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Vloga kvantitativne hemodinamske magnetne resonance pri kirurški revaskularizaciji možganskega tkiva

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Cilj kirurške revaskularizacije možganskega tkiva je izboljšati možgansko perfuzijo pri bolnikih s cerebrovaskularno steno-okluzivno boleznijo, pri katerih so določene regije možganov slabo prekrvavljene. Najpogosteje izveden poseg, anastomoza med površinsko temporalno in srednjo možgansko arterijo (STA–MCA bypass), je indiciran pri moyamoya vaskulopatiji, pri izbranih primerih kronične steno-okluzivne bolezni in akutne ishemične možganske kapi s hemodinamsko prizadetostjo. Kvantitativna hemodinamska ocena ima ključno vlogo pri odločanju o kandidatih za poseg. Med sodobnimi neinvazivnimi metodami za oceno možganske hemodinamike izstopa BOLD-CVR (blood oxygenation-level dependent cerebrovascular reactivity), posebna oblika magnetnoresonančnega slikanja, ki omogoča zaznavo regij z zmanjšano vazodilatacijsko sposobnostjo in s tem identifikacijo hemodinamsko ogroženega možganskega tkiva. V tem članku so predstavljene aktualne indikacije in postopki odločanja pri izbiri bolnikov za kirurško revaskularizacijo možganov ter institucionalne izkušnje pri selekciji bolnikov na osnovi BOLD-CVR. Poudarjen je ključni pomen te metode za uspešno načrtovanje in izvedbo revaskularizacije, kar pomembno prispeva k optimizaciji kirurških in kliničnih izidov.

Znanstvena veda:
Medicina

Ključne besede:
steno-okluzivna bolezen,
STA-MCA bypas,
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THE ROLE OF QUANTITATIVE HEMODYNAMIC MAGNETIC RESONANCE IMAGING IN THE SURGICAL REVASCULARIZATION OF CEREBRAL TISSUE

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The goal of surgical revascularization of brain tissue is to improve cerebral perfusion in patients with cerebrovascular stenotic-occlusive disease, where certain regions of the brain are hypoperfused. The most commonly performed procedure, anastomosis between the superficial temporal artery and middle cerebral artery (STA–MCA bypass), is indicated in moyamoya vasculopathy, in selected cases of chronic stenotic-occlusive disease, and in acute ischemic stroke with hemodynamic impairment. Quantitative hemodynamic assessment plays a key role in selecting candidates for the procedure. Among modern non-invasive methods for assessing cerebral hemodynamics, blood oxygenation-level dependent cerebrovascular reactivity (BOLD-CVR) stands out. This special form of magnetic resonance imaging allows detection of regions with reduced vasodilatory capacity, thereby identifying hemodynamically endangered brain tissue. This article presents the current indications and decision-making processes in selecting patients for surgical revascularization of the brain, as well as institutional experiences in patient selection based on BOLD-CVR. The critical importance of this method for successful planning and execution of revascularization is emphasized, as it significantly contributes to optimizing surgical and clinical outcomes.

Scientific science:
Medicine

Keywords:
steno-occlusive disease, STA-MCA bypass, MRI, BOLD-CVR, hemodynamics.

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1 Introduction

Stenosis or occlusion of extra- or intracranial large arteries reduces perfusion of the affected cerebral hemisphere and can lead to impaired cerebrovascular reserve capacity (1). Flow-augmentation bypass aims to restore perfusion in brain regions affected by (chronic) hypoperfusion (2). This approach is a cornerstone in the treatment of moyamoya vasculopathy and remains a viable option for carefully selected patients with atherosclerotic steno-occlusive disease who continue to experience ischemic events despite optimal medical management (3). More recently, emergency bypass procedures has been explored in the context of acute ischemic stroke with a persistent penumbra(4).

The most commonly performed surgical revascularization technique is direct bypass using the superficial temporal artery to middle cerebral artery (STA–MCA) anastomosis, which provides an immediate increase in cerebral blood flow (5). A central challenge, however, lies in accurately identifying patients who will benefit from this intervention—particularly those in whom the procedure can reduce recurrent ischemic events while maintaining a low complication rate.

