) in moyamoya disease (MMD) [2,3]. Previous studies demonstrated chronic hypoperfusion and recurrent strokes in this area would lead to declined cognitive and intellectual ability, especially in pediatric MMDs patients [4–6]. The surgical treatment for improving perfusion of ACA territory, however, is not as established as surgical revascularization for middle cerebral artery territory [7], which might be related to the lack of apparent vascular grafts in this area (grafts like superficial-temporal artery for MCA territory). It has been reported that galea and pericranium could be used as vascularized grafts (encephalo-galeo(pariosteal)-synangiosis, EGS) in the indirect revascularization of frontal lobe in MMD patients [8–10], but the application is still limited and its effect has rarely been examined.

In this study, we described our technique of a modified EGS, incorporating both periosteal and dural grafts in indirect revascularization for ACA territory with larger craniotomies, which was referred to as 'encephalo-duro-periosteal-synangiosis (EDPS)'. The effect of this technique on improving cerebral perfusion of ACA territory was studied. We hope this work may provide insights for the refinement of MMD surgeries.

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2. Material and methods

2.1. Patients and surgical modalities

This study retrospectively included 14 hemispheres of 9 MMD patients (mean: 19.36 ± 15.67 years old) with unilateral or bilateral hypoperfusion in ACA territory who had undergone EDPS at our hospital between November 2015 till July 2017. Diagnosis was made according to 2012 Guidelines set by Research Committee on the Pathology and Treatment of Spontaneous Occlusion of the Circle of Willis [11]. Indications for ACA revascularization included: a, severe hypoperfusion in ACA territory at initial presentation or after MCA territory revascularization; b, patients presenting mental retardation or decline.

This study was approved by the institutional review board of Beijing Tiantan Hospital, Capital Medical University. Due to the retrospective nature of this research, the board waived the need for written patient consent.

2.2. Encephalo-duro-periosteal-synangiosis (EDPS)

An bicoronal arc incision within the hairline (for bilateral operations), about 2 cm anterior and parallel to the coronal suture, was made through the subcutaneous tissue. Care need to be taken not to injure the superficial temporal artery, especially the trunk and posterior branch. The scalp flap was carefully lifted from the pericranium, leaving the pericranium intact. Pericranium was then cut into two 6 × 6-cm^2 quadrate flaps with anterior base, carefully elevated from the frontal bone and covered with wet gauze, preparing for later use. A bur hole was drilled adjacent to the sagittal sinus, allowing two 6 × 6-cm^2 frontal craniotomy to be elevated. The inferior border of craniotomy should not be too low in case frontal sinuses would be opened. Dura was cut in radial fashion into several triangular flaps, and then inserted into the interhemispheric fissure and inverted underneath the bone edges. Loosely place the pericranial flaps on the brain cortex, and sutured to the edges of dura. Defects of dura should be covered by artificial dura mater if necessary. The bone flap was then replaced, allowing the pericranial grafts through the crevice. At last, the scalp was closed layer by layer (Fig. 1).

If unilateral operation was about to perform, a hemicoronal incision was made to the symptomatic side. Only one pericranial flap was prepared and one bone flap was elevated. Other steps of the procedure were same to those of bilateral operations.

2.3. Evaluation of cerebral perfusion

All patients were examined by computed tomography perfusion (CTP) within 1 month before surgery and at 6 month follow-up. Cerebral perfusion was evaluated by CTP parameters calculated with General Electric Company perfusion software.

For each hemisphere, two circular regions of interests (ROI) with a diameter of 25 mm were placed in the anterior cerebral artery (ACA) territory respectively at slice levels passing through the centrum semiovale and the middle basal ganglia, covering both cortical and medullary regions [12]. ROIs placements were shown in Fig. 2. From each ROI, absolute values of cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT) and time to peak (TTP) were calculated. The relative CTP values in our study were defined as the ratios between absolute CTP values of each ROI and of cerebellum from the same side, including relative cerebral blood flow (rCBF), relative cerebral blood volume (rCBV), relative mean transit time (rMTT) and relative time to peak (rTTP) [13–15].

