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ORIGINAL RESEARCH

Outcomes of Multimodality In situ Recanalization in Hybrid Operating Room (MIRHOR) for symptomatic chronic internal carotid artery occlusions

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ABSTRACT

Background An in situ recanalization procedure of endovascular therapy (ET) or carotid endarterectomy (CEA) has been attempted in patients with symptomatic chronic internal carotid artery occlusions (ICAOs), though the recanalization rates of both are low.

Objective To investigate the outcomes of Multimodality In situ Recanalization for ICAOs in a Hybrid Operating Room (MIRHOR) at the same session.

Methods Symptomatic chronic ICAOs were classified into type A or B (short occlusion with or without a tapered residual root [TRR]), and C or D (long occlusion with or without TRR), and managed in a hybrid operating room with ET, CEA, or both, as needed. Primary efficacy outcome was technical success of recanalization with Thrombolysis in Myocardial Infarction 3. Secondary efficacy outcome was any stroke or death within 30 days (primary safety outcome) plus an ipsilateral ischemic stroke after 30 days.

Results Technical success was finally achieved in 35 (83.3%) of 42 consecutively enrolled patients with ICAO, which was significantly higher than 35.7% (15/42, p<0.001) from the initial ET or CEA alone. Furthermore, the success rate was in descending order: 100% (18/18) for type A and B occlusions, 75% (6/8) for type C occlusions, and 69% (11/16) for type D occlusions (p=0.017). Two secondary efficacy outcome events (5.1%) without mortality, including one (2.4%) primary safety outcome, were observed during a mean follow-up of 10.5 months.

Conclusion The MIRHOR for symptomatic chronic ICAOs at the same session significantly improves technical success, with low periprocedural complications and favorable clinical outcomes. The ICAO classification appears valuable in predicting technical success.

INTRODUCTION

Symptomatic chronic internal carotid artery occlusion (ICAO) with hemodynamic cerebral ischemia has a high risk of recurrent stroke despite medical therapy.[1] Carotid endarterectomy (CEA) for ICAO is relatively safe but achieves recanalization in only one-third of cases.[2] Endovascular therapy (ET) increases the rate of recanalization to about two-thirds, but is associated with a significant risk of stroke.[3] Extracranial-intracranial (EC-IC) bypass as a flow augmentation strategy appeared to be a promising therapy for this disease; however, the Carotid Occlusion Surgery Study (COSS) trial was stopped early because of futility. Of note, although the 30-day stroke rate of the surgical arm in the COSS trial was significantly higher than that of the medical arm (14.4% vs 2.0%), the rates for any stroke or death within 30 days plus the 2-year risk of ipsilateral ischemic stroke beyond 30 days were almost the same (21.0% vs 22.7%).[1] The data strongly suggested that EC-IC bypass is effective for stroke prevention beyond 30 days. The bypass efficacy appeared to hinge on the periprocedural complication rate.

Using a hybrid operating room (HOR), Shih *et al* performed combined procedures with CEA for proximal internal carotid artery (ICA) occlusion and endovascular angioplasty for distal ICA occlusion in three patients successfully.[4] The hybrid procedures may potentially reduce periprocedural complication rates from ET by removing atherosclerotic plaque with CEA and reversing blood flow with temporary proximal occlusion by the CEA technique. More importantly, the combined procedures can be performed in a HOR as a one-stage procedure. However, there have been no reports of a large case series on the combined recanalization for ICAOs. The aim of this pilot study was to investigate the outcomes of Multimodality In situ Recanalization in a Hybrid Operating Room (MIRHOR) at the same session for symptomatic chronic ICAOs with ET, CEA, or both, as needed.

METHODS

Patient selection

In this study, chronic ICAO was defined as an interval of ≥2 weeks between ICAO diagnosis and procedure. Inclusion criteria were as follows: age >18 years; transient ischemic attack (TIA) or ischemic stroke attributable to the ICAO within 3 months; total ICAO documented by ultrasound, CT angiography (CTA), magnetic resonance angiography, or catheter angiography at least 2 weeks before the revascularization procedure; patency of the ipsilateral middle cerebral artery (MCA) via the posterior or anterior communicating artery (PComA or AComA), or the ipsilateral ophthalmic artery or other external carotid-ICA collaterals (OAO); cerebral hypoperfusion in the territory of

the ICAO on CT perfusion (CTP) imaging or MR perfusion-weighted imaging (PWI). Exclusion criteria were as follows: concomitant ipsilateral MCA occlusion; infarct size greater than one-third of the territory of the ipsilateral MCA; any bleeding disorder; contraindications to heparin, aspirin, clopidogrel, iodine contrast, or general anesthesia; concomitant end-stage disease with a predicted survival of <1 year. Baseline data and follow-up information of patients were prospectively collected. Written informed consent was obtained from all patients, including for the off-label use of Enterprise stents (Codman & Shurtleff, Raynham, Massachusetts, USA). The study was approved by the institutional ethics committee.

