Original Article

# Flow-augmentation STA-MCA bypass for acute and subacute ischemic stroke due to internal carotid artery occlusion and the role of advanced neuroimaging with hemodynamic and flow-measurement in the decision-making: preliminary data

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**Background:** A major clinical challenge is the adequate identification of patients with acute (<1 week) and subacute (1–6 weeks) ischemic stroke due to internal carotid artery (ICA) occlusion who could benefit from a surgical revascularization after a failure of endovascular and/or medical treatment. Recently, two novel quantitative imaging modalities have been introduced: (I) quantitative magnetic resonance angiography (qMRA) with non-invasive optimal vessel analysis (NOVA) for quantification of blood flow in major cerebral arteries (in mL/min), and (II) blood oxygenation level-dependent (BOLD) functional magnetic resonance imaging to assess cerebrovascular reactivity (CVR). The aim of this study is to present our cohort of patients who underwent surgical revascularization in the acute and subacute phase of ischemic stroke as well as to demonstrate the importance of hemodynamic and flow assessment for the decision-making regarding surgical revascularization in patients with acute and subacute stroke and ICA-occlusion.

**Methods:** Symptomatic patients with acute and subacute ischemic stroke because of persistent ICA-occlusion despite optimal medical/endovascular recanalization therapy who were treated at the Neuroscience Clinical Center of the University Hospital Zurich underwent both BOLD-CVR and qMRA-NOVA to study the hemodynamic and collateral vessel status. Patients selected for surgical revascularization according to our previously published flowchart were included in this prospective cohort study. Repeated NOVA and BOLD-CVR investigations were done after bypass surgery as follow up as well as clinical follow up. Continuous BOLD-CVR and qMRA-NOVA variables were compared using paired Student *t*-test.

**Results:** Between May 2019 and September 2022, superficial temporal artery-middle cerebral artery (STA-MCA) bypass surgery was performed in 12 patients with acute and subacute stroke because of ICA-occlusion despite of optimal endovascular and/or medical treatment prior to the surgery. Impaired BOLD-CVR in the occluded vascular territory [MCA territory: ipsilateral *vs.* contralateral: −0.03±0.07 *vs.*

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0.11±0.07 %BOLD/mmHg$CO_2$, P<0.001] as well as reduced hemispheric flow with qMRA-NOVA (ipsilateral *vs.* contralateral: 228.00±54.62 *vs.* 384.50±70.99 mL/min, P=0.01) were measured indicating insufficient collateralization. Post-operative qMRA-NOVA showed improved hemispheric flow (via bypass) (pre-bypass *vs.* post-bypass: 236.60±76.45 *vs.* 334.20±131.33 mL/min, P=0.02) and the 3-month-follow-up with BOLD-CVR showed improved cerebral hemodynamics (MCA territory: pre-bypass *vs.* post-bypass: −0.01±0.05 *vs.* 0.06±0.03 %BOLD/mmHg$CO_2$, P=0.02) in all patients studied.

**Conclusions:** Quantitative assessment with BOLD-CVR and qMRA-NOVA allows us to evaluate the pre- and post-operative cerebral hemodynamics and collateral vessel status in patients with acute/subacute stroke due to ICA occlusion who may benefit from surgical revascularization after failure of endovascular/medical treatment.

**Keywords:** Ischemic stroke; internal carotid artery occlusion (ICA occlusion); superficial temporal artery-middle cerebral artery bypass (STA-MCA bypass); hemodynamics; quantitative flow

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## Introduction

Symptomatic patients with ischemic stroke due to internal carotid artery (ICA) occlusion often present with compromised brain hemodynamic status involving substantially larger parts of the affected vascular territory than the ischemic core itself (1-3). Despite the fact that the "Extracranial-Intracranial" (EC-IC) Bypass Study Group and the "Carotid Occlusion Surgery Study" (COSS) failed to demonstrate a benefit of bypass in comparison to medical therapy (4,5), several studies showed a significant improvement in hemodynamic parameters after superficial temporal artery-middle cerebral artery (STA-MCA) bypass surgery was performed in carefully selected patients (6-9) and even a reduction in stroke recurrence (6). Analysis showed that the failure of the COSS trial (5) to show a benefit regarding ipsilateral 2-year stroke recurrence in patients undergoing cerebral bypass revascularization was likely caused by a failure of the semiquantitative, hemispheric oxygen extraction fraction (OEF) ratio method used in the trial than by the selection of the patients for bypass based on hemodynamic compromise (10). Therefore, alternative and especially quantitative imaging techniques are needed to assess hemodynamic status in patients with ischemic stroke due to ICA occlusion.

Furthermore, patients with acute stroke have been excluded from the above-mentioned trials. In patients with acute stroke and ICA occlusion, surgical flow augmentation to penumbral tissue by an STA-MCA bypass has been reported successful in limited case series previously (11). A major clinical challenge is an adequate identification of these individuals. Recently, we published a flowchart for the selection of patients with acute stroke due to large vessel occlusion who might benefit from an urgent revascularization with STA-MCA bypass (12).

At our institution, two novel advanced magnetic resonance imaging (MRI) techniques have been introduced in the last years to evaluate the status of the cerebral hemodynamics and collateralization: (I) blood oxygenation level-dependent (BOLD) functional magnetic resonance imaging (fMRI) cerebrovascular reactivity (CVR) with a standardized $CO_2$ vasodilatory challenge to quantitatively evaluate the CVR capacity on voxel-by-voxel basis (13); and (II) non-invasive optimal vessel analysis (NOVA) quantitative magnetic resonance angiography (qMRA) to measure the volume flow rate (VFR) in mL/min in cerebral vessels and assess the cerebral collateral status and pathways (14).

With this study, our aims are: (I) to present our cohort of patients with ICA occlusion who underwent surgical revascularization in the acute and subacute phase of ischemic stroke; (II) to report on the utility of hemodynamic status and flow analysis for selecting which patients with acute and subacute stroke due to persistent ICA occlusion may profit from a revascularization via STA-MCA bypass; (III) to document the changes in cerebral hemodynamics and flow/collateral status in the patients after STA-MCA bypass surgery. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-23-876/rc).

