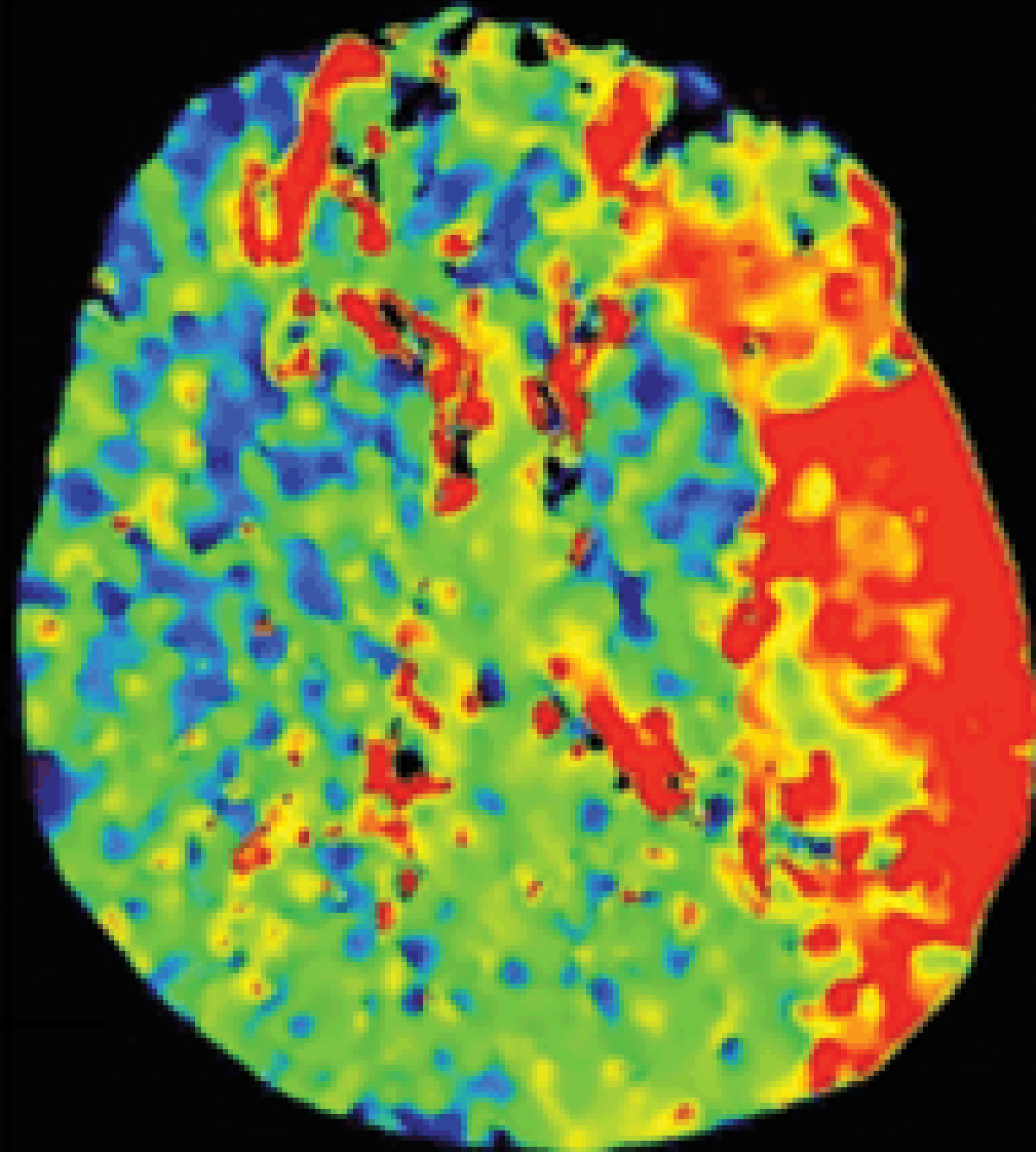

Introduction

Cerebral blood flow

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The unique characteristics of cerebral blood flow and metabolism make this topic relevant to all aspects of the care of the neurosurgical patient. One of the unique characteristics of the brain is its high consumption of total energy compared with other organs of the body relative to its weight. With little in the way of energy storage, the brain is exquisitely dependent on a constant, uninterrupted, appropriate amount of blood flow at the global and regional level. More than half of the blood flow is devoted to supporting neuronal transmission, while the remainder is necessary for maintenance of cellular function and viability. Measurement and regulation of cerebral blood flow in the neurosurgical patient is critical to optimizing outcome following any injury or disease process that may put the blood supply to all or part of the brain in jeopardy. This issue of *Neurosurgical Focus* examines the noninvasive measurement of cerebral blood flow by near-infrared spectroscopy and the treatment of a case of an embolic stroke from infective endocarditis by endovascular techniques.
(http://thejns.org/doi/abs/10.3171/2011.12.FOCUS11353)

Disclosure

The authors report no conflict of interest.

Please include this information when citing this paper: DOI: 10.3171/2011.12.FOCUS11353.

Neurosurg Focus 32 (2):E1, 2012

Endovascular intervention for acute stroke due to infective endocarditis

Case report

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The overall incidence of neurological complications due to infective endocarditis is as high as 40%, with embolic infarcts more common than hemorrhagic strokes. The standard of care for typical strokes does not apply to infective endocarditis because there is a substantial risk of hemorrhage with thrombolysis. In the last decade there have been multiple case reports of intravenous and intraarterial thrombolysis with successful outcomes for acute strokes with related infective endocarditis, but successful endovascular interventions for acute strokes associated with infective endocarditis are rarely reported. To the authors' knowledge, this report is the first case in the literature to use a mechanical retrieval device in successful vegetation retrieval in an infective endocarditis acute stroke. Although an interventional approach for treatment of acute stroke related to infective endocarditis is a promising option, it is controversial and a cautious clinical decision should be made on a case-by-case basis. The authors conclude that this approach can be tested in a case series with matched controls, because this condition is rare and a randomized clinical trial is not a realistic option.