In this context, the blood oxygenation–level dependent cerebrovascular reactivity (BOLD-CVR) method has emerged as a valuable tool, offering reproducible and quantitative assessment of cerebrovascular reserve without the need for contrast agents or radiation exposure. BOLD-CVR imaging can be readily applied in patients with chronic steno-occlusive disease and even in the setting of acute ischemic stroke (6, 7).

In this article, I aim to outline the current indications for intracranial revascularization surgery and discuss patient-selection strategies informed by hemodynamic BOLD-CVR imaging, which has been a central focus of my doctoral research.

2 STA-MCA bypass

The STA–MCA bypass is a direct revascularization technique designed to augment blood flow to the distal MCA territory. The procedure was first introduced by M. G. Yasargil in Zurich in 1967, who performed an end-to-side anastomosis connecting a distal branch of the superficial temporal artery (STA) to a cortical branch of the middle cerebral artery near the Sylvian fissure. Following a frontotemporal scalp incision—carefully preserving the STA branches—the donor vessel is dissected from the undersurface of the scalp flap. A small craniotomy, typically positioned about 6 cm above the external auditory canal, is then created to expose the Sylvian fissure and distal MCA branches. Under microscopic visualization, an appropriate recipient vessel is selected, and an end-to-side anastomosis is completed using interrupted 10-0 sutures. At the conclusion of the procedure, the bone flap is replaced, with a small segment of the bone edge removed to provide a passageway for the STA graft into the intracranial space (6, 8).

3 Overview of evidence-based indications for intracranial revascularization surgery

Table 1. Level of evidence and grade of recommendation for cerebral bypass surgery

Pathology	Clinic	Indication for bypass	Level of evidence	Grade of recomme n-dation	Randomized clinical trial
Moyamoya vasculopathy	Hemorr-hagic	YES	1B	A	Yes
	Ischemic	YES	4	C	/
Atherosclerotic vessel occlsuion	COSS patients	NO	1A	A	Yes
	Non-COSS	YES	4	C	/
	Acute stroke	?	?	?	/

3.1 Moyamoya Vasculopathy

Moyamoya disease is characterized by progressive stenosis of the distal internal carotid arteries, resulting in ischemic or hemorrhagic events. In symptomatic patients with impaired cerebral hemodynamics, surgical revascularization remains the only effective treatment. Numerous observational studies have shown that bypass surgery reduces stroke recurrence and may prevent neurocognitive decline in both pediatric and adult populations. Direct, indirect, and combined bypass techniques are used in the management of Moyamoya disease (3, 8). Although no definitive consensus exists regarding the superiority of one technique over another, direct or combined bypass procedures are typically favored in adults, whereas indirect or combined approaches are more commonly used in children (3, 5).

There are no randomized clinical trials (RCTs) evaluating the efficacy of bypass surgery in preventing ischemic stroke or cognitive decline in patients with Moyamoya disease. Nevertheless, multiple observational studies strongly suggest a therapeutic benefit of revascularization (9, 10), particularly when compared with the natural disease course. Consequently, current practice—supported by observational data—routinely recommends surgical revascularization for both pediatric and adult patients with ischemic symptoms and impaired cerebrovascular hemodynamics (level of evidence 4; grade of recommendation C, Table 1)(3).

In contrast to ischemic Moyamoya disease, hemorrhagic Moyamoya has RCT-level evidence supporting the efficacy of bypass surgery in preventing recurrent hemorrhage (11). This trial provides level 1B evidence and supports a grade A recommendation (see Table 1). The presumed mechanism is that bypass surgery improves cerebral hemodynamics and decreases hemodynamic stress on the fragile, rupture-prone collateral vessels characteristic of Moyamoya vasculopathy (3, 11).

3.2 Atherosclerotic (Chronic) Large Vessel Occlusion

Randomized clinical trials—including the Extracranial–Intracranial (EC–IC) Bypass Trial, the Carotid Occlusion Surgery Study (COSS), and the Carotid and Middle Cerebral Artery Occlusion Surgery Study (CMOSS)—have not demonstrated superiority of bypass surgery over best medical management for patients with symptomatic carotid artery occlusion (12, 13, 14). The EC–IC Bypass Trial, published in 1985 as the first prospective RCT in this field, found no significant reduction in fatal or nonfatal ischemic stroke with bypass surgery (5, 12, 15). The study was widely criticized, particularly for its failure to incorporate hemodynamic criteria to identify the subset of high-risk patients most likely to benefit from revascularization (5).