 

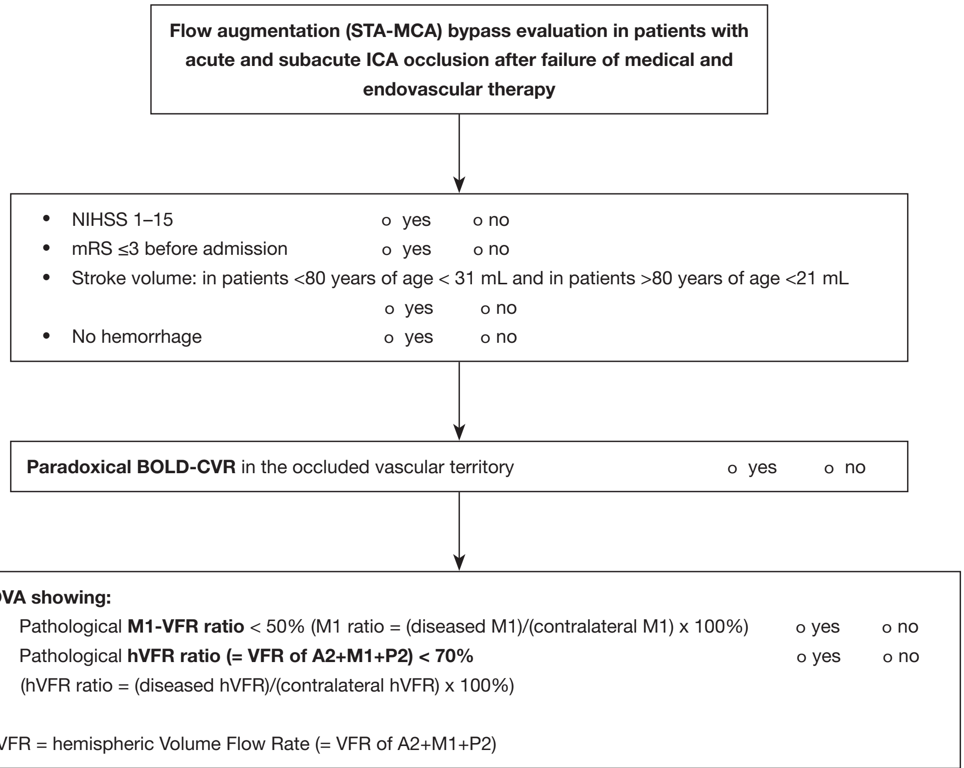


**Figure 1** The figure presents our urgent bypass flowchart [modified and reprinted with permission by Sebök *et al.* (12)] used to select patients for surgical revascularization with an STA-MCA bypass according to their clinical status and results of multimodal neuroimaging. A2, second segment of the anterior cerebral artery; CBF, cerebral blood flow; BOLD-CVR, blood oxygenation level-dependent cerebrovascular reactivity; hVFR, hemispheric volume flow rate; ICA, internal cerebral artery; i.v., intravenous; mRS, modified Rankin Scale; M1, first segment of the middle cerebral artery; M1-VFR, volume flow rate of the first segment of middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; NOVA, non-invasive optimal vessel analysis; P2, second segment of the posterior cerebral artery; STA-MCA, superficial temporal artery-middle cerebral artery.

## Methods

### *Patient inclusion*

This prospective cohort study was approved by the Cantonal Ethics Committee of the Canton Zurich, Switzerland (No. KEK 2020-02314) and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments. All the subjects signed an informed consent form before they underwent a BOLD-CVR study. The data that support the findings of this study are available upon reasonable request from the corresponding author (Dr. Martina Sebök).

From an ongoing prospective stroke database, all subjects with symptomatic ischemic stroke due to ICA occlusion in an acute (<1 week) or subacute (1–6 weeks) stage, who underwent BOLD-CVR and qMRA-NOVA imaging at the Neuroscience Clinical Center of the University Hospital Zurich, were extracted. Excluded from the study were all patients with symptomatic ischemic stroke due to chronic ICA occlusion, patients with contraindications for MRI or intolerance for the soft plastic mask or for the applied $CO_2$ stimulus during the BOLD-CVR examination.

According to our previously published bypass flowchart (*Figure 1*) (12) and results of the qMRA-NOVA and BOLD-CVR imaging, the patients who met the criteria for a surgical revascularization, underwent surgical treatment with a flow-augmentation STA-MCA bypass. Those patients were included in this study. All but two received qMRA-NOVA post-operatively before discharge. Six out of 12 received a BOLD-CVR neuroimaging by 3 months follow-up.

### Advanced MRI

All MRI data were collected on a 3 Tesla Skyra VD13 system according to previously published protocol with a three dimensional (3D) T1-weighted magnetization prepared rapid acquisition gradient echo (MP RAGE) image acquired with the same orientation as the BOLD fMRI scans for overlay purposes to acquire structural information of the whole brain (15). Furthermore, a 3D time of flight (TOF) angiography, and 2D phase contrast imaging using the 3D coordinates determined by NOVA were performed. According to standard of clinical care, patients with acute/subacute stroke also receive diffusion-weighted imaging (DWI), susceptibility-weighted imaging (SWI) and magnetic resonance perfusion (MRP) sequences (12).

### BOLD-CVR

To quantitatively assess the CVR of the whole brain, BOLD can be combined with a vasodilatory $CO_2$ stimulus and the resulting BOLD-CVR can be used as a surrogate marker of true CVR (16). The application of a precise $CO_2$ stimulus was achieved with a computer-controlled gas blender with prospective gas targeting algorithms (RespirActTM) during the BOLD-Sequence (16). The controlled $CO_2$ stimulus is administered to patients during the BOLD-CVR study in accordance with previously published detailed protocol (17,18). The protocol for the analysis of raw CVR data were previously published (15,19). The BOLD-CVR value is quantitatively assessed for the whole brain, for the grey and white matter and for the ipsilateral and contralateral hemisphere. According to our published urgent bypass flowchart (12), patients exhibiting paradoxical (= negative) CVR in at least half of the affected ipsilateral vascular territory, which indicates exhausted CVR, also known as steal phenomenon (20,21), are candidates for a revascularization with a STA-MCA bypass.

### Analysis of the MCA territory

By using a vascular atlas on the normalized CVR maps, quantitative BOLD-CVR values of the MCA territory of the ipsilateral and contralateral hemispheres were calculated using predefined brain regions listed in the standard N30R83 atlas by Hammers *et al.* (22) and Kuhn *et al.* (23).

### NOVA qMRA to assess quantitative flow

The blood flow quantification technique was completed by NOVA qMRA and has been achieved with commercially available software (NOVA, VasSol, Inc., Chicago, IL, USA) (24,25) according to our previously published NOVA protocol in acute stroke patients (12). In summary, for the quantitative measurement of the hemispheric perfusion and collateral pathways, the VFRs of the second segment of the anterior cerebral artery (A2), first segment of the MCA (M1) and second segment of the posterior cerebral artery (P2) are taken and the hemispheric volume flow rate (hVFR) is calculated as VFR of "*A2+M1+P2*".

To define the pathological flow ratios, we used the following formulas that were previously published (12):

$$\text{M1-VFR ratio} = \frac{\text{diseased M1}}{\text{contralateral M1}} \times 100\% \qquad [1]$$

and

$$\text{hVFR ratio} = \frac{\text{diseased hVFR}}{\text{contralateral hVFR}} \times 100\% \qquad [2]$$

where hVFR is determined as total of VFR of "*A2+M1+P2*".

