

Fluorescein videoangiography (FL-VAG) as a predictor of cerebral bypass patency

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ABSTRACT

Background: The fluorescein videoangiography (FL-VAG) has become a valuable adjunct tool in vascular neurosurgery. This work describes using the FL-VAG during bypass surgery and proposes a classification method for evaluating surgical results.

Methods: We analyzed 26 patients with 50 cerebral bypasses from September 2018 to September 2022. We used a three grades classification method based on the pass of intravenous fluorescein through the anastomosis. Grade 1 represents the synchronous and total filling of the "T" shape ("green T") formed by the donor and recipient vessel, Grade 2, the asynchronous filling of the anastomosis (incomplete/asynchronous "green T"), and Grade 3, a non-patent anastomosis (absence of "green T").

Results: Of the 26 patients, 8 underwent one bypass, 14 underwent double bypass, 2 underwent three bypasses, and 2 underwent four bypasses in two different interventions. The type of bypass was end-to-side anastomosis in 47 (94%) cases, internal maxillary artery to middle cerebral artery bypass with a radial artery graft (IMax-MCA anastomosis) in 2 (4%), and PICA-VA transposition in one (2%). We made 24 (48%) bypasses on the right side and 26 (52%) on the left side. After the initial surgery, thirty-nine (78%) bypasses were considered as Grade 1, 5 (10%) as Grade 2, and 6 (12%) as Grade 3. After intraoperative bypass patency assessment (IBPA), 45 (90%) of the bypasses were considered Grade 1 and remained patent on CTA.

Conclusions: Using FL-VAG and a three-tier classification method is a reliable tool to predict bypass patency. It is safe, low-risk, and available worldwide.

1. Introduction

The use of fluorescein videoangiography (FL-VAG) in vascular neurosurgery has become a valuable adjunct tool in managing cerebral aneurysms, arteriovenous malformations, and bypass procedures, among others.^{1,2} For example, cerebral bypass surgery has been used in moyamoya disease (MMD), occlusive cerebrovascular disease, and complex intracranial aneurysms to maintain adequate cerebral blood flow. Therefore, the routine use of a tool to assess the patency of a bypass, such as the FL-VAG, can be used as a fast and reproducible method for the demonstration of bypass patency intraoperatively alone or in addition to other techniques, such as the intracranial Doppler, intravenous indocyanine green video angiography (ICG-VAG) or intraoperative digital subtraction angiography (DSA).^{3,2}

In this work, we aim to describe the use of FL-VAG during bypass

surgery, and we propose a method of classification to predict the post-operative bypass patency based on the intraoperative FL-VAG findings and postoperative CT angiography (CTA) images.

2. Methodology

We analyzed twenty-six patients who underwent 50 cerebral bypasses from July 2018 to July 2022 at the department of Vascular Neurosurgery of the National Institute of Neurology and Neurosurgery "Manuel Velasco Suarez" - Mexico City. All of them had a complete clinical record, imaging studies, and recording of the surgical procedures, including the FL-VAG. As a result, the institutional review board approved this study with the number INNN 69-22.

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Abbreviation list	
CTA	Computed tomography angiography
DSA	Digital subtraction angiography
FL	Fluorescein
FL-VAG	Fluorescein videoangiography
IBPA	Intraoperative bypass patency assessment
ICG-VAG	Indocyanine green video angiography
IMax-MCA	Internal maxillary artery to middle cerebral artery
MMD	Moyamoya disease
PICA-VA	Posterior inferior cerebellar artery to vertebral artery
STA-MCA	Superficial temporal artery to the middle cerebral artery

2.1. Population

The mean age of the patients was 51 years (range, 19–83 years); of these, 11 (42.3%) were women, and 15 (57.7%) were men, with a 2:3 ratio. Fourteen (53.8%) patients had the diagnosis of complex intracranial aneurysm, 6 (23%) had acute cerebral ischemia, 5 (19.2%) had a carotid occlusion with transient ischemic symptoms, and one patient (3.8%) had moyamoya disease giving a total of 26 patients included in the study. Heart rate and blood pressure were maintained stable during surgery to avoid variations in the results. All bypasses underwent sequential FL-VAG measurements to visualize the passage of intraoperative fluorescein through the anastomosis, and a CT angiography (CTA) or ARM was made one day after surgery to corroborate postoperative patency. The senior author, a vascular neurosurgeon, performed all surgeries.