(http://thejns.org/doi/abs/10.3171/2011.11.FOCUS11263)

Key Words • **middle cerebral artery** • **infective endocarditis** • **ischemic penumbra** • **interventional endovascular procedure** • **penumbra retrieval device**

Beginning as a subtle feature such as unexplained prolonged fever, untreated infective endocarditis may end up as unstable vegetation producing infective emboli in major blood vessels supplying the brain, kidney, and other vital organs. More than one-third of cases of infective endocarditis are associated with neurological complications such as embolization, hemorrhagic conversion of infarct, cerebral mycotic aneurysm, meningitis, brain abscess, and seizures.[14] Death due to stroke that is related to infective endocarditis is substantially higher when compared with other strokes.[19] Recently the incidence of infective endocarditis has increased due to the vast number of cardiac procedures performed, and so has the secondary CNS complications.[8] The diagnosis of infective endocarditis is based on a constellation of clinical features taking into consideration a detailed medical history, physical examination, blood culture, laboratory results, and imaging.[1] The most accepted criteria used for making the diagnosis of infective endocarditis are the modified criteria of Duke.[15] Even though neurological deficits are the same, standard stroke treatment guidelines do not apply when treating stroke related to infective endocarditis in view of the high risk of hemorrhagic conversion of infarct, mycotic aneurysm formation, and underlying infection. Thus treatment is based on treating the infection with a prolonged course of antibiotics and supportive care. Intravenous thrombolytics are contraindicated in acute situations, necessitating clinicians find alternate methods to address the embolized clot or vegetation.[3,5,21] In the literature there are multiple case reports of using intravenous tPA, intraarterial tPA, and even endovascular interventions in stroke related to infective endocarditis, which embolden us to attempt interventional options for treating this otherwise devastating condition.

Abbreviations used in this paper: MCA = middle cerebral artery; tPA = tissue plasminogen activator.

