Does Advanced Imaging Aid in the Preoperative Evaluation of Patients With Moyamoya Disease?

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Abstract

Background
Moyamoya disease is characterized by progressive nonatherosclerotic stenosis and eventual occlusion of the supraclinoid cerebral arteries with the associated development of abnormal collateral vessels. Treatment of moyamoya disease revolves around restoring cerebral blood flow (CBF) distal to the steno-occlusive disease. Numerous modalities can be used to assess hemodynamic parameters. We sought to determine the impact of preoperative imaging on surgical decision-making.

Methods
A retrospective review was performed of all patients seen with the diagnosis of moyamoya. Patients were grouped on presentation based on CT/MRI findings of infarction, hemorrhage, or normal. Patients who did not have all of the preoperative tests were excluded. Preoperative radiological results were dichotomized as either normal or abnormal.

Results
During a five-year period, 34 patients with moyamoya met the inclusion criteria. All patients had an abnormal magnetic resonance angiography (MRA) Non-invasive Optimal Vessel Analysis (NOVA; VasSol, Inc, River Forest, IL). Three patients had normal initial MRI. All symptomatic patients had abnormal preoperative workup and underwent revascularization, as all were found to have abnormal single photon emission computed tomography (SPECT). The only occasion where the decision for surgery or type of surgery was influenced by imaging findings was in patients with nonclassical or minimal symptoms.

Conclusion
Although hemodynamic imaging studies can aid in establishing a preoperative baseline of CBF and cerebral vascular reserve (CVR) for follow-up studies, the true implication of these tests in the preoperative evaluation of clearly symptomatic moyamoya patients is debatable. In asymptomatic/mildly symptomatic patients, hemodynamic studies are necessary to determine the need for treatment. For symptomatic patients, surgery can be performed without an exhaustive and costly preoperative hemodynamic evaluation.

Introduction
Moyamoya disease is characterized by progressive nonatherosclerotic stenosis and eventual occlusion of the supraclinoid cerebral arteries with the associated development of abnormal collateral vessels [1,2]. The gradual occlusion of these vessels leads to cerebral perfusion pressure reductions and decreased cerebral blood flow (CBF) [3]. The capacity of the vessels to compensate for the fall in CBF is known as cerebral vascular reserve (CVR), which can be assessed by multiple imaging modalities [3].

Treatment of moyamoya disease revolves around restoring CBF distal to the steno-occlusive disease. Examination of the cerebral vasculature via angiography has long been the gold standard for diagnosis and preoperative surgical planning. Adjunct imaging methods used to measure cerebrovascular hemodynamics such as single photon emission computed tomography (SPECT), positron emission tomography (PET), xenon CT, arterial spin labeling (ASL), magnetic resonance (MR) perfusion, and magnetic resonance angiography (MRA) Non-invasive Optimal Vessel Analysis (NOVA; VasSol, Inc, River Forest, IL) have also been shown to offer advantages when determining management strategies [4]. These metabolic and flow studies allow for pre- and postoperative assessment of disease severity. However, a question of the clinical
utility of these various techniques remains. Most institutions use a variety of modalities, often letting symptomatology ultimately guide treatment. In this study, we evaluated preoperative conventional angiography, MRI, MRA NOVA, as well as pre- and post-acetazolamide challenge SPECT and their impact on the management of patients with moyamoya disease.

**Materials And Methods**

**Institutional protocol**

Patients seen at our institution with suspected moyamoya disease are investigated by a standardized institutional protocol. Initial investigations include CT, computed tomography angiography (CTA), or MRA scan depending upon the presenting symptoms. Once moyamoya disease is suspected, patients undergo a brain MRI, cerebral angiography, pre- and post-acetazolamide SPECT scan, and MRA NOVA.

Patients with the symptomatic disease are treated with revascularization when found to have hemodynamic compromise on SPECT with or without acetazolamide, while asymptomatic/mildly symptomatic patients are treated when imaging shows impaired cerebral hemodynamics on SPECT with acetazolamide. Patients with bilateral disease undergo direct and/or indirect bypass on the asymptomatic side if imaging suggests hemodynamic impairment. Direct revascularization is favored in all cases.

**Study outline**

The Feinstein Institute for Medical Research institutional review board approved a retrospective chart review of patients with moyamoya. Informed consent was waived for this study. All patients seen at our institution with a diagnosis of moyamoya disease were included. Medical records, physicians’ notes, and all radiological studies were reviewed for analysis. Descriptive statistics were used to summarize the data. Fischer’s exact test and Mann-Whitney U test were used to calculate statistical differences between datasets.