2.2. Fluorescence microscope module

We performed intraoperative FL-VAG using a ZEISS KINEVO 900 surgical microscope equipped with the YELLOW 560 fluorescence module. This module uses 460 and 500 nm light waves to illuminate the surgical field and 540 and 690 nm for focused visualization. To optimize the fluorescence image, we attenuate the ambient light.

2.3. Fluorescein video angiography

None of the patients had a previous history of allergic reactions. After completing the cerebral bypass, a bolus of 0.4 ml of FL (FL 10%, 500 mg/5 ml; Contacare Ophthalmics and Diagnostics®) was applied intravenously through a peripheral vein, followed by another bolus of 20 ml of 0.9% saline solution. The time elapsed between administering the flush with saline solution until the appearance of the fluorescence in the surgical field was measured and registered in all cases. We selected this dose based on our experience with different dosages for faster elimination during repetitive studies.⁴

2.4. Permeability scale

For the analysis of the FL-VAG after the cerebral bypass, we created a scale in which we evaluated the degree of visualization of the FL in the donor and recipient vessels, where Grade 1 represents the synchronous and total filling of the "T" shape formed by the donor and recipient vessel (complete "Green T" in the end-to-side anastomosis), Grade 2 the asynchronous, partial and slow filling of the anastomosis (incomplete/asynchronous "Green T") and Grade 3, meaning that there is no passage of FL through the anastomosis (absence of "Green T") (Table 1, Fig. 1).

Table 1
Cerebral bypass patency scale using FL-VAG.

Grade	Description	Average time for visualization after FL administration
1	Synchronous and total filling of the donor and receptor artery.	9.7 s*
2	Asynchronous and slow filling of the bypass	17.3 s*
3	There is no FS passage through the anastomosis	Not valuable*

Abbreviations: FL, fluorescein. FL-VAG, fluorescein-video angiography.

2.5. Data collection

We collected data by review of clinical records, intraoperative videos, and postoperative CTA 24 h after the procedure. Statistical analysis of the values obtained was performed using IBM SPSS Version 25 (IBM Corp., Armonk, New York, USA). To determine the normal distribution of the population, we used the Shapiro–Wilk test. In addition, we used Mann–Whitney *U* tests for nonparametric distribution. For inferential statistics, we used the Chi-square test with a *P* value < 0.05 to be considered statistically significant.

3. Results

3.1. Bypass surgery

We performed fifty bypass procedures in twenty-six patients; 8 patients (30.8%) underwent one bypass, 14 (53.8%) underwent double bypass, 2 (7.7%) underwent three bypasses, and 2 (7.7%) underwent four bypasses in two different interventions (bilateral MMD).

The number of bypasses was based on the disease to treat, the availability of the donor's vessels, and in some cases, the necessity of relocation because of malfunction of the original anastomosis. The type of bypass performed was end-to-side anastomosis from the superficial temporal artery to the middle cerebral artery (STA-MCA bypass) in 47 (94%) cases, end-to-side internal maxillary artery to middle cerebral artery with a radial artery graft (IMax-MCA anastomosis) in 2 (4%) cases. In addition, in one (2%) case, a posterior inferior cerebellar artery to vertebral artery transposition (PICA-VA bypass) was performed. We made twenty-four (48%) bypasses on the right side and 26 (52%) on the left side.

3.2. Intraoperative bypass patency assessment (IBPA)

All bypasses were assessed after completion to verify correct patency using the FL-VAG and the intraoperative Doppler as complementary flow confirmer. We described this sequence of tests as IBPA. The senior author, a vascular neurosurgeon, performed all IBPA.

We revisited eleven bypasses (22%) due to an apparent dysfunction after IBPA (Fig. 2). Of these, 5 (45.4%) were Grade 2 (slow flow), and six (54.5%) were considered Grade 3.

3.3. Transit time

We measured the time elapsed between the administration of fluorescein and its appearance under the microscope in all cases. All patients' heart rates and blood pressure were normal during the performance. For Grade 1 anastomosis, the mean time was 9.7 s; for Grade 2 was 17.3 s; and for Grade 3, more than 25 s without evidence of filling. When we compared the mean transit time of Grade 1 and Grade 2 cases, there was a significant difference among them (*P* < 0.01), considering that a slow time of transit of FL through the anastomosis is a good predictor of postoperative bypass failure.