According to our published urgent bypass flowchart, collateralization is considered insufficient if the NOVA-qMRA ratios show: a M1-VFR ratio <50% and a hVFR ratio <70%, both considered pathological (12).

According to our previously published bypass flowchart and focusing on the hemodynamic imaging with BOLD-CVR and quantitative flow measurement with qMRA-NOVA, the indication for a surgical revascularization with a STA-MCA bypass was given in patients presenting with paradoxical BOLD-CVR (= steal phenomenon) in at least half of the occluded vascular territory, a M1-VFR ratio <50% and a hVFR ratio <70%, both considered pathological.

### Follow-up advanced neuroimaging after surgical revascularization

Intraoperatively, we assessed bypass flow by employing a flexible perivascular transit-time flowprobe (Charbel MicroFlowprobe; Transonic Systems, Inc., Ithaca, NY, USA).

Patients receive a qMRA-NOVA post-operatively before discharge (to quantify the bypass flow and to study the collateral pathways). In the post-bypass qMRA-NOVA investigations the hVFR of the ipsilateral side also includes the bypass flow values and is determined as the total of VFR of A2 + M1 + P2 + the bypass. Three months post-op, patients were followed-up with BOLD-CVR to evaluate

**Table 1** Relevant clinical and baseline characteristics

| Characteristics | Total cohort (n=12) |
|---|---|
| Age, years (mean ± SD) | 63.3±8.5 |
| Sex (male), n (%) | 11 (91.7) |
| Smoking, n (%) | 10 (83.3) |
| Hypertension, n (%) | 8 (66.7) |
| Hypercholesterolemia, n (%) | 12 (100.0) |
| Diabetes, n (%) | 2 (16.7) |
| Previous ischemic event (infarction, TIA), n (%) | 3 (25.0) |
| mRS, median [IQR] | 2 [3] |
| NIHSS, median [IQR] | 4 [5] |

SD, standard deviation; TIA, transient ischemic attack; mRS, modified Rankin Scale; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale.

changes in cerebral hemodynamics.

### *Statistical analysis*

The statistical analysis was performed using SPSS Statistics 26. All continuous variables with a normal distribution are provided as mean ± SD. Categorical ordinal variables are displayed as median [interquartile range (IQR)], whereas dichotomous variables are presented as frequency (%). Continuous BOLD-CVR and qMRA-NOVA variables between the ipsilateral and contralateral hemisphere as well as BOLD-CVR and qMRA-NOVA variables before and after surgical revascularization were compared using paired Student *t*-test, where two-sided P value <0.05 was considered statistically significant.

## Results

### *Study population characteristics*

Between May 2019 and September 2022, 12 patients with acute (n=3) or subacute (n=9) ischemic stroke due to persistent ICA occlusion despite optimal medical/endovascular treatment received flow-augmentation STA-MCA bypass surgery. The relevant clinical and baseline characteristics of 12 included patients are presented in *Table 1*. Further data are reported in Table S1.

Due to limited access to MRI during the COVID pandemic, in two out of 12 patients no pre-operative BOLD-CVR investigation was performed. Ten out of 12 patients received a qMRA-NOVA follow-up before hospital discharge and 6 out of 10 patients underwent a BOLD-CVR at 3 months follow-up. In the majority of cases, we were not able to perform the follow-up investigations due to limited access to MRI during the COVID pandemic. One patient refused to undergo follow-up imaging because of claustrophobia during previous scans and one due to trouble with the mask or the applied $CO_2$ stimulus during the previous BOLD-CVR scan.

Every surgical revascularization procedure was completed within 14 days of the stroke event. After successful revascularization via bypass, post-operatively all the bypass were patent and none of patients suffered a recurrent ischemic stroke. The patients showed improvement of clinical status with pre-bypass modified Rankin Scale (mRS) score of 2 [3] to post-bypass mRS of 1 [2] as well as improvement in the NIHSS score {pre-bypass *vs.* post-bypass: 4 [5] *vs.* 2 [4]}. All of our patients were receiving antiplatelet therapy with aspirin, and none of them experienced any early hemorrhagic complications.

### *BOLD-CVR and quantitative flow in patients with acute and subacute stroke before surgical revascularization*

*Table 2* shows the BOLD-CVR and qMRA-NOVA before surgical revascularization. A significant difference was seen between the BOLD-CVR values of the ipsilateral and contralateral hemisphere (P=0.002) as well as between BOLD-CVR values of the ipsilateral and contralateral MCA-territory (P<0.001) (*Table 2*).

Similarly, a significant difference was detected in the qMRA-NOVA between the ipsilateral and contralateral M1-VFR (and hVFR). There was a significantly lower A2-VFR on the ipsilateral side compared to the contralateral side, whereas no significant difference was seen in the VFRs in the P2 segments (*Table 2*).

### *Changes in BOLD-CVR and quantitative flow after surgical revascularization*

After STA-MCA bypass an improvement of the CVR was seen with significant improvement of whole brain BOLD-CVR values, BOLD-CVR values of the ipsilateral hemisphere as well as the ipsilateral MCA-territory (*Table 3*).

When comparing pre- and post-bypass qMRA-NOVA values (*Table 4*), a significant improvement was seen in the hVFR of the ipsilateral hemisphere as well as through that in the hVFR-ratio after a revascularization via STA-MCA

**Table 2** BOLD-CVR and qMRA-NOVA quantitative flow values before revascularization

| Hemodynamic and flow measurements before revascularization | BOLD-CVR values (%BOLD/mmHg$CO_2$) |
|---|---|
| BOLD-CVR whole brain | 0.07±0.06 |
| BOLD-CVR ipsilateral hemisphere | 0.02±0.06 |
| BOLD-CVR contralateral hemisphere | 0.12±0.07 |
| BOLD-CVR ipsilateral MCA territory | −0.03±0.07 |
| BOLD-CVR contralateral MCA territory | 0.11±0.07 |
| M1-VFR ipsilateral hemisphere | 79.33±25.64 |
| M1-VFR contralateral hemisphere | 188.33±68.94 |
| A2-VFR ipsilateral hemisphere | 50.92±21.05 |
| A2-VFR contralateral hemisphere | 93.00±35.36 |
| P2-VFR ipsilateral hemisphere | 97.75±46.99 |
| P2-VFR contralateral hemisphere | 103.17±64.54 |
| Hemispheric VFR ipsilateral hemisphere | 228.00±54.62 |
| Hemispheric VFR contralateral hemisphere | 384.50±70.99 |
| M1-VFR ratio (%) | 42.93±4.84 |
| Hemispheric VFR ratio (%) | 59.33±8.71 |

All data are presented as mean value ± standard deviation. BOLD, blood oxygenation-level dependent; CVR, cerebrovascular reactivity; qMRA, quantitative magnetic resonance angiography; NOVA, Non-invasive Optimal Vessel Analysis; MCA, middle cerebral artery; M1, first segment of the middle cerebral artery; A2, second segment of the anterior cerebral artery; P2, second segment of the posterior cerebral artery; VFR, volume flow rate.

bypass. The improvement in the hVFR of the ipsilateral hemisphere is due to the added flow through the bypass. The mean STA-MCA bypass flow measured by qMRA-NOVA was 111.00±55.36 mL/min. In *Figure 2*, an illustrative case with pre- and post-bypass advanced neuroimaging data of one patient with STA-MCA bypass revascularization are presented.