2.4. Follow-up and evaluation of outcome

Conditions of patients were followed by telephone or by clinic interviews 3–6 months after surgery and annually thereafter. Modified Rankin scale (mRS) was used to evaluate neurological status on admission, at discharge and at follow-up. Recurrent cerebral hemorrhage, ischemia and seizure were recorded. Patients with complete

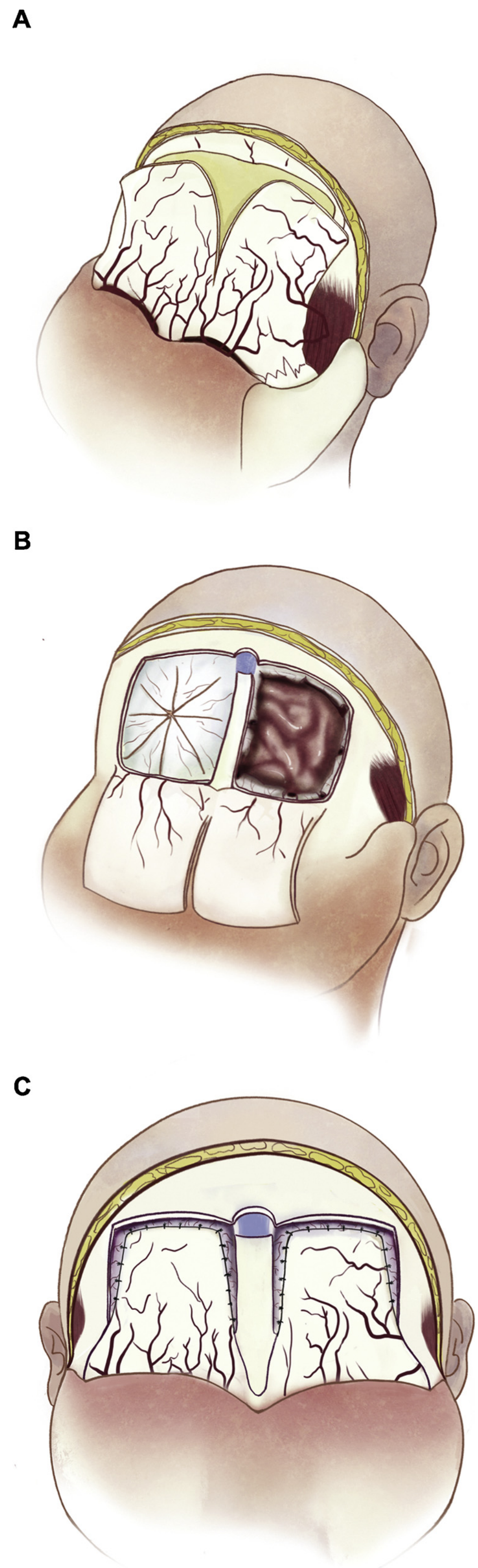

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Fig. 1. Main procedure of a bifrontal encephalo-duro-periosteal-synangiosis. A. A bicoronal arc incision within the hairline was made about 2 cm anterior and parallel to the coronal suture through the subcutaneous fat. The scalp flap was carefully lifted from the pericranium. Pericranium was then cut into two 6 × 6-cm2 quadrate flaps with anterior base, carefully elevated from the bone. B. A bur hole was drilled adjacent to the sagittal sinus, two 6 × 6 -cm2 frontal craniotomy aside being elevated. Dura was cut in radial fashion into several triangular flaps, and then inserted into the interhemispheric fissure and inverted underneath bone edges. C. Loosely place the pericranial flaps on the brain cortex, and sutured them to the edges of dura.

disappearance or self-reported decrease of symptoms were defined as 'Improvement'. Patients without significant change of previous symptoms nor newly-developed symptoms were defined as 'Stabilization'. Patients had worsened symptoms were defined as 'Deterioration'.

2.5. Data analyses

Statistical analyses were carried out using SPSS software (v.22.0; IBM Corp., Chicago, IL, USA). Group data were compared using paired *t*-test and unpaired *t*-test as appropriate. $\chi 2$ test was used in the analysis of fourfold table. A P value < 0.05 was considered statistically significant.

3. Results

3.1. Clinical characteristics of patients who underwent EDPS

Clinical characteristics of 14 operated hemispheres (9 patients) who had undergone EDPS were shown in Table 1, including 6 (66.7%) pediatric patients (under 18 years old) and 3 (33.3%) adults (mean: 19.36 ± 15.67 years; range: 6–44 years). Among 14 hemispheres, 6 (42.9%) were from male patients and 8 (57.1%) were from female patients. Seven (77.7%) patients were initially presented with ischemic symptoms, one (11.1%) with hemorrhagic symptom and the other one (11.1%) with headaches. All patients who were included in this study had mild symptoms, including eight (88.9%) patients had mRS score of 1 and one (11.1%) had mRS 0. Four patients underwent unilateral EDPS and five underwent bilateral EDPS, making a total of 14 revascularization procedures. These patients were followed for a mean of 181.93 ± 137.72 days.