Preprocedure management

Brain MRI/PWI or CT/CTP, and catheter angiography were performed to evaluate ICAO and hypoperfusion. Patients received aspirin 300 mg and clopidogrel 75 mg daily for at least 5 days before the operation. Thromboelastography was used to evaluate platelet reactivity. If the inhibition ratio of either arachidonic acid or ADP was <50%, indicating a relative resistance to aspirin or clopidogrel, then cilostazol (Zhejiang Otsuka Pharmaceutical Co, Ltd, Shanghai, China) 100 mg twice a day was added. Atherosclerotic risk factors were managed according to the American Heart Association guidelines.[5] Concomitant stenosis of ≥70% in the vertebrobasilar artery, or the contralateral MCA or ICA was stented before the ICAO operation.

ICAO classification and collateral assessment

Digital Subtraction angiography (DSA) images were assessed by two physicians, with consensus, to determine occlusion length, appearance of residual root proximal to the occlusion, and collateral circulation. Chronic ICAOs were classified as type A or B (short occlusion less than three-quarters of the cervical ICA, with tapered residual root [TRR], or without TRR or any residual root); and type C or D (long occlusion greater than three-quarters of the cervical ICA, with TRR, or without TRR or any residual root). Primary collateral pathways of AComA, PComA, and OAO were recorded.

MIRHOR strategy

Our HOR was equipped with an Artis Zeego angiographic system (Siemens AG, Forchheim, Germany). All patients were prepared to receive both ET and CEA as needed at the same session. The initial revascularization procedure with CEA or ET was chosen by experienced open and endovascular neurosurgeons. For short occlusions, or occlusions with TRR, we often performed ET first. Otherwise, CEA was chosen as the initial procedure. If the initial procedure failed, an alternative procedure was performed immediately.

Recanalization procedures

Details of the ICAO recanalization procedures are as follows:

ET as initial procedure

Intravenous infusion of nimodipine (Bayer Pharma AG, Leverkusen, Germany) at 0.6 mg/h was started 2 hours before the procedure to prevent vasospasm. Heparin bolus was given intraoperatively to maintain activated clotting time between 200 and 250 s. Under local anesthesia and via a transfemoral approach, an 8-French guiding catheter was positioned into the ipsilateral common carotid artery with continuous heparin saline solution irrigation. An assembly of 0.014" Pilot exchange microwire (Abbott Vascular, California, USA) and 3 mm×15 mm Gateway balloon catheter (Stryker Neurovascular, Fremont, California, USA) was used to cross the occluded segment. After the assembly was negotiated into the true lumen distal to the occlusion, angiography was performed via the Gateway. When the occlusion was type A or B, a FilterWire embolic protection device (Boston Scientific Corporation, Natick, Massachusetts, USA) was used. The lesion was dilated by the Gateway after successful placement of the FilterWire, followed by implantation of a Wallstent (Boston ScientificCorporation) over the FilterWire after withdrawal of the Pilot microwire and Gateway. If the FilterWire failed to pass through the lesion at the first attempt, the occlusion was predilated by the Gateway while tightly pressing the guiding catheter against the proximal end of the occlusion in order to occlude anterograde blood flow, followed by placement of the embolic protection device. If the occlusion was too long to use a FilterWire, the guiding catheter was advanced into the proximal end of the occlusion. A long Wallstent was then delivered across the occlusion over the Pilot microwire. After the distal and middle segments of the stent were opened to protect from embolization, the guiding catheter was withdrawn from the occlusion, followed by complete release of the stent. Post-dilation with the balloon was applied in patients with residual stenosis of >50% within the stent. When there was a distal dissection or stenosis, an assembly of Prowler Select Plus microcatheter (Codman & Shurtleff, Raynham, Massachusetts, USA) and 0.014" Synchro exchange microwire (Stryker Neurovascular, Fremont, California, USA) was used to pass through the lesion gently, followed by deployment of one or more self-expanding Enterprise stents. If the cervical occlusion was not passed through by the Pilot microwire and Gateway, CEA was performed.

CEA as the initial procedure or as a second option after an ET attempt

The patient was positioned with head turned to the contralateral side. Under general anesthesia, a skin incision was made along the anterior border of the sternocleidomastoid muscle in accordance with standard CEA procedure. The common carotid artery, ICA, and external carotid arteries were exposed and tightly looped with elastic tourniquets. An arteriotomy of 5–8 cm length was made at the carotid bifurcation. After removal of the carotid atherosclerotic plaque, the ICA tourniquet was loosened to observe arterial backflow. If necessary, a Fogarty thru-lumen embolectomy catheter (Edwards Lifesciences LLC, Irvine, California, USA) was used to establish arterial backflow. A 5 F sheath of 11 cm length (Medtronic, Inc, Minneapolis, USA) was then placed into the ICA at the point 1–2 cm distal to the ICA tourniquet via the arteriotomy, and secured by the double-looped ICA tourniquet. Angiography was performed through the sheath. Whenever there was a dissection or occlusion distal to the arteriotomy, ET was performed.

ET via ICA arteriotomy

A 5 F Envoy guiding catheter (Codman & Shurtleff, Raynham, Massachusetts, USA) was inserted into the neck sheath. This enabled the interventional procedure to be performed away from X-ray tube with much less radiation exposure to operators. After a microcatheter was placed in the patent ICA distal to the occlusion, one or more Enterprise stents were implanted. After recanalization was confirmed on angiography, the arteriotomy was closed.