Case Report

History and Examination. This 67-year-old woman had a history significant for a bovine mitral valve replaced 6 months prior, experienced a methicillin-resistant *Staphy-*

lococcus aureus line infection in the postoperative period, completed antibiotic treatment with no complications, and experienced intermittent atrial fibrillation on warfarin. She was admitted to the hospital for a 1-day duration of right-sided weakness, loss of appetite, and lethargy for 1 week. On admission she was found to have altered sensorium, thrombocytopenia, fever (38.8°C), atrial fibrillation (ventricular rate 107 beats per minute), and mild renal insufficiency. An examination revealed she was stuporous, had dysarthric speech, right-sided facial droop, right-sided tongue deviation, and right hemiparesis. A sensation and cerebellar system examination was not performed because of the patient's clinical condition.

Magnetic resonance imaging results were consistent with an infarct of the left posterior inferior cerebellar artery and multiple small punctate infarcts involving the posterior left temporal lobe, occipital lobe, and left precentral gyrus. A CT angiogram of the head and neck did not reveal intra- or extracranial vessel occlusion. This multiple vascular distribution raised the concern for a thromboembolic source. With the above clinical presentation, medical history, and examination, a suspicion of infective endocarditis was at the top of the differential diagnosis. The patient was not a candidate for tPA treatment given the time between the onset of the symptoms and presentation, possibility of infective endocarditis, and other risk factors. A transthoracic echocardiogram showed an ejection fraction of 30%–35%, moderate left ventricular systolic dysfunction, and mitral valve bioprosthesis with multiple elongated highly mobile masses extending into the left ventricle during diastole, likely vegetations. Blood cultures were growing Gram-negative vancomycin-resistant rods and the patient was started on antibiotics. Her right-sided weakness was improving greatly compared with admission. However, 1 week later while the patient was an inpatient she developed acute right-sided body weakness, global aphasia, and forced left gaze deviation with examination consisting of the flaccid right upper and lower extremity and a brain CT angiogram (Fig. 1), which showed a distal M_1 cutoff by either a thrombus or vegetation. After careful review of the case we decided to perform endovascular intervention to prevent poor neurological outcome from this large vessel occlusion and contraindication to use tPA.

Before the endovascular procedure was performed, a head CT angiogram with perfusion (Aquilion ONE Toshiba scanner) showed 2 hypodense lesions involving the left cerebellum and the left higher cerebral convexity involving the MCA, with no early signs of infarction or bleeding. As noted, the CT angiogram showed a left MCA occlusion between the M_1 and M_2 segments (Fig. 1). The CT perfusion scan showed increased time to peak (Fig. 2A) in the areas supplied by the left MCA, with increased cerebral blood volume (Fig. 2B), a focal area of decreased volume, and an area of increased mean transit time (Fig. 2C), indicating low volume infarct and a large area of tissue at risk; Figure 2D shows cerebral blood flow for comparison. The following day MR imaging was performed using FLAIR and diffusion-weighted MR imaging (Fig. 3). These images indicated that the area of acute restriction and infarction was much smaller than the area of ischemic penumbra on the CT perfusion.

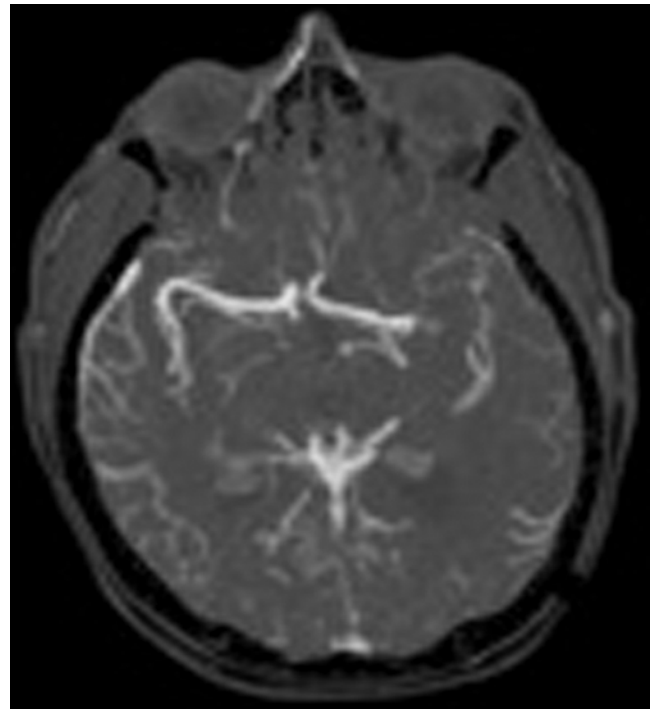

Fig. 1. Axial CT angiogram with maximum intensity projection reveals a left MCA occlusion between the M_1 and M_2 segments.