Table 1
Characteristics of patients underwent EDPS.

	Number (%)
Age, year	19.36 ± 15.67
< 18 years old[a]	10 (71.4%)
> 18 years old[a]	4 (28.6%)
Gender (Male/Female)[a]	6/8
Onset type	
Ischemic onset	7 (77.8%)
Hemorrhagic onset	1 (11.1%)
Atypical onset	1 (11.1%)
mRS at admission	
0	1 (11.1%)
1	8 (88.9%)
2	0 (0.0%)
Unilateral/bilateral surgery	4/5
Follow-up, days	181.93 ± 137.72

[a] Calculated on the basis of hemispheres (n = 14).

3.2. Encephalo-duro-periosteal-synangiosis (EDPS) improved cerebral perfusion of ACA territory

All 14 hemispheres were successfully operated with aforementioned technique of EDPS, with no procedure-related complications or death occurred. Preoperative and follow-up CT perfusion parameters were calculated and compared as shown in Fig. 3. At the level of centrum semiovale, absolute CBF and rCBF significantly increased after EDPS surgery (*P* = 0.002 and *P* = 0.045, respectively). Absolute TTP, rTTP, and MMT significantly decreased (*P* = 0.007, 0.005 and 0.039, respectively) after the operation. The increase of CBV and rCBV and the decrease of rMMT were noticed, but the difference was not statistically significant. At the level of middle basal ganglia, follow-up TTP and MMT were significant decreased compared to postoperative values (*P* = 0.028 and *P* = 0.041, respectively). The changes of other parameters were not significant.