## Discussion

Our data confirm the presence of impaired cerebral hemodynamic and collateral vessel status in symptomatic patients with acute and subacute stroke due to ICA occlusion. Moreover, we demonstrate the usefulness of advanced MRI modalities to quantify hemodynamic impairment and reduced flow (not sufficient collateral status) in acute/subacute stroke setting in case of symptomatic ICA occlusion where medical/endovascular therapy was not successful/indicated. Our data show a significant BOLD-CVR improvement in the affected MCA-territory and affected cerebral hemisphere as well as significant increase in the quantitative hemispheric flow to the ipsilateral hemisphere after surgical revascularization, due to very good flow in the bypass.

Improvement of CVR, very good flow in the bypass and good clinical outcome (no stroke recurrence) are indicators that surgical candidates have been properly selected and reinforces the role of the advanced neuroimaging via BOLD-CVR and NOVA in patients' selection.

The evidence regarding acute surgical revascularization

**Table 3** Comparison of pre- and post-bypass BOLD-CVR values in the subgroup of patients who underwent BOLD-CVR examination before and after revascularization

| Parameters | Hemodynamic measurements with BOLD-CVR (%BOLD/mmHg$CO_2$) | | P value |
|---|---|---|---|
| | Pre-bypass (n=6) | Post-bypass (n=6) | |
| BOLD-CVR whole brain | 0.10±0.03 | 0.13±0.05 | 0.04 |
| BOLD-CVR ipsilateral hemisphere | 0.04±0.05 | 0.11±0.03 | 0.004 |
| BOLD-CVR contralateral hemisphere | 0.15±0.05 | 0.14±0.08 | 0.58 |
| BOLD-CVR ipsilateral MCA territory | −0.01±0.05 | 0.06±0.03 | 0.02 |
| BOLD-CVR contralateral MCA territory | 0.13±0.05 | 0.14±0.04 | 0.67 |

All data are presented as mean value ± standard deviation. BOLD, blood oxygenation-level dependent; CVR, cerebrovascular reactivity; MCA, middle cerebral artery.

 

**Table 4** Comparison of pre- and post-bypass qMRA-NOVA values in the subgroup of patients who underwent qMRA-NOVA examination before and after revascularization

| Parameters | Flow measurements with qMRA-NOVA (mL/min) | | P value |
|---|---|---|---|
| | Pre-bypass (n=10) | Post-bypass (n=10) | |
| M1-VFR ipsilateral hemisphere | 78.80±28.53 | 67.10±40.13 | 0.38 |
| M1-VFR contralateral hemisphere | 186.10±72.24 | 174.50±74.23 | 0.11 |
| A2-VFR ipsilateral hemisphere | 42.60±17.82 | 45.90±22.70 | 0.70 |
| A2-VFR contralateral hemisphere | 90.30±32.72 | 90.10±35.11 | 0.99 |
| P2-VFR ipsilateral hemisphere | 115.20±60.91 | 115.40±55.70 | 0.99 |
| P2-VFR contralateral hemisphere | 99.90±69.42 | 96.90±72.81 | 0.65 |
| Hemispheric VFR ipsilateral hemisphere | 236.60±76.45 | 334.20±131.33 | 0.02 |
| Hemispheric VFR contralateral hemisphere | 376.30±80.70 | 361.50±105.24 | 0.43 |
| M1-VFR ratio (%) | 42.60±17.82 | 45.90±22.70 | 0.60 |
| Hemispheric VFR ratio (%) | 62.68±12.83 | 92.29±21.88 | 0.004 |

All data are presented as mean value ± standard deviation. qMRA, quantitative magnetic resonance angiography; NOVA, Non-invasive Optimal Vessel Analysis; M1, first segment of the middle cerebral artery; A2, second segment of the anterior cerebral artery; P2, second segment of the posterior cerebral artery; VFR, volume flow rate.

in patients with acute/subacute stroke due to large vessel occlusion is scarce and includes only case series or retrospective case-control cohort studies (26,27). This could be among other factors also due to limited possibility of hemodynamic and quantitative flow imaging in the acute phase of stroke in most clinical centers. At our institution, to appropriately identify the group of patients who could benefit of a revascularization after an acute/subacute ischemic stroke due to large vessel occlusion (LVO), advanced MRI-neuroimaging to non-invasively assess the cerebral hemodynamic and collateral vessel status plays a pivotal role. With our previous publication, we introduced our proposal for an urgent bypass decision protocol and introduced selection criteria regarding hemodynamic and flow assessment with novel BOLD-CVR and qMRA-NOVA imaging (12) that were used in the presented study-cohort.

### *Impaired brain hemodynamics and collateral flow status in patients with acute/subacute stroke due to ICA occlusion*

In patients who present with ischemic stroke, CVR imaging in patients who present with ischemic stroke exhibit the dynamic interplay between true ischemic lesion and the perfusion deficit (28). Patients with an exhausted CVR are at the high risk for a recurrent cerebral ischemic event (9,29,30). Therefore, an adequate identification of patients with hemodynamic failure is of huge importance, mainly for possible improvement of the collateral circulation. In fact, all studies have demonstrated that revascularization via a STA-MCA bypass significantly improves cerebral hemodynamics in a carefully selected patient cohort with ischemic stroke due to LVO (6,7,9). This underlines the importance of identifying patients with hemodynamic compromise who could benefit from surgical revascularization, even more in the acute/subacute phase for those patients where endovascular and medical treatment were not effective/indicated.

Our cohort includes 12 patients with acute/subacute ischemic stroke due to ICA occlusion who presented with significant hemodynamic impairment measured by BOLD fMRI CVR in the ipsilateral MCA territory with on average paradoxical BOLD-CVR values (= steal phenomenon) as well as in the ipsilateral hemisphere. Furthermore, by quantifying the flow in mL/min by qMRA-NOVA a significantly lower flow was measured in the affected M1 and A2 as well as in the whole hemisphere when compared to the contralateral unaffected hemisphere. Beside the importance of studying the hemodynamic status, this highlights the importance of investigating the collateral blood supply when evaluating a surgical revascularization since brain perfusion and hemodynamics are influenced by the collateral blood flow (14,31).

