

Risk Profile In Extracranial/Intracranial Bypass Surgery—The Role of Antiplatelet Agents, Disease Pathology, and Surgical Technique In 168 Direct Revascularization Procedures

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Key words

- Antiplatelet treatment
- Cerebrovascular insufficiency
- Extra-/intracranial bypass surgery
- Hemorrhage
- Ischemia
- Moyamoya disease
- Patency rate
- Postoperative complication

Abbreviations and Acronyms

CAD: Cerebrovascular atherosclerotic disease

COSS: Carotid Occlusion Surgery Study

EC-IC: Extra-/intracranial

EMS: Encephalomyosynangiosis

MMD: Moyamoya disease



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Citation: *World Neurosurg.* (2014) 82, 5:672-677.

<http://dx.doi.org/10.1016/j.wneu.2013.06.010>

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

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INTRODUCTION

Revascularization procedures, and extra-/intracranial (EC-IC) bypass surgery in particular (Figure 1), were originally devised to treat patients with internal carotid artery or middle cerebral artery stenosis or occlusion (9). The EC-IC bypass trial in 1985 (5), however, demonstrated that broad application of this procedure based on angiographic and clinical findings alone does not improve outcome, compared to conservative treatment alone. Later studies provided evidence that specific, high-risk subgroups of patients

■ **OBJECTIVE:** Cerebral revascularization procedures are a treatment option in moyamoya disease patients, but recent studies failed to show an immediate benefit in cerebrovascular atherosclerotic disease. To facilitate optimal efficacy of the procedure, a detailed characterization of a representative perioperative complication rate and the role of potential risk factors such as underlying pathology, antiplatelet therapy, and the type of surgery performed is warranted and the purpose of this study.

■ **METHODS:** We included 158 consecutive patients with moyamoya disease or cerebrovascular atherosclerotic disease undergoing 168 direct revascularization procedures. Type of disease, antiplatelet therapy, coagulation disorders, surgical technique, intraoperative complications, postoperative imaging, the need for revision, and outcome at time of discharge were analyzed.

■ **RESULTS:** Complication rate was low, with a high patency rate of 97%. Six hemispheres (3.6%) needed to undergo surgical revision; early morbidity was 10.7% with no mortality, with evidence of ischemia in 6.9% of patients. Type of pathology treated and surgical technique did not influence outcome. Antiplatelet treatment was not associated with an increased risk for hemorrhage or revision, but improved outcome ($P < 0.05$). Ischemia, hemorrhage, and the need for revision aggravated outcome at time of discharge.

■ **CONCLUSION:** Extra-/intracranial bypass surgery remains a treatment option in patients with moyamoya disease, although its use in the context of atherosclerotic disease was recently put into question. Regardless, a detailed characterization of perioperative risk factors is needed to optimize a potential long-term benefit of surgery. At a high-volume center, the complication rate is low independent from the underlying pathology with a high patency rate. Antiplatelet treatment does not increase the risk of hemorrhagic complications, but may improve outcome. Longer follow-up is required to adequately assess the true efficacy of revascularization on stroke prevention.

may still be amenable to surgical intervention and that stricter selection criteria are crucial to effectively filter those patients at highest risk for impending ischemic stroke, despite maximized medical treatment. Patients with angiographic evidence of cerebrovascular atherosclerotic disease (CAD) or moyamoya disease (MMD) may present with a history of (mostly transitory) neurologic events and borderzone infarctions on recent imaging. However, one of the most important selection criteria—which was not included in the EC-IC bypass trial—is evidence of cerebrovascular

hemodynamic insufficiency, as the risk of future stroke increases dramatically (15), oftentimes despite aggressive antiplatelet treatment and high-normal blood pressure management. Hemodynamic insufficiency or the failure of an adequate response to a vasodilatory stimulus as characterized by the cerebrovascular reserve capacity constitutes a mandatory selection criterion (12), and EC-IC bypasses have repeatedly been shown to effectively improve cerebrovascular reserve capacity (3, 13).