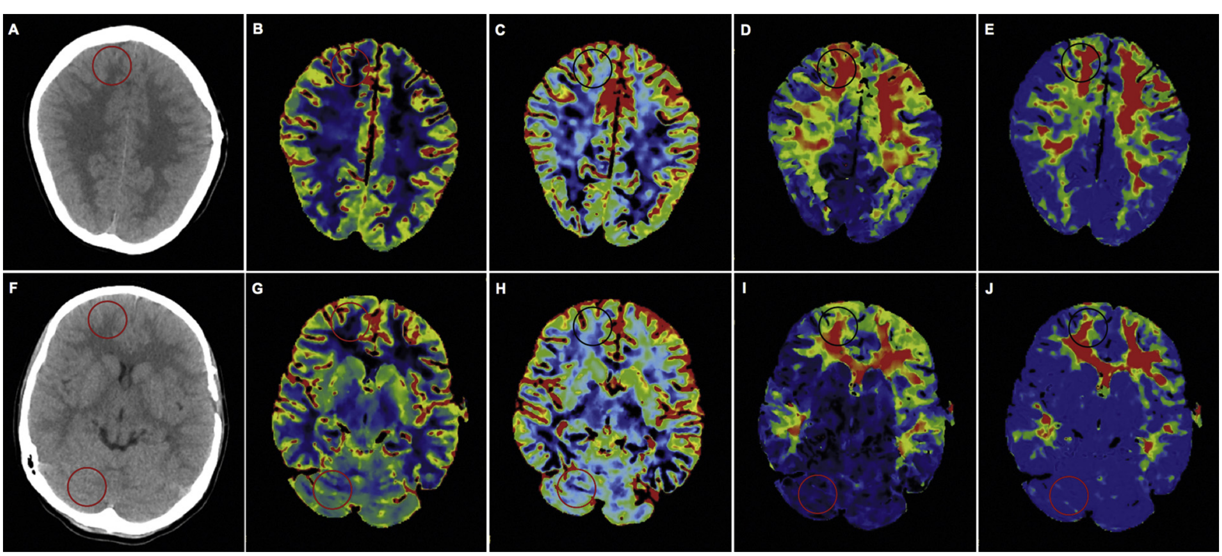

Fig. 2. The placement of regions of Interest (ROI) on computed tomography perfusion (CTP). For each hemisphere, three circular ROIs (diameter = 25 mm) were placed on the structural scan and automatically propagate to four functional scans. A. ROI 1 was placed on the ACA territory at the level of centrum semiovale. B–E. Propagation of ROI 1 on cerebral blood flow (CBF), cerebral blood volume (CBV), time to peak (TTP) and mean transit time (MTT), respectively. F. ROI 2 was placed on the ACA territory at the level of middle basal ganglia. ROI 3 was placed on the cerebellum at the same level, which was used as a reference value in calculating relative CTP parameters. G-J: Propagation of ROI 2 and 3 on cerebral blood flow (CBF), cerebral blood volume (CBV), time to peak (TTP) and mean transit time (MTT), respectively.