**Results**

**Patient characteristics**

A total of 34 patients with moyamoya disease were evaluated from January 1, 2011, to January 1, 2016, and received a complete imaging workup as discussed in the methods. The majority of patients were females (76%, 26/34), with an average age of 43 years (range: 17-72; Table 1). Transient or permanent neurological deficit likely due to ischemia was the most common presenting disease process found in 56% of patients (19/34). Three of these patients had transient symptoms (e.g. transient numbness). These three patients had no impaired CVR. Table 2 demonstrates imaging findings categorized by presenting symptoms of the patients.

| Demographics | Age  | 43 (17-72) |
|--------------|------|------------|
| Sex (F)      | 76%  | 26 (26/34) |
| Side         | Left | 44% (15/34) |
|              | Right| 35% (12/34) |
|              | Bilateral | 21% (7/34) |
| Major ischemia |         | 47% (16/34) |
| Transient neurological symptoms | 9% (3/34) |
| Hemorrhage   | 26%  | (9/34)     |
| Headache     | 6%   | (2/34)     |
| Syncope      | 6%   | (2/34)     |
| Seizure      | 3%   | (1/34)     |
| Tinnitus     | 3%   | (1/34)     |

**TABLE 1: Patient demographics**
**Surgery (% of 26 patients) | No surgery (% of 8 patients)**
---|---
**Presentation**
Transient or minor | 3 (11.54%) | 3 (37.50%)
Hemorrhage | 6 (23.08%) | 2 (25.00%)
Ischemic stroke | 17 (65.38%) | 3 (37.50%)
Normal | 3 (11.54%) | 0.00%
**MRI findings**
Ischemia | 17 (65.38%) | 6 (75.00%)
Hemorrhage | 6 (23.08%) | 2 (25.00%)
**SPECT post Diamox**
No change | 12 (46.15%) | 2 (25.00%)
Improved | 0.00% | 3 (37.50%)
Decreased | 14 (53.85%) | 3 (37.50%)
**NOVA**
Abnormal | 26 (100.00%) | 8 (100.00%)
Normal flow | 0.00% | 0.00%

**TABLE 2: Imaging findings based on presentation**
SPECT: single photon emission computed tomography; NOVA: Non-invasive Optimal Vessel Analysis.

**MRI findings**
Brain MRI was abnormal in all but three patients. In total, 65% of patients (22/34) had findings of ischemia (this includes symptomatic and asymptomatic patients), including white matter ischemic disease, or acute infarcts. Of the patients, 26% (9/34) had hemorrhage (Table 1). There was no relationship between MRI findings and the likelihood of a patient undergoing surgery (P > 0.05).

Of the three patients with normal MRI, all patients underwent surgery due to findings of perfusion deficits on SPECT or impaired CVR based on SPECT with acetazolamide. Of the six patients with minor symptoms of moyamoya (headache, transient paresthesia), three were the patients with no significant findings on conventional MRI but impaired hemodynamic imaging. The other three had only radiological findings suggestive of ischemia (Table 2).

**Angiographic findings**
Findings on conventional cerebral angiography were used as the gold standard for moyamoya disease diagnosis. All patients were found to have evidence of moyamoya on angiography. Suzuki grades ranged from II to VI [2]. In total, 70% of patients presented with Suzuki grade II-IV (Table 1). Only one patient presented with Suzuki grade I.

The six patients with nonclassical symptoms were found to have Suzuki grade III disease in four cases, grade IV in one case, and one with grade V. In three patients (9%), angiography demonstrated a diminutive superficial temporal artery (STA) leading to surgical planning changes and indirect bypass alone.

**SPECT method**
Post-acetazolamide results were characterized as increased perfusion, decreased perfusion, and no change. In total, 50% (17/34) of patients were found to have decreased perfusion after the addition of acetazolamide and 38% (13/34) had abnormal SPECT with no change after acetazolamide.

In the subcategory of patients with no or minimal symptoms, three patients had normal SPECT before acetazolamide. Another three patients were found to have increased perfusion with the addition of acetazolamide. None of these six patients underwent surgery. Patients who underwent surgery were more likely to have decreased perfusion with the administration of acetazolamide (P < 0.05). There was no significant association between type of presentation (hemorrhage vs. ischemia vs. other) and SPECT findings post acetazolamide (P > 0.05).

**MRA NOVA**
All patients were found to have abnormal MRA NOVA. For the four patients with normal brain MRI, the MRA
NOVA showed decreased flow in the diseased vessels seen on angiography. Flow values were found to be abnormal in all vessels. The average vessel flow on the affected M1 was 13 ml/min, significantly lower than historical controls ($P < 0.05$) [5].

**Treatment**

In total, 26 out of 34 patients underwent 32 surgical bypass procedures. Of the 32 bypasses, 11 were indirect in the form of encephaloduroarteriosynangiosis (EDAS) and the remaining 21 were direct or combined bypasses. Indirect bypass alone was done whenever the donor or recipient vessel size was deemed sub-optimal for a direct bypass and per the surgeon’s discretion. Six patients had follow-up revascularization procedures of their contralateral hemisphere. Eight out of the 34 patients did not undergo surgical revascularization as mentioned above (Table 3). An example case can be seen in Figure 1.