ET via a femoral approach

Angiography via a femoral approach was performed in patients with recanalization distal to the arteriotomy. If there was a dissection near the arteriotomy, a Wallstent was implanted. The stent length was at least 2 cm longer than the arteriotomy, so that each end of the stent extended at least 1 cm into the normal artery on either side of the arteriotomy. This reduced the radial force of the stent against the arteriotomy and prevented tearing of the closed arteriotomy.

Postoperative management

A patient's blood pressure was maintained at about 80% of baseline level for 3 days to prevent hyperperfusion syndrome with an intravenous ß blocker, calcium channel blocker, or both. Edaravone (Simcere Pharmaceutical Group, Nanjing, Jiangsu, China), an oxygen free radical scavenger, was also used intravenously for 3 days. Brain CT immediately after the operation was performed to rule out intracranial hemorrhage. Patients were given 5000 IU Fragmin (Vetter Pharma-Ferrtigung GmbH, Germany) every 12 hours subcutaneously for 3 days and monitored until discharge. Dual or triple (in cases relatively resistant to aspirin or clopidogrel) antiplatelet agents were administered for 3 months, and then a single agent for life.

Outcome measures

Primary efficacy outcome was technical success of recanalization with Thrombolysis in Myocardial Infarction (TIMI) 3 on catheter angiography at the end of the final procedure, assessed by endovascular neurosurgeons. Primary safety outcome was any stroke or death within 30 days, and secondary efficacy outcome was any stroke or death within 30 days plus an ipsilateral ischemic stroke after 30 days, both of which were independently evaluated by neurologists, who assessed daily during hospitalization, and followed up in clinic or by telephone after hospital discharge. Stroke was defined as a focal neurologic deficit persisting longer than 24 hours. Recanalization durability was assessed by reocclusion on follow-up CTA or DSA.

Statistical analysis

All continuous variables were expressed as mean±SD or median with IQR each for normal or skewed distribution data. Categorical variables were expressed as numbers and percentages. A χ^2 test was used to compare the recanalization rates after initial ET or CEA and hybrid surgeries, and between the ICAO classifications. The cumulative probability of secondary efficacy end points over time was estimated by the product-limit method. Data for patients lost to follow-up were censored on the last contact date. A p value <0.05 was considered to be statistically significant.

RESULTS

Baseline characteristics

Between January 2014 and October 2015, 42 consecutive patients (36 male and six female) were enrolled (figure 1A, table 1). Their average age was 60.7±11 years. Stroke as the last qualifying event occurred in 32 patients, and TIA in 10. The median duration between diagnosis of occlusion and procedure was 56 days (IQR, 30–144 days) for all patients, 50 days (IQR, 17–71 days) for type A, 62 days (IQR, 30–109 days) for type B, 61.5 days (IQR, 22.5–156.75 days) type C, and 49.5 days (IQR, 31.5–297.75 days) for type D. The median baseline National Institutes of Health Scale score was 0 (IQR, 0–2). Nine patients had concomitant ≥70% stenosis of a vertebral artery ostium or the contralateral ICA, which was stented before their ICAO procedures. Three patients had contralateral asymptomatic ICA occlusion, which was not managed surgically. All patients had at least one primary collateral pathway which supplied the ipsilateral MCA trunk, including 50% of patients with one pathway (AComA in nine patients, PComA in 6, and OAO in 6), 45.2% with two pathways (AComA and OAO in 10 patients, PComA and OAO in 5, and AComA and PComA in 4), and 4.8% with three pathways (AComA, PComA and OAO in two patients). As a collateral donor, AComA was found in 59.5% patients, OAO in 54.8%, and PComA in 40.5%. Of the 42 target ICAOs, three were classified as type A, 15 as type B, eight as type C, and 16 as type D occlusions.

Primary efficacy outcome and procedural data

Technical success was finally achieved in 35 patients (figure 1 and table 2). In detail, the initial ET procedure revascularized 12 of 15 occlusions (3 type A, 6 of 9 type B, and 3 type C); the initial CEA recanalized 3 of 27 occlusions (3 of 6 type B, 0 of 5 type C, and 0 of 16 type D); the CEA after ET failure revascularized the three remaining type B occlusions, and the ET after CEA failure (figure 2) recanalized 17 of 24 occlusions (3 of 3 type B, 3 of 5 type C, and 11 of 16 type D). The success rate of 83.3% (35/42) at the end of the final procedure was significantly higher than 35.7% (15/42, $p<0.001$) from the initial ET or CEA alone. Furthermore, the success rate, in descending order, was 100% (18/18) for type A and B occlusions, 75% (6/8) for type C, and 69% (11/16) for type D ($p=0.017$). Postoperative hospitalization length of stay was 7.6±4.0 days. Before discharge, the 35 patients with TIMI 3 recanalization had a CTA/CTP study, which showed a patent target ICA with improved ipsilateral brain perfusion.