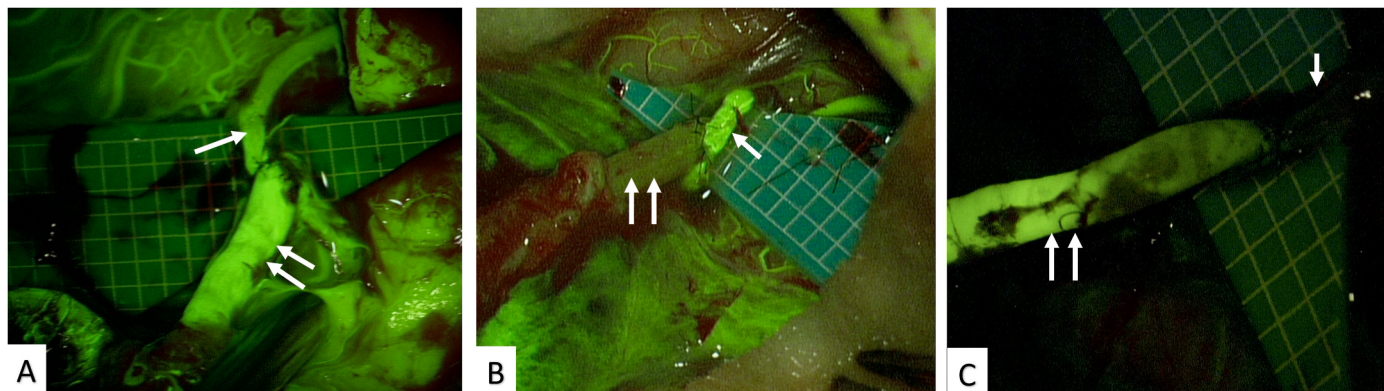


Fig. 1. FL-VAG bypass patency grades. **A**, Grade 1. (Complete “Green T”), showing a synchronous filling of the donor and recipient arteries (arrows). **B**, Grade 2 (incomplete “green T”). In this case, the recipient artery is visible (arrow), but the donor artery fluorescence is not seen (double arrow). **C**, Grade 3, an FL fluctuant column in the donor’s vessel is seen (double arrow). When present, this fluctuant column is a reliable sign of occlusion of the anastomosis. The site of anastomosis does not show fluorescence (arrow).

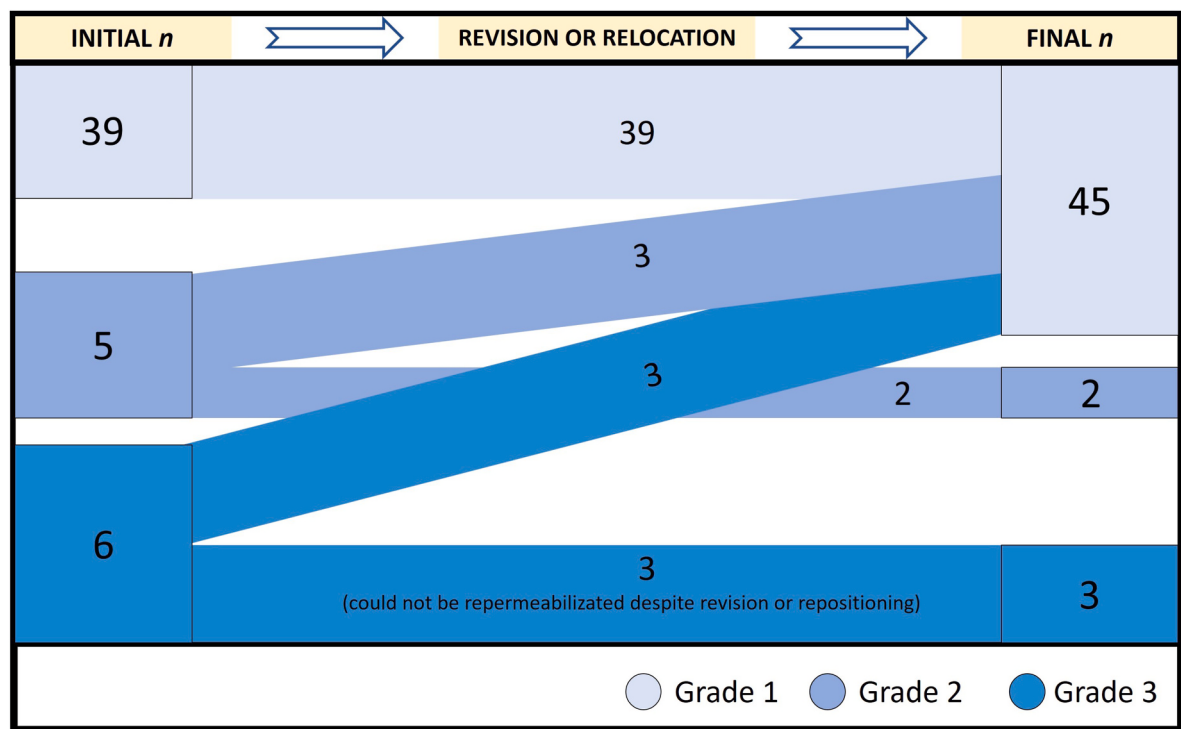


Fig. 2. Permeability rate in the initial surgery and after IBPA.