COSS, published in 2011, attempted to address this limitation by enrolling only patients with strictly defined hemodynamic impairment. However, even in this carefully selected cohort, STA–MCA bypass combined with medical therapy provided no clinical advantage over medical therapy alone (3, 13). Together, the EC–IC Bypass Trial and COSS provide level I evidence showing no benefit of bypass in patients with recently symptomatic carotid occlusion compared with medical management (3, 5). The lack of benefit is attributed both to improvements in contemporary medical therapy and to a relatively high perioperative complication rate—most of which was unrelated to the bypass itself—likely reflecting the vulnerability of these hemodynamically compromised patients.(13) Consequently, bypass surgery is not recommended for these patients (level of evidence 1A; grade of recommendation A) (3). More recently, the CMOSS trial reached similar conclusions: in patients with symptomatic ICA or MCA occlusion and hemodynamic insufficiency, the addition of bypass surgery to medical therapy did not significantly alter the composite endpoint of stroke or death within 30 days, nor did it reduce ipsilateral ischemic stroke beyond 30 days up to two years of follow-up (14).

However, there are subgroups of patients—excluded from the EC–IC Bypass Trial and COSS—for whom flow-augmentation bypass may still offer meaningful benefit. These include individuals with ongoing hemodynamic symptoms (e.g., posture- or blood-pressure–dependent deficits) and those who remain severely (hemodynamically) affected despite maximal medical and interventional therapy. In such cases, bypass may serve as a last resort to prevent a disabling stroke. Moreover, even in the context of negative RCTs, carefully selected patients are still believed to experience improvements in impaired cerebral hemodynamics and reductions in recurrent ischemic events following STA–MCA bypass (2, 3). Contemporary case series demonstrate better outcomes than those reported in earlier trials, reflecting the centralization of bypass surgery in high-volume specialized centers and the incorporation of refined hemodynamic criteria into decision-making (2).

3.3 Acute ischemic stroke due to large vessel occlusion

The role of flow-augmentation STA–MCA bypass in the treatment of acute ischemic stroke remains highly controversial, largely due to the absence of definitive evidence and the limited success of medical and endovascular therapies in certain cases. A recent systematic review identified nineteen studies and highlighted the need for further investigation to clarify the potential utility of EC–IC bypass in acute ischemic stroke—specifically those who remain symptomatic with a persistent penumbra despite optimal medical and/or endovascular management (16).

A key challenge is the accurate identification of patients with persistent hypoperfusion and inadequate collateral circulation who are most likely to benefit from microsurgical revascularization. In this context, BOLD-CVR provides an efficient, noninvasive method for evaluating cerebral hemodynamics and stratifying stroke risk in patients with symptomatic steno-occlusive atherosclerotic disease. This technique allows quantitative assessment of hemodynamic impairment, including in the setting of acute stroke, and can detect paradoxical BOLD-CVR responses, such as the steal phenomenon (4, 6, 7).

4 BOLD-CVR quantitative hemodynamic magnetic resonance imaging

Accurate evaluation of cerebral blood flow capacity and vasodilatory reserve is critical for identifying patients who may benefit from surgical revascularization. At our institution, we have standardized this assessment through a quantitative, MRI-based blood oxygenation–level dependent cerebrovascular reactivity (BOLD-CVR) protocol (6).

BOLD-CVR identifies impaired or paradoxical vascular responses to a standardized carbon dioxide (CO_2) challenge. The BOLD signal encompasses complex neurophysiological processes that cause a shift in hemoglobin species. This shift occurs because deoxyhemoglobin molecules are paramagnetic (thus reducing the T2/T2* relaxation time in 3 Tesla MRI), while oxyhemoglobin molecules are diamagnetic (resulting in no effect on the T2/T2* relaxation time). Consequently, alterations in hemoglobin oxygenation due to increased cerebral blood flow predominantly influence the BOLD signal. The addition of a standardized CO2 stimulus leads to iso-metabolic changes, enabling BOLD-CVR to serve as a surrogate measure for cerebral blood flow (17, 18).