Clinical outcome

During 10.5±5.2 months' follow-up, 2 (4.8%) secondary efficacy outcome events without mortality occurred. One patient (case 9) had a minor embolic stroke at day 2 (2.4% of primary safety outcome). The other patient (case 15) had a minor ipsilateral ischemic stroke on day 151. The cumulative probability of secondary efficacy outcome events was 2.4% (95% CI 0% to 7.0%) at 1 and 3 months, and 5.1% (95% CI 0% to 12.0%) at 6 months and 1 year. Additionally, one patient (case 1) had a non-fatal acute myocardial infarction on day 3; two patients (case 28 and case 9) experienced TIAs on days 102 and 407, respectively; and one patient (case 13) had gastrointestinal tract bleeding on day 43.

Durability

Follow-up CTA or DSA was performed at 7.7±4.2 months in 31 patients. ICA reocclusion was seen in three patients (9.7%), including two which were symptomatic (cases 15 and 28).

DISCUSSION

This study showed the advantage of an HOR, in which all patients with symptomatic chronic ICAO were managed with CEA, ET, or both, as needed in a one-stage procedure. To our knowledge, this is the largest prospective cohort study on Multimodality In situ Recanalization in Hybrid Operating Room (MIRHOR) for symptomatic chronic ICAO with ipsilateral MCA patency so far. Our results show that the MIRHOR at the same session significantly improves technical success of TIMI 3 recanalization, with low periprocedural complications and favorable clinical outcomes.