3.4. Grade 1

After the initial surgery, thirty-nine (78%) bypasses had a synchronous and total filling of the vessels (Grade 1); all of them exhibited patency in the postoperative image, showing a complete "Green T" shape. Consequently, the statistical analysis showed that visualization of a "Green T" in an end-to-side anastomosis was significantly associated with postoperative patency for a Grade 1 bypass ($P = 0.0003$).

3.5. Grade 2

In five (10 %) cases, there was a partial and slow filling in the FL-VAG (Grade 2, incomplete or asynchronous "Green T"). Two were left without further revision because they showed a discrete filling. Both bypasses did not show postoperative patency. We submitted all remaining 3 cases to revision due to a slow flow (>20 s), and postoperative patency was re-

established in all three. This result suggests the association between slow flow through the anastomosis during IBPA and early occlusion if not revisited ($P = 0.011$).

3.6. Grade 3

Six (12%) bypasses did not show the passage of fluorescein through the anastomosis and were defined as Grade 3 (absent "Green T"). Three of them became Grade 1 after the bypass was relocated to another close cortical branch. Still, in the remaining 3 cases, the anastomosis could not be permeabilized or relocated, and none showed postoperative patency. In the statistical analysis, Grade three was significantly associated with postoperative occlusion ($P = 0.0005$).

3.7. Permeability rate

The number of patent bypasses was evaluated immediately after finishing the anastomosis and after IBPA using the FL-VAG as a leading indicator and intraoperative qualitative Doppler as a secondary indicator. From the original number of 39 (78%) anastomoses in Grade 1, this number increased to 45 (90%) after IBPA. Then, we obtained a 90% bypass permeability rate in this study (Fig. 2).

3.8. Fluctuant column

We observed a fluctuant column of FL in the donor artery in 4 (8%) cases, of which three were Grade 3 and one Grade 2 that did not show postoperative flow. So then, a fluctuant column in the donor artery without a good flow of FL through the anastomosis indicates imminent occlusion ($P = 0.007$). Therefore, in these cases, the bypass should be considered as grade 3. In all these cases, the Doppler signal was present but weak, even when the fluorescein did not show pass through the anastomosis. In this sense, the FL VAG was more reliable than the qualitative Doppler signal.

3.9. Complications

Any of the patients showed adverse reactions to the FL administration. Five patients (19.2%) showed complications after surgery; three grade 3 (11.5%) developed a cerebral infarction despite the bypass revealed by the presence of low-density areas in the postoperative CT. Two (7.6%) patients died due to causes not related to the surgery (hospital-acquired pneumonia).

3.10. Illustrative cases

Representative Grade 1 case (Fig. 3). A 72-year-old man presented with occlusion of the left internal carotid artery with repetitive transient ischemic symptoms (Fig. 3A). We decided to perform an STA-MCA bypass. Preoperative perfusion studies showed a blood flow reduction in the left MCA territory with a limited parietal infarction zone (Fig. 3B). The bypass showed good functioning with a total and synchronous filling of the vascular anastomosis (Grade 1) (Fig. 3C and D). Postoperative imaging studies showed bypass patency with improved perfusion values (Fig. 3E and F). The patient was discharged one week after the operation, with a modified Rankin scale of 1, without added deficits.

Representative Grade 2 case (Fig. 4). A 70-year-old male presented to the emergency room with left MCA ischemic symptoms because of atherosclerotic disease (Fig. 4A). The study showed a prolonged transit time at the left MCA territory (Fig. 4B). The patient underwent a double STA-MCA bypass using the frontal and parietal branches. After completing both anastomoses, we used the FL-VAG for confirmation of patency. In the first graft, we observed total and synchronous filling of anastomosis (Grade 1) (Fig. 4C). Still, in the second one, a partial and asynchronous Grade 2 filling was present (Fig. 4D). Then, we reconstructed the second anastomosis, and postoperative imaging studies showed patency in both anastomoses (Fig. 4E).