The use of a standardized CO_2 stimulus provides a quantitative assessment of hemodynamic changes with high spatial resolution and excellent reproducibility. This allows for detailed evaluation of the hemodynamic alterations associated with cerebrovascular diseases, both in pre- and post-treatment assessments as well as in longitudinal natural-history studies (4, 6, 7).

5 The role of quantitative BOLD-CVR assessment in surgical revascularization

5 .1 Cerebral hemodynamics and revascularization strategies in Moyamoya vasculopathy

The evaluation of cerebrovascular reactivity impairment in patients with Moyamoya vasculopathy has been extensively studied. The availability of a quantitative hemodynamic imaging marker to assess CVR in candidates for STA–MCA bypass is of critical importance. In patients with ischemic Moyamoya disease and compromised hemodynamics, surgical revascularization is recommended (3, 5, 19). Optimal patient selection, however, should ideally be guided by multimodal structural and hemodynamic imaging (20, 21). Previous studies have demonstrated that impaired BOLD-CVR can identify patients most likely to benefit from bypass surgery. These studies further showed that revascularization leads to improved cerebrovascular reactivity in the operated hemisphere (22, 23, 24).

At our institution, BOLD-CVR is employed as a standard imaging modality to identify patients with hemodynamic impairment who may benefit from STA–MCA bypass. Additionally, it is used at three months postoperatively to assess the impact of surgery on cerebral hemodynamics. In our preliminary cohort of 12 Moyamoya patients who underwent pre- and post-operative BOLD-CVR, nine of twelve patients (75%) showed improved absolute CVR in the affected hemisphere and symptomatic MCA territory (21).

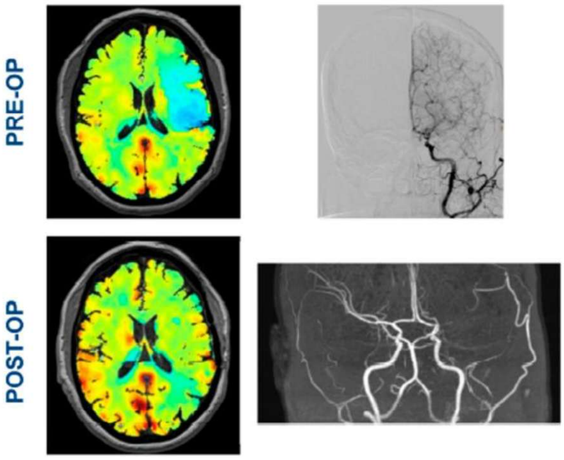

Figure 1: Illustrative case: A 49-year-old patient with Moyamoya vasculopathy presented with bilateral supraclinoid ICA stenosis and left MCA-M1 occlusion. The patient had experienced two transient ischemic attacks, with transient weakness of the right arm and leg. Digital subtraction angiography confirmed the diagnosis. Preoperative BOLD-CVR revealed a steal phenomenon with markedly impaired cerebrovascular reactivity in the left MCA territory. The patient underwent a left-sided STA–MCA flow-augmentation bypass combined with encephalo-duro-synangiosis. Postoperative imaging demonstrated a patent bypass with a flow of 73 mL/min, and follow-up BOLD-CVR showed significant improvement in cerebrovascular reactivity in the left MCA territory. (Adapted from Garbani Nerini et al.(21).)

5 .2 The role of an STA-MCA bypass in an atherosclerotic (chronic) large vessel occlusion

Surgical revascularization via flow-augmentation STA–MCA bypass has been shown to reduce the risk of recurrent ischemia in selected cases of atherosclerotic large-vessel occlusion (5). Based on current evidence and insights from prior randomized clinical trials, we identify three subgroups of patients with ICA or MCA occlusion who may benefit from bypass and should be considered as candidates:

- Patients with recurrent neurological symptoms despite optimal medical therapy.
- Patients with severely impaired hemodynamic status (e.g., markedly reduced BOLD-CVR or ongoing, often blood-pressure–dependent, hemodynamic symptoms).
- Patients with multiple chronic cerebral artery occlusions (e.g., ICA/MCA occlusion with contralateral ICA and/or vertebral artery involvement).