As more data such as those from the recent Carotid Occlusion Surgery Study

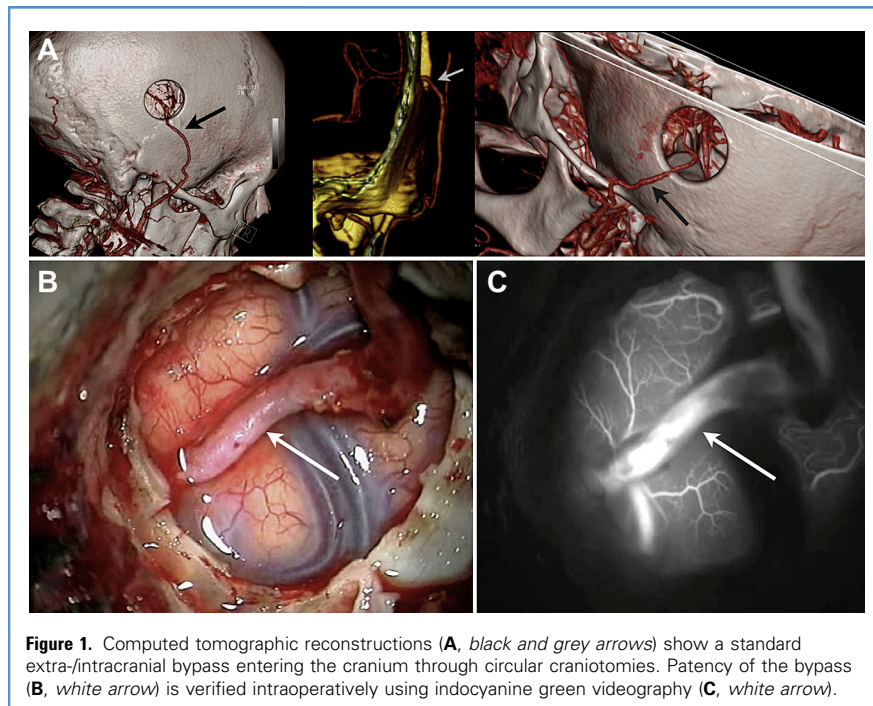


Figure 1. Computed tomographic reconstructions (A, black and grey arrows) show a standard extra-intracranial bypass entering the cranium through circular craniotomies. Patency of the bypass (B, white arrow) is verified intraoperatively using indocyanine green videography (C, white arrow).

(COSS) study emerge (11), questioning the immediate efficacy of bypass surgery to reduce stroke risk in atherosclerotic patients and at the same time pointing out the inherent perioperative risks of the procedure, it is not only of the essence to define and agree on the most appropriate selection criteria. Although an evaluation of selection criteria particularly for patients with CAD is beyond the scope of this study, it is mandatory to determine a representative and likely more detailed complication rate of the surgical procedure itself in dedicated neurovascular centers as well as the association with potential risk factors, in order to optimize a potential long-term benefit over medical treatment alone.

It is the purpose of this observational analysis to describe the complication rate at our institution, and—as a next step—to identify a potential association with variables such as surgical technique, disease pathology (CAD vs. MMD), and antiplatelet treatment.

MATERIAL AND METHODS

For this purpose, we retrospectively analyzed patients undergoing a direct revascularization procedure at the Department of Neurosurgery, Universitätsmedizin

Mannheim, University of Heidelberg, Germany. To be considered for a surgical procedure at our institution, among other considerations patients have to have evidence of recurrent ischemic symptoms with watershed but not territorial infarctions on magnetic resonance imaging, with the last neurologic event more than 6 weeks ago. Patients require angiographic evidence of chronic, either extracranial carotid occlusion or intracranial internal carotid artery or middle cerebral artery stenosis or occlusion, as well as functional evidence of compromised cerebrovascular reserve capacity of less than 30% as determined by territory-specific xenon-enhanced computed tomography analysis. If eligible, patients undergo a standardized end-to-side anastomosis of a branch of the superficial temporal artery to a cortical M₃ branch, with or without addition of an encephalomyosynangiosis (EMS).

To ensure homogeneity of the patient cohort in this stratification, we excluded all patients not meeting all of the above-mentioned criteria, if they received a revascularization procedure for pathologies other than atherosclerotic disease or MMD (such as acute dissection, tumors, or complex aneurysms requiring vessel sacrifice) or if they received only an EMS.

The following data were available for review: patient demographics (sex, age, symptomatology); pre- and postoperative imaging (angiography, CT); pre- and postoperative lab work (including complete blood count, coagulation panel); pre-, intra-, and postoperative anti-coagulation and antiplatelet treatment; surgical technique; intraoperative complication (prolonged hypo- or hypertension); and outcome at time of discharge. A summary of the definitions used for variables and outcome parameters is given in Table 1. Some items may function as both variable and outcome parameter; bypass patency, for instance, was characterized as an important outcome measure, as well as a relevant variable for ischemia or neurologic outcome.

Statistics

Data are presented as mean \pm standard deviation (SD) as well as percentage. All variables and outcome parameters were dichotomized (yes/no) for further analysis as defined in Table 1. Student t-test and Fisher exact test were used as applicable (Numbers; Apple Inc., Cupertino, California, USA; and GraphPad Prism; GraphPad Software, Inc., La Jolla, California, USA). Logistic regression analysis was included for multiple variable analysis. Statistical significance was set at $P < 0.05$, $P < 0.01$, and $P < 0.001$, respectively, including the odds ratio (OR).

RESULTS

Of a total of 280 revascularization procedures performed on 246 patients at our institution from 2004 to 2009, only 158 patients (mean age 51.4 ± 13.2 years) undergoing a total of 168 direct revascularization procedures (demographic data, Table 2) were eligible for inclusion into this particular analysis, and only CAD or MMD patients were considered for our risk stratification. Of the remaining patients, all of the above-mentioned criteria were observed and complete data sets were available for review, including postoperative angiography.

Preoperative conventional angiography showed evidence of CAD in 99 patients (62.7%), whereas 59 patients (37.3%) were diagnosed with MMD. Patients with MMD were significantly younger (41.6 ± 10.7 years vs. 57.7 ± 10.2 years, $P < 0.001$) with

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