Operation and Postoperative Course. A conventional angiogram-directed Penumbra retrieval device (Penumbra Inc.) was used to gain access by canalizing the femoral artery with a 6 Fr sheath, and a 90-cm guiding catheter was used and advanced via the left internal carotid artery to the M_1 segment, where the thrombus was evacuated. The aspiration catheter, along with a separator, was used to debulk and remove the thrombus. Control cerebral angiograms were obtained every 3–4 minutes per manufacturer recommendations to monitor the progression of the aspiration and to reposition the reperfusion catheter to the new thrombus interface. Recanalization was established and Thrombolysis in Cerebral Infarction scores of 2 or 3 of the left MCA and its major branches were recorded. The following day MR imaging showed the area of restriction was significantly decreased compared with the volume of brain tissue loss, due to infarction. The patient was showing some improvement but a week later developed sudden shortness of breath and relative hypoxemia, concerning for a pulmonary embolism. The patient and family requested "do not resuscitate" status and did not want any more interventions, therefore she was transferred to hospice care.

Discussion

Infective endocarditis, the infection of the inner layer of the heart valves, is most commonly caused by the *Streptococcus viridans* group and *S. aureus*.[6,24] In advanced cases when antibiotic treatment is not initiated in a timely fashion, unstable infective vegetations frequently develop, which exhibit a high propensity to embolize into the blood stream causing ischemic events in the brain,

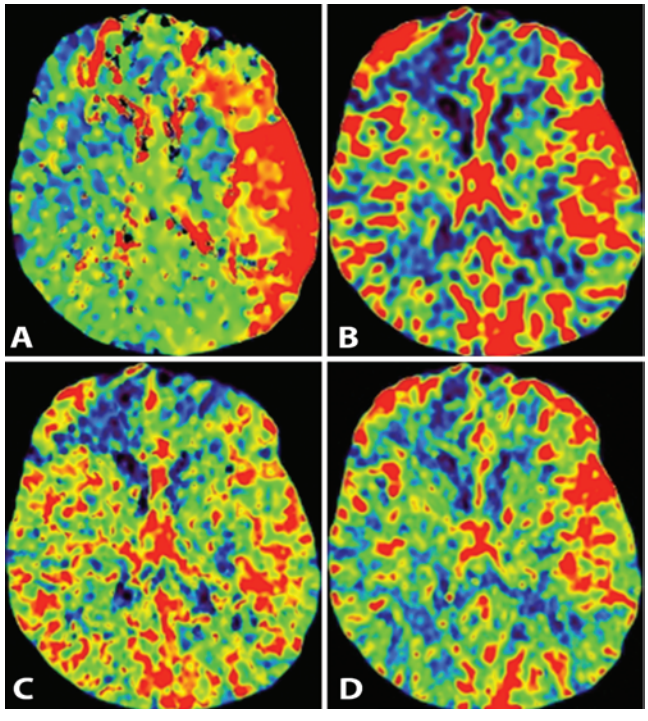

Fig. 2. Preoperative axial CT perfusion images of the patient. Images show increased time to peak **(A)** in the areas supplied by the left MCA, a matched area of increased cerebral blood volume **(B)**, and an area of increased mean transit time **(C)** with a small focal area of decreased volume and decreased mean transit time, indicating low volume infarct and a large area of tissue at risk. Cerebral blood flow is shown for comparison **(D)**.