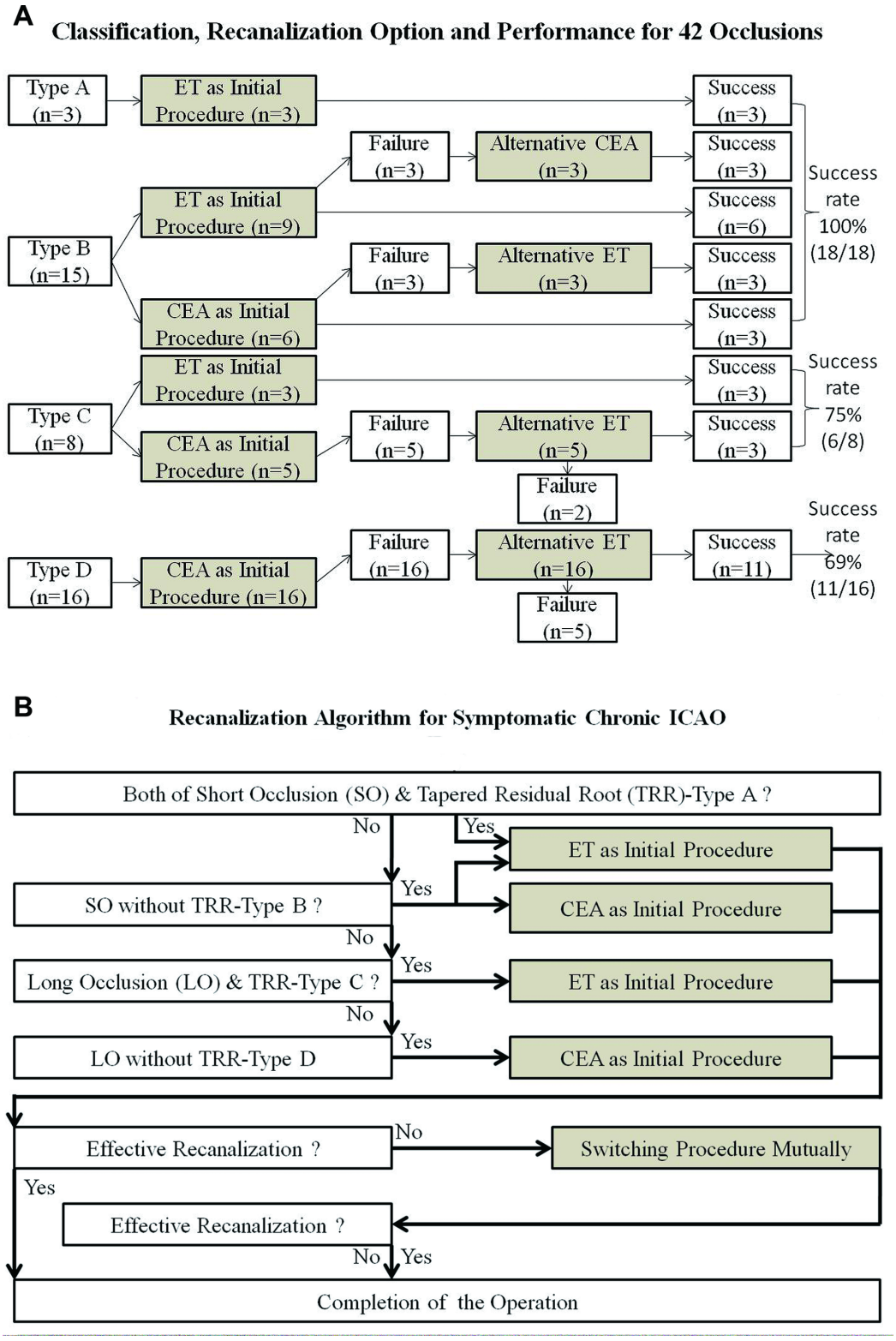

Figure 1 Recanalization of chronic internal carotid artery occlusions (ICAOs) and revised revascularization algorithm. (1-A) Symptomatic chronic ICAOs were classified as type A or B (short occlusion with or without tapered residual root [TRR]), and C or D (long occlusion with or without TRR). Initial endovascular therapy (ET) opened 12 of 15 occlusions (3 type A, 6 of 9 type B and 3 type C occlusions). In contrast, initial carotid endarterectomy (CEA) recanalized only 3 of 27 cases (3 of 6 type B, 0 of 5 type C, and 0 of 16 type D occlusions). After ET failure, CEA revascularized all 3 type B occlusions. After CEA failure, ET opened 17 of 24 occlusions (3 type B, 3 of 5 type C, and 11 of 16 type D occlusions). The technical success rate of Thrombolysis in Myocardial Infarction 3 recanalization was 83.3% (35/42) at the procedural end, significantly higher than 35.7% (15/42; p<0.001) from the initial CEA or ET. The rate was 100% (18/18) for type A and B, 75% (6/8) for type C, and 69% (11/16) for type D occlusions (p=0.017). (1-B) We recommend initial endovascular therapy (ET) procedure for short occlusion (SO) with TRR (type A) and long occlusion (LO) with TRR (type C), initial carotid endarterectomy (CEA) or ET procedure for SO without TRR (type B), with alternative procedure as needed; and CEA before ET for LO with TRR (type D).

Table 1 Baseline characteristics of 42 patients with symptomatic chronic internal carotid artery occlusions*

No	Age*	Risk factors	Qualified events	Duration† (days)	Collaterals	Occlusion side/ classification‡	Other stenosis/ stenting
1	70s	CS, DM, HL, HT	TIA	834	AComA, OAO	L/B	LV1 70%/Yes
2	60s	CS, DM, HT	Stroke	147	AComA, OAO	R/B	
3	60s	CS	Stroke	16	OAO	L/B	
4	60s	HL	Stroke	1834	AComA, OAO	R/D	
5	50s	CS, DM	TIA	36	AComA, PComA	R/D	
6	60s	CS	Stroke	67	AComA, OAO	R/D	
7	70s	CS, HT	TIA	21	AComA, OAO	R/D	LV1 70%/Yes
8	50s	CS, HT	Stroke	369	AComA	R/D	
9	40s	HL, HT	TIA	25	PComA	L/D	RC1 70%/Yes
10	50s	CS, HT	Stroke	31	AComA	L/D	
11	60s	CS, DM, HL	Stroke	33	AComA, OAO	R/D	
12	50s	CS, DM, HT	TIA	80	OAO	R/C	
13	70s	HL	Stroke	44	AComA, OAO	R/B	
14	70s	HT	TIA	77	AComA	R/B	
15	50s	CS, HT	Stroke	524	PComA	R/B	LICA 100%/No
16	60s	HL	TIA	50	PComA, OAO	R/A	LC1 90%/Yes
17	60s	CS, DM, HT	TIA	398	AComA	R/D	
18	60s	DM, HT	TIA	66	AComA, OAO, PComA	R/B	LC1 70%/Yes
19	60s	CS, DM, HL	Stroke	63	PComA	R/D	
20	70s	CS, DM, HL, HT	Stroke	144	AComA, OAO	L/C	LV1 95%/Yes
21	50s	CS, HL, HT	Stroke	62	PComA, OAO	R/B	
22	70s	DM, HT	Stroke	46	AComA, OAO	R/B	
23	60s	CS, DM	Stroke	71	AComA	R/A	
24	40s		Stroke	36	AComA, PComA	L/C	
25	60s	CS, HT	Stroke	31	AComA, OAO, PComA	L/B	LV1 80%/Yes
26	40s	CS, HL, HT	Stroke	81	AComA	L/B	
27	70s	CS, DM, HT	TIA	147	AComA	R/D	
28	50s	CS, HL, HT	Stroke	109	AComA, PComA	R/B	
29	50s	DM, HT	Stroke	17	OAO	R/A	
30	60s	CS	Stroke	30	AComA	R/B	
31	60s	CS, HT	Stroke	35	AComA, PComA	R/D	LC1 75%/Yes
32	70s	CS, DM	Stroke	348	OAO	R/D	
33	40s		Stroke	43	AComA, OAO	R/C	
34	40s	CS, HT	Stroke	161	PComA	L/C	
35	50s	HT	Stroke	175	PComA	L/C	RICA 100%/No
36	40s		Stroke	16	PComA, OAO	R/C	
37	50s	DM, HT	Stroke	22	OAO	R/B	
38	80s	CS, HL, HT	Stroke	96	PComA, OAO	L/D	RC1 70%/Yes
39	50s	CS, HL, HT	Stroke	18	OAO	L/C	
40	50s	CS, HL	Stroke	35	AComA	L/D	
41	60s	DM, HL, HT	Stroke	21	PComA	R/B	
42	40s	CS, HL, HT	Stroke	16	PComA, OAO	R/D	LICA 100%/No

*AComA, anterior communicating artery; CS, cigarette smoking; DM, diabetes mellitus; F, female; HL, hyperlipidemia; HT, hypertension; ICAO, internal carotid artery occlusion; L, left; M, male; OAO, ipsilateral ophthalmic artery or other external carotid-ICA collaterals; PComA, posterior communicating artery; R, right; TIA, transient ischemic attack; V1, vertebral artery ostium

†Days from ICAO documentation to procedure.