All these subgroups exhibit exhausted cerebrovascular reserve and symptomatic oligoemia exacerbated by hemodynamic stress. Importantly, these patients were excluded from prior RCTs and represent potential bypass candidates if surgery can be performed with low morbidity. The goal is to achieve high bypass patency (>95%) with minimal complications (<5%). The potential benefit of bypass over medical therapy in these individuals is unlikely to be tested in RCTs, highlighting the critical role of advanced hemodynamic neuroimaging in patient selection.(1, 20) Our studies confirm that carefully selected bypass candidates derive long-term benefit from surgical revascularization. Additionally, the flow through a flow-augmentation STA–MCA bypass is dynamically influenced by the demand of the revascularized territory and can increase substantially to meet physiological requirements (1, 20).

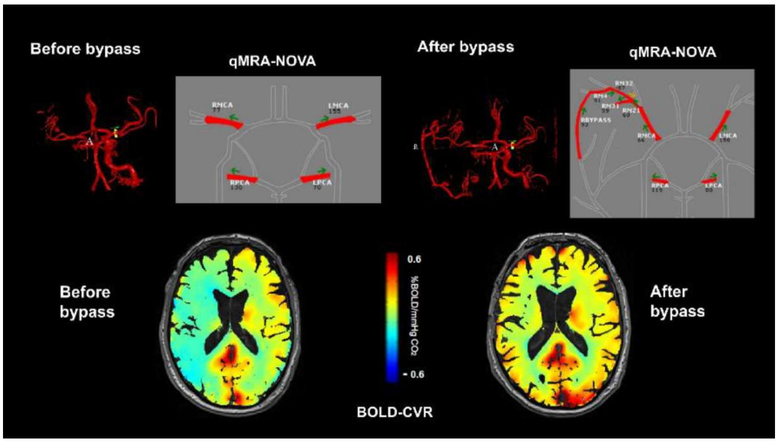

Figure 2. Illustrative case: A 70-year-old male with chronic right-sided ICA occlusion presented with recurrent ischemic stroke symptoms. Preoperative BOLD-CVR demonstrated impaired cerebrovascular reactivity in the right hemisphere and reduced flow in the right MCA, supporting the indication for STA–MCA bypass surgery. Postoperative imaging revealed a bypass flow of 93 mL/min, and BOLD-CVR at three months demonstrated significant improvement in cerebrovascular reactivity throughout the right hemisphere. At two-year follow-up, the patient remained free of ischemic symptoms.

5 .3 Urgent evaluation flowchart for STA-MCA bypass in acute large vessel occlusion

Finally, another subgroup that may benefit from bypass surgery comprises patients with acute ischemic stroke who have brain tissue at risk of infarction due to persistent oligoemia in the acute phase (penumbra), despite optimal medical and endovascular management (5, 16).
Among patients with acute or evolving stroke, those who may benefit from bypass surgery typically meet three criteria: (1) acute stroke or stroke in progress (with fluctuating or worsening symptoms) despite maximal medical and interventional endovascular treatment; (2) major cerebral artery occlusion, with a documented penumbra; and (3) a small infarct core, to minimize the risk of hemorrhagic conversion. The rationale for this approach is that restoring blood flow to ischemic but salvageable tissue may prevent infarct progression. Although promising, this strategy is reserved for highly selected patients with severe hemodynamic compromise and inadequate collateral circulation (6).