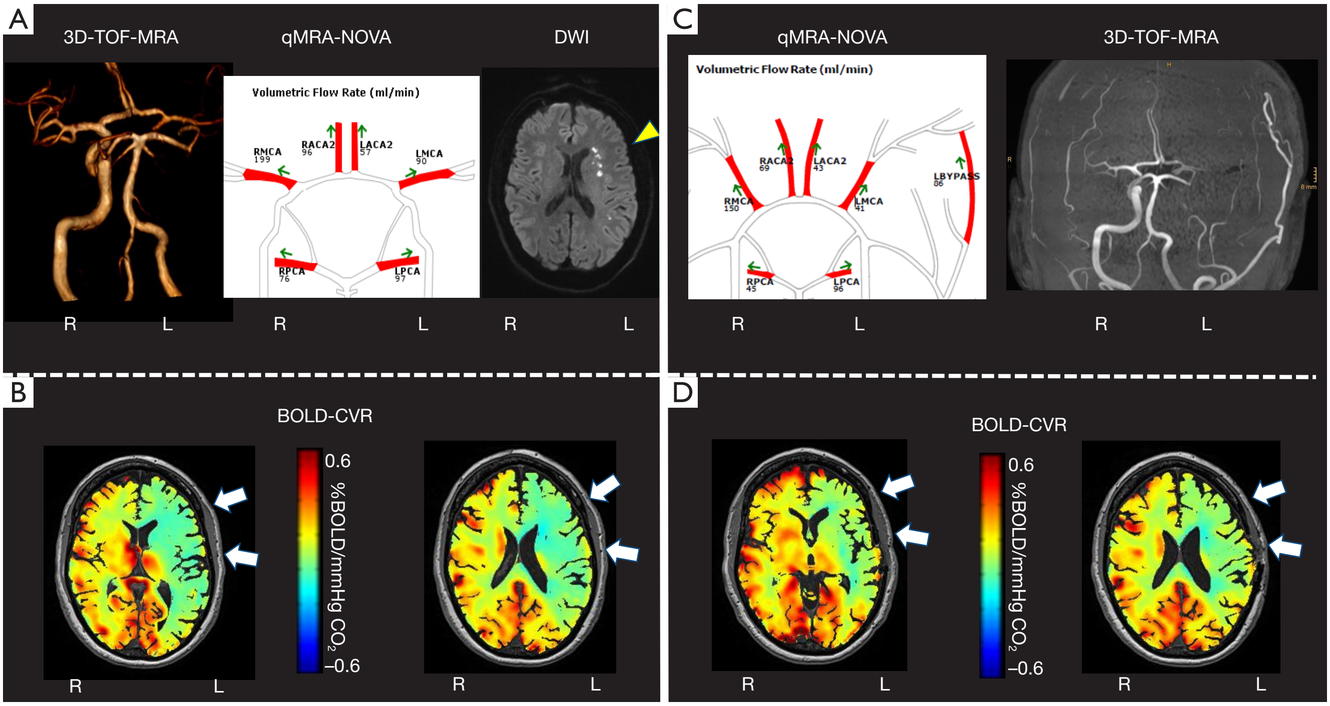


**Figure 2** This 61-year-old man presented with subacute ischemia in multiple locations (yellow triangle) in the left hemisphere (notably inner watershed zone as well as the territory of the middle cerebral artery) due to an ICA-occlusion (A). He experienced sensory troubles of the right 3rd and 4th finger 5 days before admission, which worsened the day before the admission with motor troubles of the right hand and dysphasia. At admission, the patient presented with a NIHSS score of 5/42 and a mRS score 3. On neurological examination, a discrete motor aphasia could be noted as well as a left facial palsy and a pronator drift as well as sensory troubles of the right arm. BOLD fMRI showed paradoxical CVR (= steal phenomenon) in the left ACA- and MCA-territory (B, white arrows). qMRA-NOVA showed a clear asymmetry in M1-VFR with a pathological ratio of 45.23% (<50%) as well as a pathological hVFR rate of 65.77% (<70%) (A). According to our previously published bypass flowchart, as well as clear hemodynamic compromise (i.e., paradoxical CVR in the left ACA- and MCA territory) there was an indication for surgical revascularization. The patient underwent STA-MCA flow augmentation bypass surgery on the left side. On the qMRA-NOVA performed after surgery, an improvement in hVFR to 100.76% could be seen (C). At the 3-month follow-up there were no neurological deficits (NIHSS score 0), Doppler confirmed the bypass was patent and significant CVR improvement in the left ACA- and MCA-territory were shown by BOLD fMRI (D). ACA, anterior cerebral artery; BOLD, blood oxygenation-level dependent; fMRI, functional magnetic resonance imaging; CVR, cerebrovascular reactivity; hVFR, hemispheric volume flow rate; ICA, internal carotid artery; MCA, middle cerebral artery; mRS, modified Rankin Scale; M1,first segment of the middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; NOVA, non-invasive optimal vessel analysis; qMRA, quantitative magnetic resonance angiography; STA, superficial temporal artery; VFR, volume flow rate; 3D-TOF-MRA, three dimensional time of flight magnetic resonance angiography; DWI, diffusion-weighted imaging.

qMRA-NOVA is regarded as a useful tool also in the management of anterior circulation stroke to study the status of collateral circulation. Whereas in the very early phase of the acute ischemic stroke, the collateral circulation plays an important role in maintaining the blood flow to the tissue at risk of progressing into ischemia, activated secondary collaterals additional to primary collaterals were related to a compromised cerebral hemodynamics in a number of investigations (32-35).

### *Impact of revascularization with flow-augmentation bypass on hemodynamic status and collateral blood flow*

Limited number of previous studies investigated the changes in cerebrovascular creativity after a successful surgical revascularization via STA-MCA bypass (20,36). Otsuka *et al.* (36) used N-isopropyl-[$^{123}$I] p-iodoamphetamine SPECT and showed that STA-MCA bypass was effective for improving CVR in included patients with hemodynamic failure stage 2. Another study (20) using the BOLD technique to evaluate CVR found a significant post-revascularization change only in the vascular territory of the bypass (ipsilateral MCA territory) and the degree of post-revascularization CVR improvement was correlated with the severity of hemodynamic impairment. Because a normal to near-normal CVR was reported in the non-operated hemisphere, there was little room for post-bypass CVR improvement (20). Similarly, our data demonstrate a clear CVR improvement with normalization of BOLD-CVR values in the affected MCA territory and affected hemisphere. The BOLD-CVR method offers several advantages over SPECT or PET techniques, including the absence of an external tracer or contrast agent, avoidance of radiation exposure, the ability to promptly cease the vascular stimulus ($CO_2$) when needed, and the capability to generate quantitative and reproducible CVR measurements (16,37).