‡Type A or B, short occlusion within 3/4 portion of the cervical ICA towards its origin, with tapered residual root (TRR), or without TRR or residual root; type C or D, long occlusion beyond the 3/4 portion of the cervical ICA, with TRR, or without TRR or residual root.

Table 2 Procedures of multimodality in situ recanalization and outcomes*

No.	Initial procedure/ recanalization	Alternative procedure/ recanalization	Recanalization on FA angiography/ recanalization after ET	Clinical FU (months) /event/mRS	Angiography FU (months)/ reocclusion
1	CEA/no	ET/yes	yes/ND	18/AMI on day 3/2	13/no
2	CEA/no	ET/yes	yes/ND	18/no/1	12/no
3	CEA/no	ET/yes	yes/ND	17/no/2	NA
4	CEA/no	ET/no	ND/ND	16/no/1	NA
5	CEA/no	ET/no	ND/ND	16/no/1	NA
6	CEA/no	ET/yes	yes/ND	16/no/2	9/no
7	CEA/no	ET/yes	no/yes†	16/no/1	10/no
8	CEA/no	ET/no	ND/ND	16/no/2	NA
9	CEA/no	ET/yes	no/yes†	16/minor stroke on day2, TIA on day407/2	15/no
10	CEA/no	ET/yes	yes/ND	16/no/1	15/no
11	CEA/no	ET/yes	no/yes†	16/no/1	11/no
12	CEA/no	ET/yes	yes/ND	15/no/1	NA
13	ET/no	CEA/yes	yes/ND	15/GIB on day43/1	15/no
14	ET/yes	ND/ND	ND/ND	15/no/1	9/no
15	ET/yes	ND/ND	ND/ND	15/minor stroke on day151/2	4/yes (CTA)
16	ET/yes	ND/ND	ND/ND	15/no/1	12/no
17	CEA/no	ET/no	ND/ND	13/no/1	NA
18	CEA/yes	ND/ND	yes/ND	12/no/0	12/no
19	CEA/no	ET/no	ND/ND	13/no/1	NA
20	CEA/no	ET/no	ND/ND	13/no/2	NA
21	ET/no	CEA/yes	yes/ND	14/no/1	12/no
22	ET/no	CEA/yes	yes/ND	12/no/1	12/no
23	ET/yes	ND/ND	ND/ND	12/no/2	12/no
24	ET/yes	ND/ND	ND/ND	12/no/0	NA
25	CEA/yes	ND/ND	yes/ND	11/no/1	12/no
26	ET/yes	ND/ND	ND/ND	11/no/1	13/no
27	CEA/no	ET/yes	yes/ND	9/no/1	12/no
28	ET/yes	ND/ND	ND/ND	9/TIA on day102/1	6/yes (DSA)
29	ET/yes	ND/ND	ND/ND	9/no/0	12/no
30	CEA/yes	ND/ND	yes/ND	7/no/0	16/no
31	CEA/no	ET/yes	yes/ND	7/no/1	12/no
32	CEA/no	ET/yes	yes/ND	6/no/2	5/yes (CTA)
33	CEA/no	ET/no	ND/ND	6/no/2	NA
34	CEA/no	ET/yes	yes/ND	5/no/1	12/no
35	ET/no	CEA/yes	yes/ND	5/no/1	12/no
36	ET/yes	ND/ND	ND/ND	5/no/1	12/no
37	ET/yes	ND/ND	ND/ND	5/no/1	12/no
38	CEA/no	ET/yes	no/yes†	4/no/1	14/no
39	ET/yes	ND/ND	ND/ND	4/no/1	12/no
40	CEA/yes	ND/ND	no/yes†	3/no/1	12/no
41	ET/yes	ND/ND	ND/ND	3/no/0	12/no
42	CEA/yes	ND/ND	no/yes†	1/no/0	6/no

*AMI, acute myocardial infarction; Angio, angiography; C1-C6, segments of internal carotid artery according to the Bouthillier's classification: C1 (cervical), C2 (petrous), C3 (lacerum), C4 (cavernous), C5 (clinoid), C6 (ophthalmic), and C7 (communicating); CEA, carotid endarterectomy; ET, endovascular therapy; FA, femoral artery; ND, not done; FU, follow-up; GIB, gastrointestinal tract bleeding; ICA, internal carotid artery; mRS, modified Rankin Scale; NA, not available; TIA, transient ischemic attack.
†Six patients underwent a Wallstent (Boston Scientific, Natick, Massachusetts, USA) deployment across the closed ICA arteriotomy with no event due to dissection near the arteriotomy found by angiography via the femoral artery.