At the University Hospital Zurich, BOLD-CVR is now used to assess cerebral hemodynamics in acute bypass candidates. NOVA-qMRA is also employed to quantify collateral vessel status, providing precise blood flow measurements (in ml/min). Using advanced quantitative MRI to evaluate hemodynamic impairment and collateral circulation, combined with relevant clinical data, we developed an institutional flowchart for urgent bypass candidate selection. This flowchart identifies symptomatic patients with acute ischemic stroke due to persistent large vessel occlusion, significant hemodynamic compromise, and inadequate collateral circulation who may benefit from urgent flow-augmentation bypass surgery (6).
According to the flowchart, a bypass is considered for patients 1) with low or moderate neurological impairment (National Institutes of Health Stroke Scale score 1–15, modified Rankin Scale score ≤ 3), 2) without large or malignant stroke, 3) without intracranial hemorrhage, 4) with MR perfusion/diffusion mismatch > 120%, 5) with paradoxical BOLD-CVR (=steal) in the occluded vascular territory, and 6) with insufficient collateral circulation (6).

Exhausted CVR (i.e., the steal phenomenon) is a major risk factor for recurrent stroke, making the accurate identification of hemodynamic impairment crucial.(7) Our institutional criteria for urgent bypass in symptomatic acute stroke patients combine clinical evaluation with advanced multimodal MRI to assess hemodynamic impairment (steal phenomenon), which serves as a key decision factor. Given that exhausted CVR is a significant predictor of recurrent cerebral infarction(25), prompt identification of patients with impaired hemodynamics is essential, as STA–MCA bypass can improve collateral circulation and enhance cerebral flow (4).

In our preliminary study of acute bypass patients, 3-month follow-up with BOLD-CVR showed improved cerebral hemodynamics in the MCA territory (pre-bypass: -0.01 ± 0.05 vs. post-bypass: 0.06 ± 0.03 %BOLD/mmHgCO_2, $P=0.02$). These findings confirm that quantitative BOLD-CVR effectively assesses pre- and post-operative hemodynamic status in patients with acute stroke due to large vessel occlusion who may benefit from revascularization following failure of endovascular or medical treatment (4).

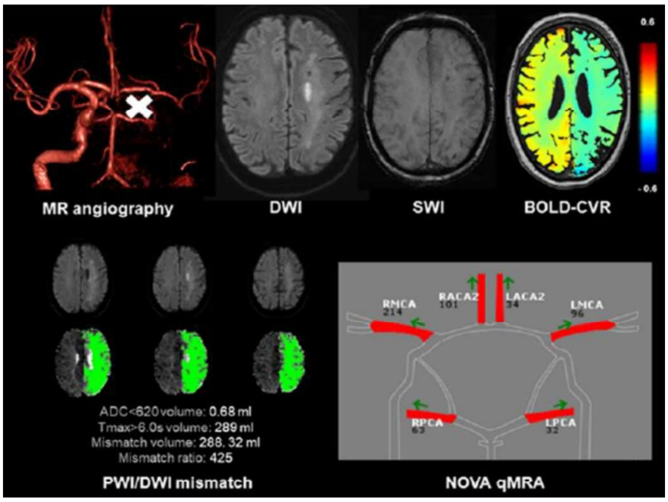

Figure 3: Illustrative case: A 60-year-old man presented with acute ischemia in the left centrum semiovale due to left ICA occlusion. Neurological examination revealed mild right facial palsy and pronator drift of the right arm (NIHSS score 2/42). Given the low NIHSS score, he did not undergo intravenous thrombolysis or thrombectomy. Prior to the event, the patient had no disability (mRS score 0). Stroke volume was 0.68 mL, with no hemorrhage on SWI. The mismatch volume was 289 mL. BOLD MRI revealed paradoxical cerebrovascular reactivity in the entire left hemisphere. NOVA-qMRA demonstrated impairment of collateral circulation. Based on our institutional bypass flowchart, STA-MCA flow-augmentation bypass was indicated. (Adapted from Sebök et al.(6).)

6 Conclusion

Flow-augmentation bypass remains a key surgical intervention for symptomatic Moyamoya vasculopathy, as well as for carefully selected patients with chronic atherosclerotic large vessel occlusion with severe hemodynamic impairment, and acute stroke due to persistent occlusion despite optimal medical or endovascular therapy. This approach is particularly beneficial for patients with hemodynamic impairment who are at increased risk of recurrent ischemic events. Advanced hemodynamic imaging techniques, such as BOLD-CVR, are essential for precise patient selection, ensuring safer surgery and better clinical outcomes.

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