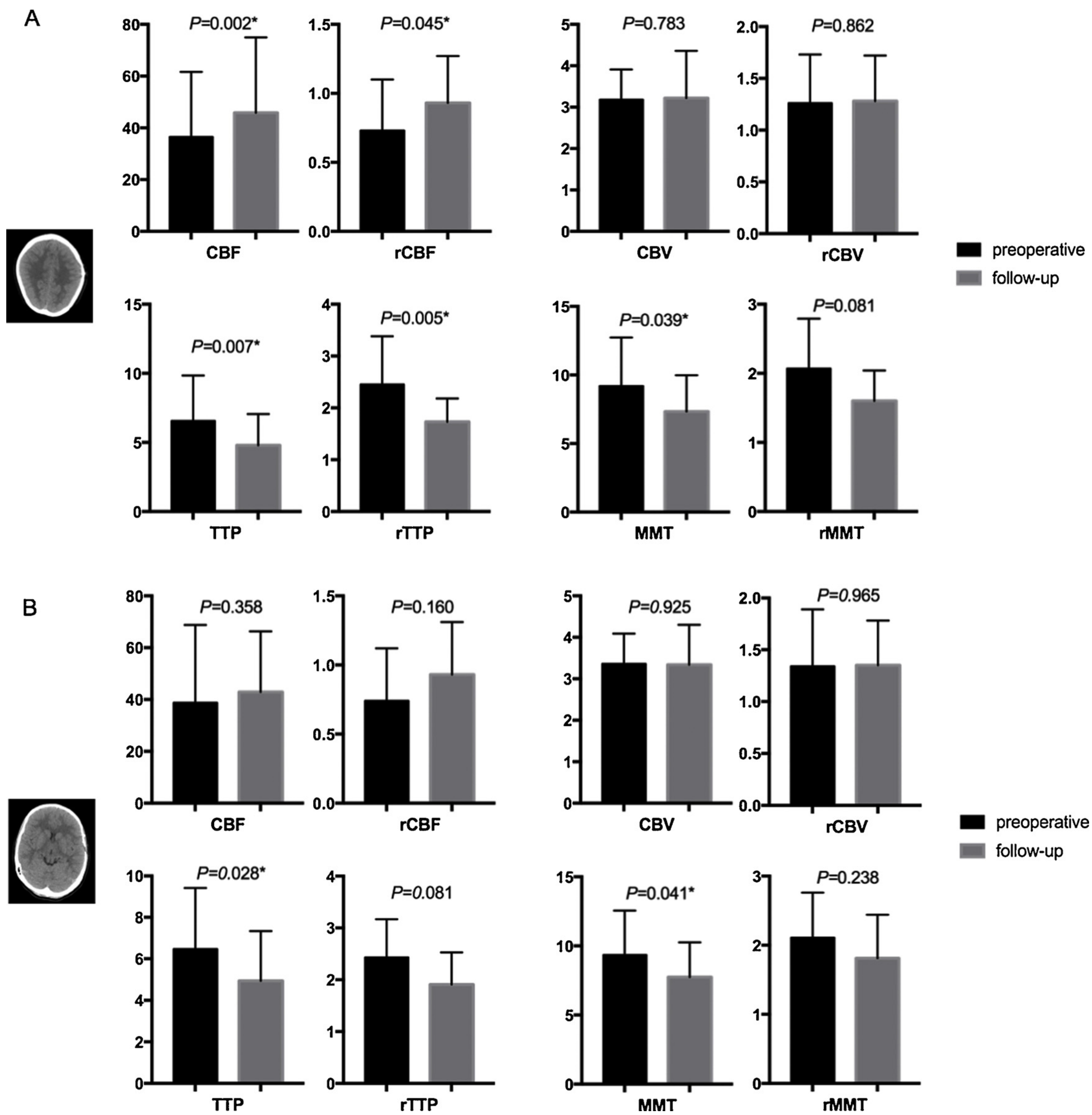

Fig. 3. Preoperative and follow-up CT perfusion parameters of patients underwent EDPS indirect revascularization, including cerebral blood flow (CBF), relative CBF (rCBF), cerebral blood volume (CBV), relative CBV (rCBV), time to peak (TTP), relative TTP (rTTP), mean transit time (MTT) and relative MTT (rMTT). A. Comparison of preoperative and follow-up CTP parameters at the level of centrum semiovale. B. Comparison of preoperative and follow-up CTP parameters at the level of middle basal ganglia.

3.3. Postoperative complications and long-term outcome after EDPS

Postoperative complications and long-term outcome after EDPS surgery were listed in Table 2. The mean duration of EDPS procedure was 75.00 ± 22.53 min per hemisphere. In the whole series, no postoperative complication occurred (including ischemic or hemorrhagic events, epilepsy or wound infection). Mean postoperative hospital stays were 7.36 ± 1.39 days. During long-term follow-up, one patient had an episode of TIA, of which the symptoms diminished within 24 h, and one patient had recurrent intraventricular hemorrhage leading to worsened neurological status. At the last follow-up, five (55.6%) patients had improved outcomes and three (33.3%) were stabilized. One (11.1%) patient had deteriorated outcome because of re-bleeding.

Table 2
Postoperative complications and long-term outcome after EDPS (n = 9).

	Number (%)
Operation time per hemisphere (min)[a]	75.00 ± 22.53
Postoperative complications	
Ischemic events	0 (0.0%)
Hemorrhagic events	0 (0.0%)
Wound infection	0 (0.0%)
Epilepsy	0 (0.0%)
Postoperative hospital stays (d)	7.36 ± 1.39
Recurrent symptoms during follow-up	
Ischemic events	1 (11.1%)
Hemorrhagic events	1 (11.1%)
Epilepsy	0 (0.0%)
Outcome	
Improvement	5 (55.6%)
Stabilization	3 (33.3%)
Deterioration	1 (11.1%)

[a] Calculated on the basis of hemispheres (n = 14).

4. Discussion

Hypoperfusion of ACA territory is frequently seen along the progressive stenosis and occlusion of internal carotid artery in moyamoya disease [2,3], however, revascularization of this area has not drawn as