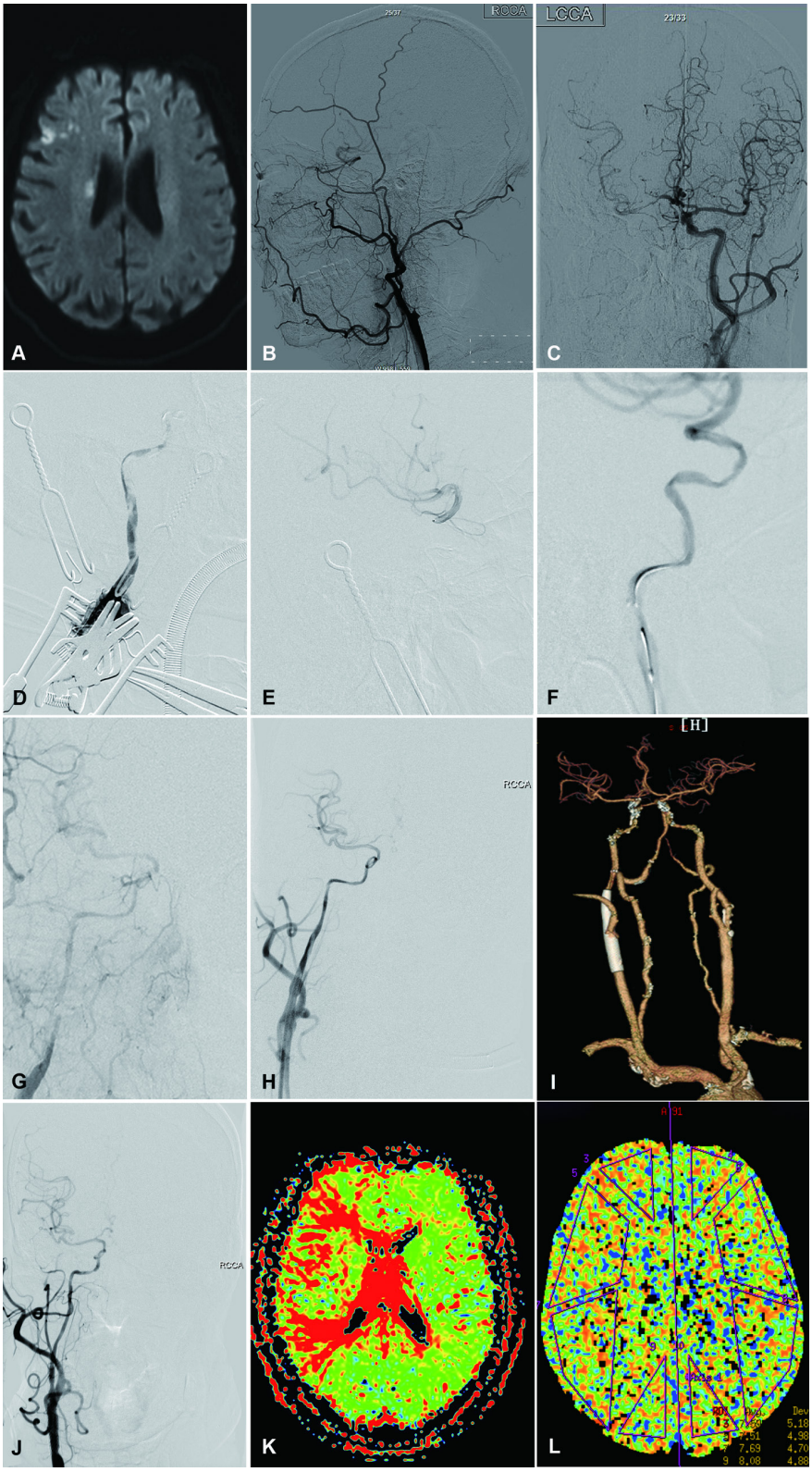

Figure 2 Case example. Case 11 with paroxysmal left-sided limb weakness and dysphasia underwent hybrid procedures for a symptomatic chronic internal carotid artery occlusion (ICAO). Diffusion-weighted imaging showed new infarcts in the right hemisphere (A). Preoperative angiography confirmed right ICAO, with ophthalmic artery collateral (B) and anterior communicating artery collateral (C). Angiography through the carotid sheath after carotid endarterectomy showed C4 occlusion with C1 and C2 dissection. After the microcatheter was placed in C6 (E), three Enterprise stents (two 4.5×37 mm and one 4.5×28 mm) were implanted in tandem from C6 to distal C1 across the lesion with Thrombolysis in Myocardial Infarction 3 recanalization (F). Angiography via a femoral approach after closing the internal carotid artery (ICA) arteriotomy showed a C1 dissection (G), which was reconstructed by implantation of a 9×50 mm Wallstent (H). The ICA remained patent on CT angiography at 6 days (I) and angiography at 11 months after the procedure (J). Mean transit time on preoperative perfusion-weighted imaging was prolonged in the right hemisphere (K) and normalized on postoperative CT perfusion (L).