Representative Grade 3 case (Fig. 5). A 63-year-old woman reported left cerebral artery ischemic symptoms from the atherosclerotic disease (Fig. 5A). We performed an STA-MCA bypass. After IBPA, it was shown the absence of flow through the anastomosis (Grade 3) (Fig. 5B and C). In consequence, we reconstructed the anastomosis. A second FL-VAG showed total and synchronous filling of anastomosis (Grade 1) (Fig. 5D). The postoperative imaging studies showed improved bypass flow and perfusion values (Fig. 4D–F).

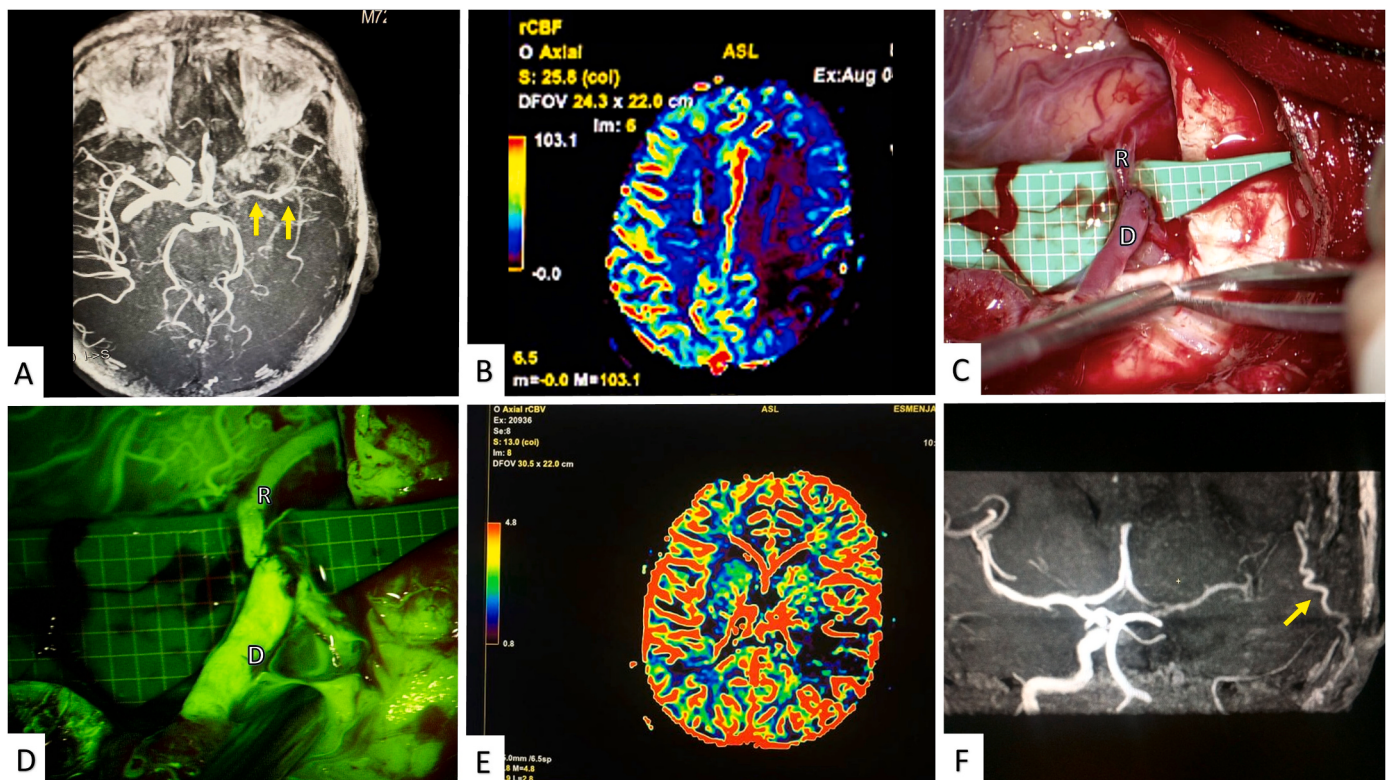


Fig. 3. Grade 1 bypass. A, Left internal carotid artery occlusion with collateral circulation in the MCA (arrows). B, Regional cerebral blood flow is reduced in the left MCA territory. A well-established and limited infarction is present in the parietal area with an extensive penumbra zone. C, An STA-MCA bypass was completed (D, donor artery, R, recipient artery). D, A complete “Green T” is visible after administration of Fluoresceine. E, Improvement of flow values in the MCA after the bypass. F, Postoperative CTA showing a functional bypass (arrow).