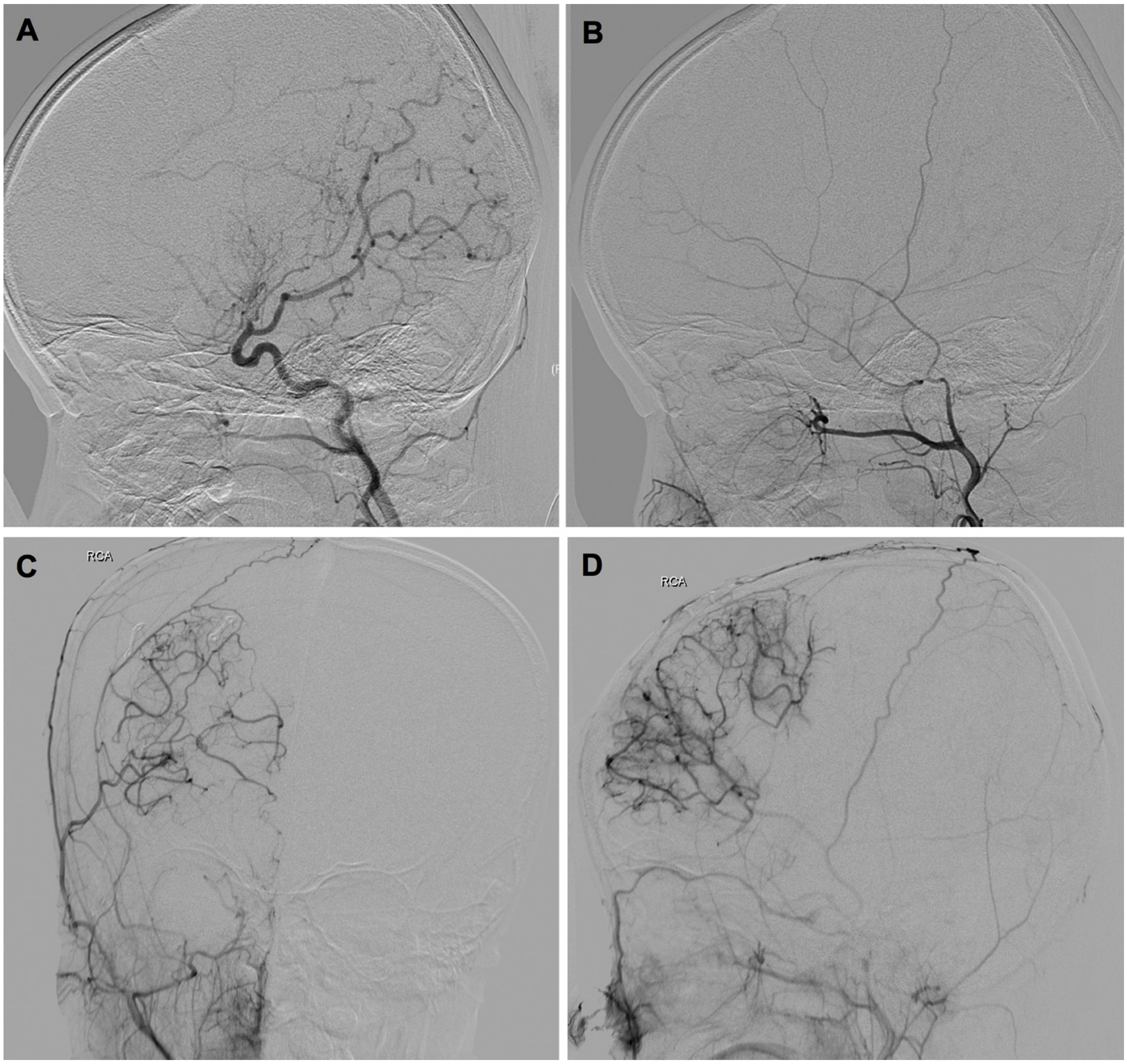

Fig. 4. A case illustration of a 7-year-old MMD patient who underwent right-side EDPS. Digital subtract angiography (DSA) was conducted preoperatively and at 1-year follow-up. A. Pre-operative DSA showing stenosis of right internal carotid artery, disappear of anterior cerebral artery (ACA) and middle cerebral artery and formation of moyamoya vessels. B. Pre-operative DSA showing external carotid artery with no formation of spontaneous extracranial-intracranial collateral vessels. C. Follow-up DSA showing abundant neo-angiogenisis at ACA territory (anteroposterior position). D. Follow-up DSA showing abundant neo-angiogenisis at ACA territory (Lateral position).

high attention as of MCA territory. A few studies have reported experience of treating MMD presented with ACA hypoperfusion with encephalo-galeo(peristeal)-synangiosis (EGS) or MBH surgery[8, 2], however, such procedures have not been standardized yet. In this study, we described our single-center experience of treating ACA territory hypoperfusion in MMD with a modified technique using pericranium as vascularized grafts, namely encephalo-duro-periosteal-synangiosis (EDPS).

The application of galea and pericranium (periosteum) as grafts in indirect revascularization for ACA territory in moyamoya disease had been through evolution [16]. A 'ribbon' procedure was described by Kinugasa et al. in 1994, inserting a strip of galeal tissue into interhemispheric fissure, receiving positive effect [17]. This procedure was then modified by Kim et al, using a small bifrontal rectangular craniotomy over midline [8,9]. Considering the small craniotomy of current procedures might limit the scope of future angiogenesis [18] and periosteal grafts alone would not provide enough revascularization [19], in our practices, we further modified the original technique by enlarging the craniotomies in order to gain more exposure and make sure larger area can be covered by vascularized grafts. Large pericranial flaps with abundant blood supply are used as the main grafts. Also, revascularization is reinforced by inversion of dural flaps under the bone edge of craniotomy. The details of this procedure had been described in the Method section.