In this cohort, a TIMI 3 recanalization was finally achieved in 83.3% patients, which was significantly higher than 35.7% from initial CEA or ET alone, with a 2.4% periprocedural stroke rate and no death. The technical success rate was much higher than the 34% after CEA alone reported by Paty *et al*,[2] and 61.6% after ET alone by Chen *et al*,[3] with comparable rates of severe complications (1.1% to 4.3%).[2 3] The 30-day risk of stroke or death is also much lower than 14.4% (14/97) of the surgical arm, and similar to 2.0% (2/98) of the medical arm in the COSS trial.[1] In that study the much higher rate of periprocedural complications in the surgical arm than in the medical arm could be partially explained by stage 2 hemodynamic failure and vulnerability of the affected brain territory during temporary occlusion of the MCA during the bypass surgery.[6 7] In contrast, our MIRHOR does not require MCA occlusion and therefore has an advantage over EC-IC bypass. Of note, we also developed comprehensive medical management and multiple embolic prevention strategies for risk reduction. The former includes the use of thromboelastography-guided antiplatelet therapy to prevent acute thrombosis, intravenous infusion of nimodipine to prevent procedure-related vasospasm, and strict blood pressure control after the procedure to prevent hyperperfusion. The last of these is described in the 'Methods' section in detail. This management of combined standard and individualized medicine (Customized Medicine) in this study is essential to ensure the safety of MIRHOR.

This study showed a 5.1% (95% CI 0% to 12.0%) cumulative probability of any stroke and death within 30 days plus ischemic ipsilateral stroke beyond 30 days at 6 months and 1 year. The probability seems much lower than that of the COSS trial, which showed 21.0% (95% CI 12.8% to 29.2%) in the surgical arm and 22.7% (95% CI 13.9% to 31.6%) in the medical arm at 2 years, with more than 50% events occurring within 6 months.[1] The findings above demonstrate that MIRHOR may be optimal solution for symptomatic chronic ICAOs with ipsilateral MCA patency, implying that a randomized clinical trial should be performed to confirm its efficacy.

The reocclusion rate in this study was 9.7%, slightly higher than the 5.7% after ET for chronic ICAOs found by Lin *et al*.[8] This disparity may be partly because predilatation with a balloon before stent placement was not used in our patients. However, predilatation before stenting might increase the risk of embolic stroke events. Further study is needed to balance the durability and procedural safety of MIRHOR.

We also showed that the ICAO classification may predict the technical success of MIRHOR. The technical success was associated with ICAO classifications, which in descending order was achieved in 100% of type A and B occlusions (short ones with and without a TRR), 75% of type C or 69% of type D occlusions (long ones with or without TRR). Thus, a stratified randomization for each lesion classification should be considered in the design of future randomized clinical trials.

ET effectively recanalizes TRR occlusions, with success rates as high as 100% in our study (6/6; type A [3/3] and C [3/3])). ET is comparable to CEA for type B occlusions (66.7% [6/9] vs 66.7% [6/9]). The higher recanalization for A, B ,and C occlusions may be related to the use of the assembly of a Pilot microwire with a stiffer microwire tip than neurovascular microwires and Gateway balloon catheter with a tapered catheter tip, just as Cohen *et al* reported an improvement of procedural success by wire escalation to high tip stiffness guidewires.[9] CEA alone did not recanalize any long segmental occlusion. However, CEA followed by ET resulted in 100% (3/3) TICI 3 recanalization for type B occlusion, and 60% (3/5) recanalization for type C occlusions, and 68.8% (11/16) recanalization for type D occlusions. CEA improved the recanalization rate of subsequent ET possibly by removing a large volume of atherosclerotic plaque and creating access to the true lumens of long segmental occlusions. The hybrid procedures with CEA followed by ET appear to be the best option for type D occlusions, because it is very difficult to safely negotiate an assembly of microcatheter and microwire through long occlusions without TRR via the femoral artery. In contrast, it is not difficult to navigate the assembly into true lumen of type C occlusions via the femoral artery.[3] Based on these findings, we recommend initial ET for type A and C, initial CEA or ET for type B, with an alternative procedure as needed; and CEA before ET for type D occlusions (figure 1B).

Limitations

Our study has some limitations. First, our sample size was not sufficiently large to compare differences in the durability between ET, CEA, and ET after CEA for each type of ICAO. We are dealing with this limitation with additional cases and longer follow-up. Second, although the clinical efficacy end point events in this cohort seemed lower than in the medical arm of the COSS trial, we cannot prove the clinical efficacy of MIRHOR at the same session because our study was not a randomized controlled trial. Third, the preprocedural DSA, on which our individualized recanalization algorithm was based, may overestimate the ICA occlusion length. A more accurate imaging diagnostic tool may be further developed. Finally, this study did not consider new silent infarction (subclinical ischemic event) after the procedures, observed after stenting of carotid stenosis under proximal or distal embolic protection[10]; further study may be needed. Nevertheless, this pilot study shows that the MIRHOR is clinically feasible and safe for revascularization of chronic ICAOs, with favorable clinical outcome. Further studies are warranted to validate these findings.

CONCLUSION

The Multimodality In situ Recanalization in Hybrid Operating Room (MIRHOR) at the same session significantly improves technical success of recanalization for symptomatic chronic ICAOs with ipsilateral MCA patency, with low periprocedural complications, and favorable clinical outcomes. The ICAO classification appears valuable in predicting technical success and guiding individualized revascularization strategy.

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