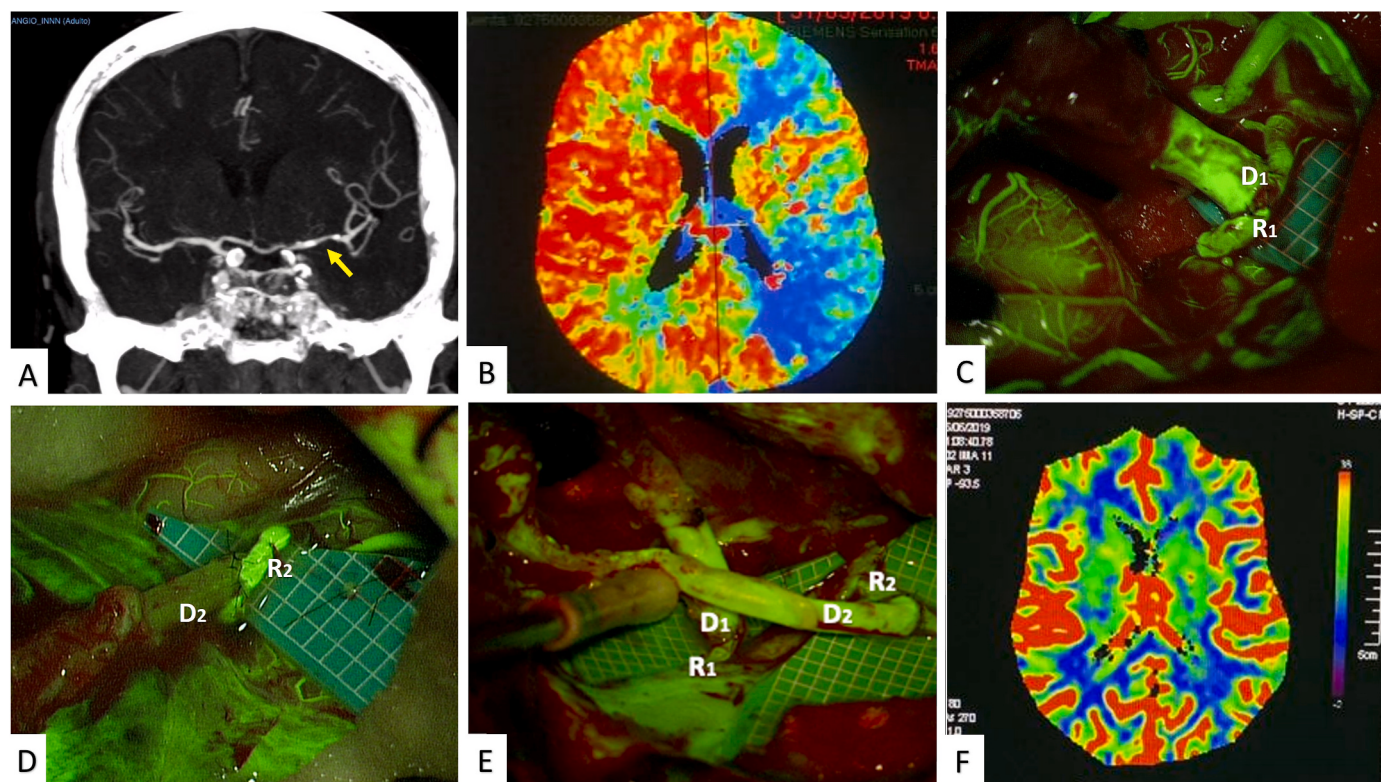


Fig. 4. Grade 2 bypass. A, CTA showing atherosclerotic changes in the left MCA in a 70 y-o man. B, The perfusion MRI study shows low flow in the left MCA territory. C, The first STA-MCA bypass showed a complete “green T” (Grade 1 anastomosis). D, The second bypass was considered grade 2, with an asynchronous “green T”. E, After revision, both bypasses were grade 1 and showed a good “green T,” anastomosis. F, Postoperative perfusion study showing improvement in the regional circulation values.

