Assessment of Hemodynamic Changes and Hyperperfusion Risk After Extracranial-to-Intracranial Bypass Surgery Using Intraoperative Indocyanine Green–Based Flow Analysis

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■ BACKGROUND: **Intraoperative blood flow assessments during cerebral bypass would ideally assess vessel patency, downstream perfusion, and risk of postoperative hyperperfusion syndrome (HPS). Previous studies using indocyanine green–based flow analyses (ICG-BFA) have identified multiple parameters that can intraoperatively track bypass-related changes in cerebral perfusion and potentially predict postoperative risk of HPS. Herein, we determine the most robust parameter and anatomic location for intraoperative ICG-BFA assessment of bypass-related perfusion changes and prediction of postoperative risk of HPS.**

■ METHODS: **Retrospective analysis of an institutional review board–approved prospective database identified patients undergoing superficial temporal artery-to-middle cerebral artery bypass. Demographic and clinical information, as well as manually calculated and automated pre- and postbypass intraoperative ICG-BFA data from cortical, arterial, and venous regions of interest were recorded and analyzed.**

■ RESULTS: **Seven patients underwent superficial temporal artery-to-middle cerebral artery bypass (4 Moyamoya, 3 carotid occlusions). Average age was 48.2 ± 13.9 years (3 female, 4 male). Although all parameters measured showed trends toward improvement postbypass, only changes in arterial and venous automated ICG-BFA slope (also known as blood flow index [maximum intensity/rise time]) reached significance. None of the patients experienced symptomatic HPS, despite 5 of 7 (71.4%) having an increased HPS risk based on previously published ICG-BFA data.**

■ CONCLUSIONS: **ICG-BFA has utility for the intraoperative assessment of bypass-related changes in cerebral perfusion, with automated blood flow index being the most robustly affected parameter. Although previously published ICG-BFA indices did not predict the development of symptomatic postoperative HPS, larger-scale studies correlating observed ICG-BFA changes with risk of HPS are warranted.**

INTRODUCTION

Cerebral bypass is an important surgical option for progressive Moyamoya disease (MMD) and medically refractory, symptomatic carotid occlusive disease.[1,2] Potential complications of cerebral revascularization nonetheless include ischemia (typically from intraoperative hypotension), and hyperperfusion syndrome (HPS). HPS results from the rapid increase of blood flow to a chronically underperfused brain, with clinical manifestations ranging from severe headache to

Key words
- Cerebral bypass
- Flow 800
- Hyperperfusion syndrome

Abbreviations and Acronyms
BFI: Blood flow index
DLCFA: Descending lateral circumflex artery
EC-IC: Extracranial-to-intracranial
HPS: Hyperperfusion syndrome
ICG: Indocyanine green
ICG-BFA: Indocyanine green–based flow analyses
Max I: Maximum intensity
MCA: Middle cerebral artery
MMD: Moyamoya disease
MRI: Magnetic resonance imaging
MVTT: Microvascular transit time
TTP: Time to peak
ROI: Region of interest
RT: Rise time
STA: Superficial temporal artery

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neurologic deficits.[3] Cerebral edema and hemorrhage also are possible. Symptomatic HPS occurs in 11.6%–24.7% of patients undergoing cerebral bypass,[4,5] but incidence of HPS postbypass can be significantly lowered with strict blood pressure control.[5] Balancing postoperative ischemia and risk of hyperperfusion is thus challenging. Intraoperative assessments of blood flow would ideally be used to not only ensure bypass patency but also assess downstream cerebral perfusion and risk-stratify patients for postoperative complications such as HPS.

Current options for intraoperative blood flow assessments include magnetic resonance imaging (MRI), quantitative Doppler, laser speckle imaging, and indocyanine green–based flow analyses (ICG-BFA) with Flow 800 (Carl Zeiss, Oberkochen, Germany). MRI perfusion studies can identify cerebrovascular changes in downstream parenchyma and potentially predict patients at risk for HPS,[3] but this technique is costly, time intensive, and limited to centers with intraoperative MRI capacity. Quantitative Doppler is easily incorporated into an operating room workflow and has been described as a predictive measure of bypass patency[6] yet can only measure flow within the donor vessel to infer downstream parenchymal perfusion. Predictions of HPS based on quantitative Doppler also have not been described. Laser speckle imaging can detect microcirculatory flow changes postbypass,[7] but its predictive value for HPS remains unclear. Laser speckle also is not currently integrated into any intraoperative microscope or other imaging systems, presenting logistical challenges to widespread use.