Previous studies showed no advantage of EC-IC bypass over medical therapy in a group of patients with cerebral blood flow (CBF) >80% or CVR >10% (21,23). Currently, no BOLD-CVR threshold suggesting the optimal CVR threshold for surgical revascularization is available. Based on our clinical experience and daily observation, we defined significant (at least half of the vascular territory) paradoxical BOLD-CVR (= steal phenomenon) in the occluded vascular territory as an indication for revascularization (12). Further studies are needed to evaluate the proposed selection criteria for surgical revascularization, especially regarding the cut-offs for evaluation of hemodynamic status at brain parenchymal level as well as the status of collateral vessels.

Using qMRA-NOVA, the patency as well as the quantitative flow through the bypass can be noninvasively measured; furthermore, collateral status and pathways may be analyzed (38,39). Our previous study evaluated the reliability and usefulness of this noninvasive modality in a serial follow up of bypass function and concluded that qMRA might be an alternative to standard angiography for bypass graft-follow up (39). Beside the value in assessing bypass patency, our data underlines the importance of quantitative flow evaluation, especially on the hemispheric level. It is important to underline how the concept of defining the flow of the bypass according to the used graft (STA = low flow) could be nowadays considered obsolete. Intra-operative (using intraoperative flowmeter) (40) and post-operative quantification (using qMRA-NOVA) (39) of bypass flow shows how a STA can on average bring more than 100 mL/min flow, if needed. In fact, the flow in the bypass depends on the flow demand of the vascular territory. If the indication for revascularization is correct and the flow demand is high, the flow in the bypass can reach values over 100 mL/min. If even more flow is needed, the STA will grow with time and further flow improvement can be quantified with qMRA-NOVA.

### *Future directions*

Our findings highlight the value of advanced quantitative hemodynamic and flow studies in patients being candidates for surgical revascularization after failure of endovascular and/or medical therapy. The next step is a prospective study with an external and multicentric validation of presented selection criteria. Furthermore, the future aim should be a prospective randomized multicentric trial including patients who underwent hemodynamic and quantitative cerebral flow imaging after an ICA occlusion and unsuccessful medical/endovascular treatment that can be randomized into surgical and medical group and followed-up.

### *Limitations*

This is a single center study with a small sample size demonstrating our experience of surgical revascularization after an advanced multimodal MRI evaluation to assess cerebral hemodynamics and collateral vessel flow status. Further studies are needed to evaluate the proposed selection criteria for surgical revascularization.

## Conclusions

The advanced neuroimaging via BOLD-CVR and qMRA-NOVA showed impaired cerebral hemodynamics and insufficient collateral vessel status in symptomatic patients with acute/subacute stroke due to ICA occlusion. After flow-augmentation bypass surgery, the same neuroimaging showed a significant CVR improvement in the affected MCA-territory and affected cerebral hemisphere as well as significant increase in the quantitative hemispheric flow to the ipsilateral hemisphere. Further studies are needed to value the impact of both investigations in the decision making regarding surgical revascularization after failure of endovascular/medical treatment.

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## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-23-876/rc

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This prospective cohort study was approved by the Cantonal Ethics Committee of the Canton Zurich, Switzerland (No. KEK 2020-02314) and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments. All the subjects signed an informed consent form before they underwent a BOLD-CVR study.



## References

1. Pindzola RR, Sashin D, Nemoto EM, Kuwabara H, Wilson JW, Yonas H. Identifying regions of compromised hemodynamics in symptomatic carotid occlusion by cerebrovascular reactivity and oxygen extraction fraction. Neurol Res 2006;28:149-54.
2. Nemoto E, Lin R, Uchino K, Billigen J, Bircher N, Zaidi S, Reddy V, Jumma M, Kuwabara H, Sashin D, Boada F, Chang YF, Vora N, Hammer M, Jovin T, Massaro L, Zhang T, Matsumoto K, Yonas H. Comparison of Quantitative and Qualitative Oxygen Extraction Fraction (OEF) in Acute Stroke Patients with Large Vessel Occlusion. Adv Exp Med Biol 2018;1072:45-51.
3. Powers WJ. Cerebral hemodynamics in ischemic cerebrovascular disease. Ann Neurol 1991;29:231-40.
4. Failure of extracranial-intracranial arterial bypass to reduce the risk of ischemic stroke. Results of an international randomized trial. N Engl J Med 1985;313:1191-200.
5. Powers WJ, Clarke WR, Grubb RL Jr, Videen TO, Adams HP Jr, Derdeyn CP; . Extracranial-intracranial bypass surgery for stroke prevention in hemodynamic cerebral ischemia: the Carotid Occlusion Surgery Study randomized trial. JAMA 2011;306:1983-92.
6. Low SW, Teo K, Lwin S, Yeo LL, Paliwal PR, Ahmad A, Sinha AK, Teoh HL, Wong LY, Chong VF, Seet RC, Chan BP, Yeo TT, Chou N, Sharma VK. Improvement in cerebral hemodynamic parameters and outcomes after superficial temporal artery-middle cerebral artery bypass in patients with severe stenoocclusive disease of the intracranial internal carotid or middle cerebral arteries. J Neurosurg 2015;123:662-9.
7. Ishikawa T, Houkin K, Abe H, Isobe M, Kamiyama H. Cerebral haemodynamics and long-term prognosis after extracranial-intracranial bypass surgery. J Neurol Neurosurg Psychiatry 1995;59:625-8.
8. Klijn CJ, Kappelle LJ, van der Zwan A, van Gijn J, Tulleken CA. Excimer laser-assisted high-flow extracranial/intracranial bypass in patients with symptomatic carotid artery occlusion at high risk of recurrent cerebral ischemia: safety and long-term outcome. Stroke 2002;33:2451-8.
9. Schmiedek P, Piepgras A, Leinsinger G, Kirsch CM, Einhüpl K. Improvement of cerebrovascular reserve capacity by EC-IC arterial bypass surgery in patients with ICA occlusion and hemodynamic cerebral ischemia. J Neurosurg 1994;81:236-44.
10. Carlson AP, Yonas H, Chang YF, Nemoto EM. Failure of cerebral hemodynamic selection in general or of specific positron emission tomography methodology?: Carotid Occlusion Surgery Study (COSS). Stroke 2011;42:3637-9.
11. Burkhardt JK, Winklhofer S, Fierstra J, Wegener S, Esposito G, Luft A, Bozinov O, Regli L. Emergency Extracranial-Intracranial Bypass to Revascularize Salvageable Brain Tissue in Acute Ischemic Stroke