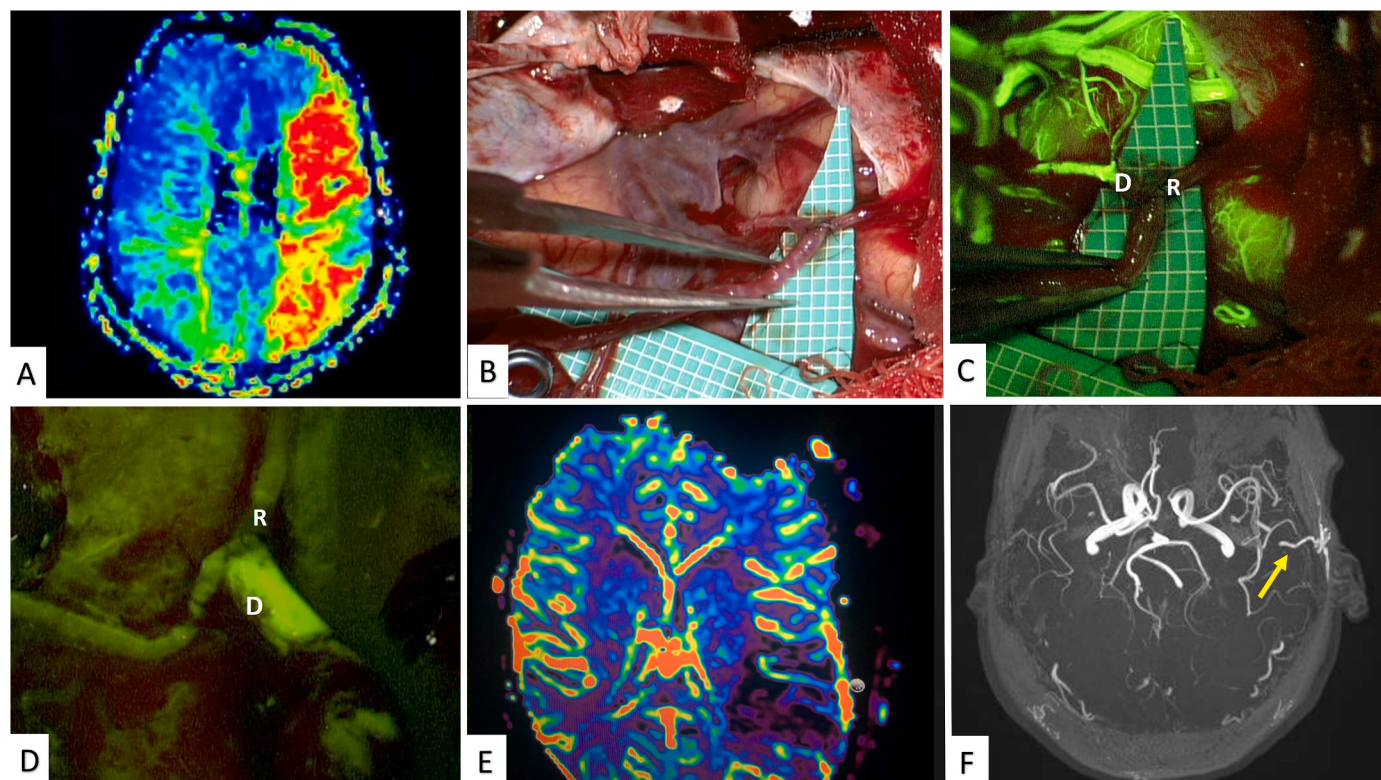


Fig. 5. Grade 3 bypass. A, Perfusion study shows a prolonged transit time in the left hemisphere. B, An STA-MCA bypass was completed. C, The FL-VAG shows a non-functioning Grade 3 bypass. D, After revision, the bypass was converted into a Grade 1. E, The perfusion values showed improvement in the affected territory. F, The postoperative CTA shows the flow augmentation in the left MCA territory with a functional bypass (arrow).

4. Discussion

Bypass surgery is divided into different types according to their expected function. Accordingly, they are classified as "flow augmentation" and "flow preservation" bypasses.^{5,6} It is a well-established and accepted procedure in patients with complex aneurysms, hemodynamic atherosclerotic cerebrovascular disease, MMD, and in some cases, for resection of skull base tumors and flows preservation when needed to sacrifice a vessel or there exists an entrapped vessel segment.⁷ For this purpose, the neurosurgeon may use one or more intraoperative tools: DSA, Doppler ultrasonography, ICG-VAG, dual image videoangiography, FL-VAG, and quantitative flowmetry.⁸