In order to evaluate the effect of EDPS, CTP was used to compare cerebral perfusion before and after surgery. Results showed that EDPS was able to significantly increase cerebral blood flow and reduce transit time of the ACA territory. The improvement of blood flow (CBF and rCBF) was more obviously seen at the level of centrum semiovale than the level of basal ganglion, but shorten of transit time was significant at both levels, indicating the broad region of revascularization induced by EDPS (Fig. 3). A case illustration showing abundant neovascularization after EDPS on DSA can be seen on Fig. 4, underlined the satisfying revascularization that EDPS could provide. In the long-term, improvement and stabilization of symptoms were achieved in 88.9% patients (5 and 3, respectively). Only one patient resulted in deterioration because of intracranial hemorrhage during follow-up (Table 2), again confirming the favorable effect of this method.

On the other hand, the advantage of EDPS is quite easily seen. It is a simple method, with a mean operation time of 75.00 ± 22.53 min for each hemisphere (Table 2), technically much less challenging comparing to STA-ACA bypass [20,21]. The short duration of this procedure may reduce potential risks raised by long-time anesthesia and operating [22], which brought about the low incidence of perioperative complications (0% in this series comparing to 4–10% after bypass and EDAS in previous literature) [23,24]. The incision should always be placed within hairline and only one bur hole need to be drilled in the frontal bone, therefore it is less likely to leave postoperative cosmetic defects compared to multiple bur holes operation and STA-ACA bypass, which in our series no patients had complains about at follow-up (data not shown).

Comparing to past EGS surgery, one improvement of our modification is to adapt larger craniotomies with larger periosteal flaps, theoretically broadening the potential revascularized area, as demonstrated by our findings that improvement in perfusion could be detected down to the plane of middle basal ganglia. On the other hand, dural grafts are combined in this technique along with periosteal grafts, providing two kinds of vascularized grafts and doubling the potential effect of neo-angiogenesis. EDPS could be an effective method to address hypoperfusion of ACA territory when STA-ACA bypass was not advantageous (ie. STA anterior branch courses over forehead) or not optional (ie. STA anterior branch does not exist), as an individual procedure to treat initial presentation of MMD, or as a salvage procedure for frontal hypoperfusion after MCA territory revascularization. Moreover, EDPS is of high flexibility that it could merge with EDAS or direct bypass to establish a one-staged revascularization covering both ACA and MCA territory for MMD, as had been reported by previous literature [25].

Previous studies had emphasized the importance of ACA territory involvement for cognitive decline especially in pediatric MMD patients [4–6,26], moreover, early revascularization of this area might contribute to later-life intellectual improvement [1,27–29]. However, compared to MCA territory, ACA territory hypoperfusion is much underestimated and overlooked, even though infarction and hypoperfusion of frontal lobe is just as common and vital at bedside practice. The current situation might be related to the lack of apparent vascular grafts (grafts like superficial-temporal artery for MCA territory) in ACA territory, the poor understanding of periosteal revascularization, and the lack of standard, widely-established surgical method. In this study, we again proved the effectiveness of periosteal revascularization for moyamoya disease, and described a simple, practical technique which could be universally applied. Hopefully our experience will bring solution to ACA territory revascularization, for both pediatric and adult MMD patients.

The current study has a few limitations. The evaluation of cerebral perfusion was only by CT perfusion, which was though usable but less quantitative than single photon emission computed tomography (SPECT). Evaluation of neo-angiogenesis by digital subtraction angiography was not included in this study, because few patients in this study were willing to receive another invasive examination at follow-up. Also, small sample size and retrospective design might lead to compromised efficiency and bias in statistics. Most of patients who have underwent this EDPS were under age of 18, which might contribute to the success of this technique as it is agreed that indirect bypass generally functions well in pediatric patients. Last, the effect of EDPS was not compared with other procedures. Although we intended to include historical controls of cases that had undergone multiple bur hole surgery, however, due to the uneven baseline characteristics out of retrospectively inclusion, the value of such comparison was very limited (see Supplementary materials 1 and 2). All in all, this paper was mainly about introducing our surgical experience. Future studies with prospective design, larger sample size and longer-time follow-up are needed to further validate the potential of periosteal grafts in revascularization for moyamoya disease.

5. Conclusion

In this article, we described our method of using periosteal and dural flaps to revascularize ACA territory in moyamoya disease, knowing as 'encephalo-duro-periosteal-synangiosis (EDPS)'.EDPS significantly improved cerebral blood perfusion of frontal area, as a simple but effective technique, providing a great potential in the surgical treatment of moyamoya disease.

Conflict of interests and disclosure

We declare that we have no conflict of interest for the current study.

Acknowledgement

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.clineuro.2019.02.002.

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