| Presentation          | Transient symptoms or minor | Permanent deficit due to ischemia | Permanent deficit due to hemorrhage |
|-----------------------|-----------------------------|---------------------------------|-----------------------------------|
|                       | 17.6% (9/34)                | 47% (16/34)                     | 26.4% (9/34)                      |

| MRI                   | MRI                          | MRI                             |
|-----------------------|------------------------------|---------------------------------|
| Negative              | 33% (3/9)                    | Negative                        | 0                                |
| Ischemia              | 56% (6/9)                    | Ischemia                        | 16/16 (100%)                     |
| Hemorrhage            | 0                            | Hemorrhage                      | 0                                |

| MRA NOVA              | MRA NOVA                     | MRA NOVA                        |
|-----------------------|------------------------------|---------------------------------|
| Normal                | 0                            | Normal                          | 0                                |
| Abnormal              | 100% (9/9)                   | Abnormal                        | 100% (16/16)                     |

| SPECT with acetazolamide | Increased perfusion | 33% (3/9) | No change | 33% (3/9) | Decreased perfusion | 33% (3/9) |
|--------------------------|--------------------|-----------|-----------|-----------|--------------------|-----------|
| Increased perfusion      | 0                  | 50% (5/10)| 50% (5/10)| 50% (8/15) |
| No change                |                    | 22% (2/9) |           |           |
| Decreased perfusion      |                    |           | 78% (7/9) |

| Surgery | Yes | 33.3% (3/9) | Yes | 100% (16/16) | Yes | 78% (7/9) |
|---------|-----|-------------|-----|-------------|-----|-----------|
| No      | 66.7% (6/9) | 0         | 0   | 22% (2/9)   |

**TABLE 3: Patient imaging findings based on surgical decision**

SPECT: single photon emission computed tomography; MRA: magnetic resonance angiography; NOVA: Non-invasive Optimal Vessel Analysis.
FIGURE 1: Case example

Imaging of an example patient undergoing surgical revascularization. (A) Preoperative angiogram demonstrating supraclinoidal ICA and MCA stenosis as well as early moyamoya collaterals with (B) MRA NOVA demonstrating no flow in the RMCA and (C) showing DWI restriction on initial MRI in a watershed region. The patient underwent right-sided STA to MCA bypass with (D) postoperative MRA NOVA showing bypass flow of 37 ml/min and (E) postoperative angiography of the external carotid artery demonstrating good flow in the bypass graft.

ICA: internal carotid artery; MCA: middle cerebral artery; RMCA: right middle cerebral artery; DWI: diffusion-weighted imaging; STA: superficial temporal artery; MRA: magnetic resonance angiography; NOVA: Non-invasive Optimal Vessel Analysis; RACA2: right anterior cerebral artery A2; LACA2: left anterior cerebral artery A2; LMCA: left middle cerebral artery; RACA: right anterior cerebral artery; LPCOM: left posterior communicating artery; RPCA: right posterior cerebral artery; BA: basilar artery; LPCA: left posterior cerebral artery; RICA: right internal carotid artery; LICA: left internal carotid artery; RSTA: right superficial temporal artery.

In total, 15% (4/26) of patients experienced complications: one hyperperfusion syndrome, one postoperative stroke, one pseudomeningocele, and one patient with deep vein thrombosis. All complications, except for the postoperative stroke, occurred in patients with direct bypass. In patients undergoing direct bypass, bypass patency was confirmed in all but one patient (20/21 patients, 95% patency). The long-term bypass patency and hemodynamic evaluation are beyond the scope of this paper.

Surgical decision-making and preoperative imaging impact

Surgical decision-making was predominantly influenced by symptomatology for symptomatic patients and by SPECT findings. In total, 76% of patients underwent surgery. Standard MRI failed to change the decision for surgery as the patients with normal MRI all underwent surgery. MRA NOVA was abnormal in all patients, so its impact on decision-making is unclear. Eight patients did not undergo surgery because of their symptomatology or workup. Of those eight, three did not receive surgery as they were minimally symptomatic with normal SPECT findings. Three patients had a SPECT demonstrating increased perfusion (Table 3). Two died prior to surgery due to the initial hemorrhage. However, those two patients would have been surgical candidates had they not passed. Preoperative formal cerebral angiography did alter surgical strategy in three of the minimally symptomatic patients (11%) prompting indirect bypass due to a small STA.

Discussion

Most patients with moyamoya initially present with symptoms related to their pathology: transient ischemic attack (TIA), infarct, or hemorrhage [1]. Inevitably, a CT or MRI is done. For symptomatic patients, noninvasive vascular imaging is typically obtained with either a CTA or MRA [6,7]. Subsequently, the patient will typically undergo cerebral angiography to confirm the moyamoya diagnosis [6]. At this point, there are currently many diagnostic studies to choose from to aid in the formation of a therapeutic plan. However, we demonstrated in this paper that these modalities may offer little utility in therapeutic decision-making. In the era of rising healthcare costs, efficient and appropriate utilization of resources without jeopardizing...
Conclusions

In our cohort of patients with moyamoya disease and syndrome, it was initial presenting symptoms that...
drew the decision for surgery. Advanced hemodynamic imaging was useful as a noninvasive tool to track surgery to evaluate patients with only minor symptomatology and to assess contralateral disease burden.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Feinstein Institute for Medical Research issued approval 16-0357. This research has been approved by the Feinstein Institute for Medical Research IRB. Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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