Flow 800 is a relatively new software tool integrated into the operative microscope that can be used to assess temporal distribution dynamics of intraoperative indocyanine green (ICG) dye infusion. This system automatically calculates the time to half-maximum intensity (delay) and slope of the intensity curve at this timepoint (slope; also known as blood flow index [BFI]) at user-defined region of interest (ROIs) within the operative field. Data also can be downloaded from the system to manually calculate other flow-based parameters. Previous studies using Flow 800 for ICG-BFA for cerebral bypass have demonstrated that various manually calculated and automated parameters can detect changes in pre- and postbypass perfusion and predict the risk of HPS.[8-12] The reproducibility, and therefore clinical importance, of these parameters nonetheless remains unknown. In this work, we assess the robustness of previously described ICG-BFA parameters for detecting intraoperative perfusion changes after cerebral bypass and predicting postoperative symptomatic risk of HPS.

METHODS

This study was approved by the local institutional review board and was completed in compliance with Health Insurance Portability and Accountability Act regulations. Patient consent was obtained based on institutional guidelines for procedures, data collection, and review.

A retrospective analysis was performed on an institutional review board–approved prospective database to identify patients undergoing superficial temporal artery (STA)-to-middle cerebral artery (MCA) extracranial-to-intracranial (EC-IC) bypass at a single institution over a 1-year period (August 2016 to August 2017). Patients meeting these criteria were included only if they had complete pre- and postbypass ICG-BFA data ($n = 7$). Information recorded included patient demographics (age, sex), underlying cerebrovascular disease, bypass/graft specifics, surgical complications, and clinical outcomes.

The senior author (J.J.R.) performed all surgeries, with plastic surgery assistance in cases using an interposition graft. Patients in this series with MMD or carotid occlusions were considered for bypass in the setting of recurrent/progressive ischemic events with underlying reductions in cerebral perfusion reserve, despite optimal medical therapy. Choice of a direct STA-MCA bypass versus use of an interposition graft was based on the suitability of the STA as a donor vessel. The STA was assessed preoperatively with either computed tomography or formal angiography, although the ultimate assessment of STA suitability as a donor vessel was made intraoperatively.

EC-IC Bypass Procedures

All STA-MCA bypasses were performed in a similar fashion. To summarize, after obtaining informed consent, the patient was brought to the operating room, intubated, and neurophysiologic monitoring was established. Their head was fixed in a Mayfield head holder and turned contralateral to the side of the operation. The STA was mapped with Doppler, then dissected free starting above the zygoma. If the distal STA was deemed an inadequate donor at this point, a descending branch of the lateral circumflex artery (DLCFA) interposition graft was dissected in conjunction with plastic surgery. A craniotomy was then performed over the sylvian fissure, and a distal MCA branch was identified and dissected free for anastomosis. An STA-MCA bypass was then performed in an end-to-side fashion (with or without a DLCFA interposition graft).

ICG-BFA Data Acquisition and Analysis

ICG was given intravenously (0.2 mg/kg) in the operating room both before and after cerebral bypass, with recordings via Flow 800 software integrated into the PENTERO operative microscope (Carl Zeiss AG, Oberkochen, Germany). The microscope was set to approximately 3.0× magnification and positioned at a focal distance of 300 mm for all recordings. After data recordings, user-generated ROIs were placed in an even distribution on the cortical surface (5 total, avoiding large cortical vessels), and one each on a downstream cortical artery and vein (**Figure 1**). Time–intensity curves were generated for each ROI, and automatically generated ICG-BFA parameters (delay and slope; see below for definition) for all ROIs were recorded (**Figure 2**). Intrapatient cortical ROI data were averaged before analysis. Delay and intensity were comparatively visualized via scaled images (**Figure 2**). Raw time–intensity curve data also were downloaded for secondary analyses on a personal computer.

Based on previous reports on ICG-BFA for cerebral bypass,[8-13] the following manually calculated parameters were analyzed: maximum intensity (Max I), time to peak (TTP; time from initial to peak fluorescence intensity), rise time