Patients. World Neurosurg 2018;109:e476-85.
12. Sebök M, Esposito G, Niftrik CHBV, Fierstra J, Schubert T, Wegener S, Held J, Kulcsár Z, Luft AR, Regli L. Flow augmentation STA-MCA bypass evaluation for patients with acute stroke and unilateral large vessel occlusion: a proposal for an urgent bypass flowchart. J Neurosurg 2022. [Epub ahead of print]. doi: 10.3171/2021.10.JNS21986.
13. Sebök M, van Niftrik CHB, Winklhofer S, Wegener S, Esposito G, Stippich C, Luft A, Regli L, Fierstra J. Mapping Cerebrovascular Reactivity Impairment in Patients With Symptomatic Unilateral Carotid Artery Disease. J Am Heart Assoc 2021;10:e020792.
14. Bae YJ, Jung C, Kim JH, Choi BS, Kim E. Quantitative Magnetic Resonance Angiography in Internal Carotid Artery Occlusion with Primary Collateral Pathway. J Stroke 2015;17:320-6.
15. van Niftrik CHB, Piccirelli M, Bozinov O, Pangalu A, Fisher JA, Valavanis A, Luft AR, Weller M, Regli L, Fierstra J. Iterative analysis of cerebrovascular reactivity dynamic response by temporal decomposition. Brain Behav 2017;7:e00705.
16. Slessarev M, Han J, Mardimae A, Prisman E, Preiss D, Volgyesi G, Ansel C, Duffin J, Fisher JA. Prospective targeting and control of end-tidal CO2 and O2 concentrations. J Physiol 2007;581:1207-19.
17. Sebök M, van Niftrik CHB, Piccirelli M, Bozinov O, Wegener S, Esposito G, Pangalu A, Valavanis A, Buck A, Luft AR, Regli L, Fierstra J. BOLD cerebrovascular reactivity as a novel marker for crossed cerebellar diaschisis. Neurology 2018;91:e1328-37.
18. Sebök M, van Niftrik CHB, Piccirelli M, Muscas G, Pangalu A, Wegener S, Stippich C, Regli L, Fierstra J. Crossed Cerebellar Diaschisis in Patients With Symptomatic Unilateral Anterior Circulation Stroke Is Associated With Hemodynamic Impairment in the Ipsilateral MCA Territory. J Magn Reson Imaging 2021;53:1190-7.
19. Sebök M, van Niftrik CHB, Wegener S, Luft A, Regli L, Fierstra J. Agreement of novel hemodynamic imaging parameters for the acute and chronic stages of ischemic stroke: a matched-pair cohort study. Neurosurg Focus 2021;51:E12.
20. Mandell DM, Han JS, Poublanc J, Crawley AP, Fierstra J, Tymianski M, Fisher JA, Mikulis DJ. Quantitative measurement of cerebrovascular reactivity by blood oxygen level-dependent MR imaging in patients with intracranial stenosis: preoperative cerebrovascular reactivity predicts the effect of extracranial-intracranial bypass surgery. AJNR Am J Neuroradiol 2011;32:721-7.
21. Fierstra J, van Niftrik C, Warnock G, Wegener S, Piccirelli M, Pangalu A, Esposito G, Valavanis A, Buck A, Luft A, Bozinov O, Regli L. Staging Hemodynamic Failure With Blood Oxygen-Level-Dependent Functional Magnetic Resonance Imaging Cerebrovascular Reactivity: A Comparison Versus Gold Standard ((15)O-)H(2)O-Positron Emission Tomography. Stroke 2018;49:621-9.
22. Hammers A, Allom R, Koepp MJ, Free SL, Myers R, Lemieux L, Mitchell TN, Brooks DJ, Duncan JS. Three-dimensional maximum probability atlas of the human brain, with particular reference to the temporal lobe. Hum Brain Mapp 2003;19:224-47.
23. Kuhn FP, Warnock G, Schweingruber T, Sommerauer M, Buck A, Khan N. Quantitative H2[(15)O]-PET in Pediatric Moyamoya Disease: Evaluating Perfusion before and after Cerebral Revascularization. J Stroke Cerebrovasc Dis 2015;24:965-71.
24. Calderon-Arnulphi M, Amin-Hanjani S, Alaraj A, Zhao M, Du X, Ruland S, Zhou XJ, Thulborn KR, Charbel FT. In vivo evaluation of quantitative MR angiography in a canine carotid artery stenosis model. AJNR Am J Neuroradiol 2011;32:1552-9.
25. Zhao M, Charbel FT, Alperin N, Loth F, Clark ME. Improved phase-contrast flow quantification by three-dimensional vessel localization. Magn Reson Imaging 2000;18:697-706.
26. Guida L, Sebök M, Wegener S, Fierstra J, van Niftrik B, Luft AR, Regli L, Esposito G. Flow-augmentation bypass in the treatment of acute ischemic stroke. J Neurosurg Sci 2021;65:269-76.
27. Esposito G, Sebök M, Amin-Hanjani S, Regli L. Cerebral Bypass Surgery: Level of Evidence and Grade of Recommendation. Acta Neurochir Suppl 2018;129:73-7.
28. Juttukonda MR, Donahue MJ. Neuroimaging of vascular reserve in patients with cerebrovascular diseases. Neuroimage 2019;187:192-208.
29. Yonas H, Smith HA, Durham SR, Pentheny SL, Johnson DW. Increased stroke risk predicted by compromised cerebral blood flow reactivity. J Neurosurg 1993;79:483-9.
30. Kleiser B, Widder B. Course of carotid artery occlusions with impaired cerebrovascular reactivity. Stroke 1992;23:171-4.
31. Ruland S, Ahmed A, Thomas K, Zhao M, Amin-Hanjani S, Du X, Charbel FT. Leptomeningeal collateral volume flow assessed by quantitative magnetic resonance angiography in large-vessel cerebrovascular disease. J Neuroimaging 2009;19:27-30.