DSA remains the gold standard technique for evaluating graft/bypass patency; however, this technique has several disadvantages, namely invasiveness, high costs, ionizing radiation used in the operating room, and prolonged procedure time.⁹ Since the introduction of the ICG-VAG, it has become one of the most extended methods to verify graft patency during bypass surgery. ICG represents a non-invasive, easy-to-use technique with a poor complication rate between 0.05 and 0.2%.¹⁰ However, visualization through microscope eyepieces, evaluation of the surrounding tissue, and visualization of fine cortical vessels is still a concern.¹¹

FL in neurosurgery has confirmed its utility in vascular and tumor surgery.^{4,12,13} It is a low-cost, well-tolerated compound with minimal adverse effects and is readily available worldwide.¹⁴ However, its utility in bypass surgery has yet to be well established. It has advantages over the ICG-VAG in terms of visualization of delicate vascular structures; however, its clearance from brain tissue is slow.¹⁵ In this sense, we have found that administration of 0.4 ml of a 10% Fluorescein solution, followed by a 20 ml saline solution flush, permits repeated doses with an acceptable grade of tissue impregnation, not affecting the visualization of the anastomosis flow.

Retrospective clinical studies had already been performed using FL-VAG to evaluate the intraoperative patency of cerebral bypass, as reported by Narducci et al, which included 11 patients in their case series demonstrating the excellent functioning of the bypass with FL-VAG. They were confirmed later through postoperative DSA or CTA.¹⁶ Furthermore, Woitzik et al showed that FL is beneficial not only in the early diagnosis of intraoperative flow failure but even for detecting the occlusion site, which, as in our cases, allowed the revision and correction of the bypass.¹⁷ Then, the present study's goal was to propose a three grades method that would allow us to classify the bypasses according to the intensity and filling of the FL. The time of transit through the anastomosis, to define the necessity for an early revision and eventual relocation of the anastomosis, as well as to predict the patency of the anastomosis in the first 24 h (a crucial time to detect an early occlusion of a bypass).

4.1. Permeability scale

The concept of an IBPA represents the necessity to corroborate the well-functioning of a bypass after the completion of the anastomosis. Therefore, we should use all the tools available to achieve this goal, including visual inspection, intraoperative Doppler, flowmeter, DSA, or novel techniques such as the ICG-VAG or the FL-VAG.

In this study, we analyzed the utility of a systematic method using the FL-VAG to evaluate the proper function of an anastomosis based on the transit time of FL through the bypass and the visual image created by the FL flow as a predictor for good functioning. Visualization of a "Green T" with a transit time <10 s is a reliable predictor of good postoperative patency. On the contrary, an incomplete "Green T," a transit time >12 s, or no visualization at all of the bypass, is an indicator for rebuilding or relocating the anastomosis without hesitation (Figs. 1–4). All this could help novel and experienced neurosurgeons to evaluate the quality and functioning of the anastomosis with relative confidence.

5. Conclusions

FL-VAG demonstrates the patency of cerebral vessels in real-time when performing bypass anastomosis. This procedure is easy to use, fast, low risk and can be implemented routinely in cerebral revascularization surgery. Measuring patency by grades helps us to predict a good postoperative function of the bypass. Grade 1 was associated with intraoperative and postoperative permeability, demonstrating that it is a good predictor of bypass functioning; on the contrary, Grade 3 was statistically associated with a lack of intraoperative permeability, indicating that it is a reliable predictor of occlusion in the short term. Grade 2 was an indicator of the necessity of revision and eventual reassembling or relocation of the bypass until Grade 1 was obtained.

Thus, we can conclude that the intraoperative use of FL-VAG is a valuable short-term predictor of patency of the bypass, being a safe and inexpensive alternative; however, studies are needed to prove its prediction over a more extended period.

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Limitations

The retrospective nature of the present study is a limitation in collecting additional data about the bypass procedure. However, we consider that the objective of the work could be completed with the information obtained from the clinical records, surgical videos, and imaging studies. Long-term follow-up is also desirable for these patients.

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None.

CRediT authorship contribution statement

Edgar Nathal: Writing – original draft, Conceptualization, Validation, Supervision, Visualization, Writing – review & editing. **Javier Degollado-García:** Conceptualization, Writing – original draft, Validation, Supervision, Visualization. **Héctor A. Rodríguez-Rubio:** Investigation, Data curation, Formal analysis, Methodology, Resources, Writing – review & editing, Writing – original draft. **Alfredo Bonilla-Suástegui:** Visualization, Data curation, Resources, Methodology, Investigation. **Alejandro Serrano-Rubio:** Funding acquisition, Writing – review & editing, Investigation, Methodology, Supervision, Writing – original draft.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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