 

32. Schneider J, Sick B, Luft AR, Wegener S. Ultrasound and Clinical Predictors of Recurrent Ischemia in Symptomatic Internal Carotid Artery Occlusion. Stroke 2015;46:3274-6.
33. Hofmeijer J, Klijn CJ, Kappelle LJ, Van Huffelen AC, Van Gijn J. Collateral circulation via the ophthalmic artery or leptomeningeal vessels is associated with impaired cerebral vasoreactivity in patients with symptomatic carotid artery occlusion. Cerebrovasc Dis 2002;14:22-6.
34. Hartkamp NS, Petersen ET, Chappell MA, Okell TW, Uyttenboogaart M, Zeebregts CJ, Bokkers RP. Relationship between haemodynamic impairment and collateral blood flow in carotid artery disease. J Cereb Blood Flow Metab 2018;38:2021-32.
35. Sebök M, Niftrik CHBV, Lohaus N, Esposito G, Amki ME, Winklhofer S, Wegener S, Regli L, Fierstra J. Leptomeningeal collateral activation indicates severely impaired cerebrovascular reserve capacity in patients with symptomatic unilateral carotid artery occlusion. J Cereb Blood Flow Metab 2021;41:3039-51.
36. Otsuka M, Kikkawa Y, Kamide T, Suzuki K, Shibata A, Ikeda T, Kurita H. Factors related to improvement of cerebrovascular reserve after superficial temporal artery to middle cerebral artery anastomosis for patients with atherosclerotic steno-occlusive disease. Acta Neurochir (Wien) 2019;161:799-805.
37. Spano VR, Mandell DM, Poublanc J, Sam K, Battisti-Charbonney A, Pucci O, Han JS, Crawley AP, Fisher JA, Mikulis DJ. CO2 blood oxygen level-dependent MR mapping of cerebrovascular reserve in a clinical population: safety, tolerability, and technical feasibility. Radiology 2013;266:592-8.
38. Zhu F, Qian Y, Xu B, Gu Y, Karunanithi K, Zhu W, Chen L, Mao Y, Morgan MK. Quantitative assessment of changes in hemodynamics of the internal carotid artery after bypass surgery for moyamoya disease. J Neurosurg 2018;129:677-83.
39. Amin-Hanjani S, Shin JH, Zhao M, Du X, Charbel FT. Evaluation of extracranial-intracranial bypass using quantitative magnetic resonance angiography. J Neurosurg 2007;106:291-8.
40. Amin-Hanjani S, Charbel FT. Flow-assisted surgical technique in cerebrovascular surgery. Surg Neurol 2007;68 Suppl 1:S4-11.


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**Table S1** Overview of clinical and quantitative imaging data for all included patients

| | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | Case 7 | Case 8 | Case 9 | Case 10 | Case 11 | Case 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Age (years), sex | 56, M | 78, F | 69, M | 66, M | 59, M | 69, M | 70, M | 61, M | 46, M | 57, M | 62, M | 58, M |
| Occluded vessel | L ICA | R ICA | R ICA | L ICA | L ICA | L ICA | L ICA | L ICA | R ICA | L ICA | R ICA | L ICA |
| Clinical presentation | R hemisyndrome, dysarthria | L hemisyndrome, L facial palsy | Dysarthria, L facial palsy | R hemisyndrome | R hemisyndrome, aphasia, dysarthria | R hemisyndrome, aphasia, dysarthria | R hemisyndrome | R hemisyndrome, aphasia | L hemisyndrome, speech trouble | R hemisyndrome | L hemisyndrome, dysarthria | R hemisyndrome, R facial palsy |
| Smoking | Yes | Yes | Yes | No | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes |
| Hypertension | No | Yes | Yes | Yes | No | Yes | No | Yes | Yes | No | Yes | Yes |
| Dyslipedemia | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Obesity (BMI >25 kg/m$^2$) | No | Yes | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes |
| Diabetes | No | Yes | No | No | No | No | No | No | No | No | No | Yes |
| Previous stroke | Yes | No | No | No | No | Yes | No | No | Yes | No | No | Yes |
| NIHSS score pre-bypass | 9 | 4 | 1 | 7 | 11 | 4 | 2 | 5 | 2 | 3 | 4 | 2 |
| mRS score pre-bypass | 4 | 1 | 1 | 4 | 4 | 4 | 1 | 3 | 1 | 2 | 2 | 2 |
| BOLD-CVR | | | | | | | | | | | | |
| Whole-brain pre-op | 0.09 | –0.06 | 0.11 | N/A | 0.04 | 0.14 | 0.02 | 0.11 | N/A | 0.05 | 0.09 | 0.07 |
| Affected hemisphere pre-op | 0.07 | –0.11 | 0.04 | N/A | 0.02 | 0.10 | –0.03 | 0.08 | N/A | –0.01 | 0.03 | –0.01 |
| Unaffected hemisphere pre-op | 0.12 | –0.01 | 0.17 | N/A | 0.07 | 0.16 | 0.07 | 0.23 | N/A | 0.07 | 0.17 | 0.12 |
| Affected MCA territory pre-op | –0.03 | –0.16 | –0.05 | N/A | -0.07 | 0.04 | –0.10 | 0.07 | N/A | –0.01 | 0.02 | –0.05 |
| Unaffected MCA territory pre-op | 0.09 | 0.02 | 0.14 | N/A | 0.06 | 0.18 | 0.06 | 0.20 | N/A | 0.06 | 0.17 | 0.12 |
| qMRA-NOVA | | | | | | | | | | | | |
| Affected M1-flow pre-op | 18 | 85 | 75 | 88 | 74 | 52 | 119 | 90 | 79 | 103 | 73 | 96 |
| Contralateral M1-flow pre-op | 38 | 195 | 163 | 179 | 178 | 158 | 327 | 199 | 175 | 272 | 162 | 214 |
| M1-ratio pre-op, % | 47.37 | 43.59 | 46.01 | 49.16 | 41.57 | 32.91 | 36.39 | 48.76 | 45.14 | 37.87 | 45.06 | 44.86 |
| Affected A2-flow pre-op | 22 | 65 | 78 | 34 | 73 | 89 | 36 | 57 | 46 | 40 | 37 | 34 |
| contralateral A2-flow pre-op | 33 | 57 | 138 | 134 | 68 | 61 | 76 | 96 | 107 | 147 | 98 | 101 |
| Affected P2-flow pre-op | 119 | 58 | 104 | 113 | 92 | 46 | 106 | 97 | 116 | 216 | 74 | 32 |
| Contralateral P2-flow pre-op | 291 | 97 | 68 | 67 | 141 | 65 | 94 | 76 | 89 | 127 | 60 | 63 |
| Affected hemispheric VFR pre-op | 159 | 208 | 257 | 235 | 239 | 187 | 261 | 244 | 241 | 359 | 184 | 162 |
| Contralateral hemispheric VFR pre-op | 362 | 349 | 369 | 380 | 387 | 284 | 497 | 371 | 371 | 546 | 320 | 378 |
| Hemispheric VFR-ratio pre-op, % | 43.92 | 59.60 | 69.65 | 61.84 | 61.76 | 65.85 | 52.52 | 65.77 | 64.96 | 65.75 | 57.50 | 42.86 |

A2, second segment of the anterior cerebral artery; BMI, body mass index; BOLD, blood oxygenation-level dependent; CVR, cerebrovascular reactivity; F, female; ICA, internal carotid artery; L, left; M, male; MCA, middle cerebral artery; M1, first segment of the middle cerebral artery; NOVA, non-invasive vessel analysis; P2, second segment of the posterior cerebral artery; qMRA, quantitative magnetic resonance angiography; R, right; VFR, volume flow rate

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