heart, lungs, and intestines.[3,7,11,13] Intracranial hemorrhage occurs in 5% of patients with infective endocarditis,[24] either due to hemorrhagic conversion of acute ischemic strokes or the formation of mycotic aneurysms.[16,22] Generally, treatment with intravenous thrombolysis up to 4.5 hours from symptom onset has become the standard of care in acute ischemic strokes.[10,17] To date, there has been much debate on how to treat ischemic embolic strokes from infective endocarditis. Administration of tPA to patients with acute ischemic stroke and infective endocarditis is not well documented and therefore not considered

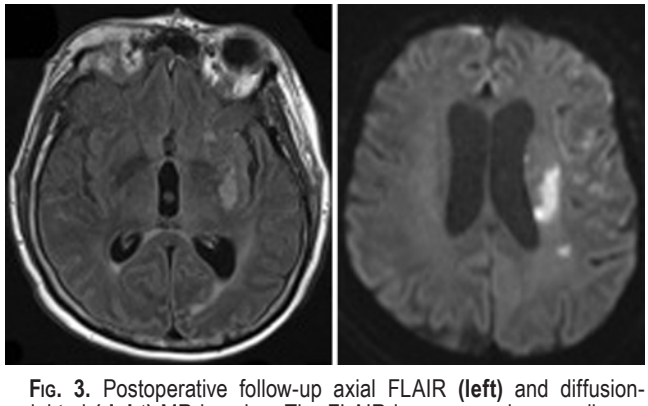

Fig. 3. Postoperative follow-up axial FLAIR **(left)** and diffusion-weighted **(right)** MR imaging. The FLAIR image reveals a small area of signal hyperintensity in the left basal ganglia representing the final infarct core. The diffusion-weighted image shows a small area of acute restriction in the left periventricular subcortical white matter.

safe by the American Heart Association, Stroke Council, and American Stroke Association.[1] For instance, although the use of thrombolytic therapy in patients with infective endocarditis has been reported without hemorrhagic complications,[12,20] many cases show the use of tPA for acute ischemic stroke significantly increases the risk of bleeding. In a report by Bhuva et al.,[3] 3 patients suffering from acute ischemic stroke due to infective endocarditis developed multifocal intracranial hemorrhages. Intracranial hemorrhage has also been reported in patients receiving intravenous tPA for myocardial infarction due to infective endocarditis.[6] Another option is administration of recombinant prourokinase up to 6 hours after the onset of symptoms, but this treatment has not been approved by the US FDA.[9] Therefore, a more conservative approach is treatment of the blood infection and the complications thereafter once they develop, as has been the policy used in infective endocarditis-associated acute ischemic stroke.

In the past few years, the use of interventional endovascular methods in treating infective endocarditis–associated acute ischemic stroke has not been extensively reported nor implemented. Several cases initially addressed the use of endovascular intervention to treat mycotic aneurysms resulting from infective endocarditis,[4,11,12,18,23] but only a few cases have been reported using interventional endovascular methods in infective endocarditis–associated ischemic strokes, including catheter-guided intraarterial tPA.[2,21]

In this article we present a potential option in the treatment of infective endocarditis-associated acute ischemic stroke: the successful use of an endovascular method in a case in which thrombolytic therapy was not an option. Using a Penumbra retrieval device, we were able to remove the clot and decrease the volume of brain tissue loss due to infarction, without significantly increasing the patient's risk of hemorrhage. From these results, it appears that endovascular intervention can provide a promising treatment for stroke patients who are not eligible for thrombolytic therapy. These results need further validation for safety and effectiveness, but this initial study is promising.

Disclosure

Dr. Peters serves on the speakers bureau for Toshiba America Medical Systems. Dr. Mocco received research support from ev3; has served as a consultant to Concentric and Actelion; serves on the advisory board of Lazarus Effect, Edge Therapeutics, and NFocus; and has ownership in Codman Neurovacular.

Author contributions to the study and manuscript preparation include the following. Conception and design: Waters, Dababneh, Ford, Taimeh, Mocco. Acquisition of data: Waters, Dababneh, Ford, Taimeh. Analysis and interpretation of data: Waters, Dababneh, Ford, Taimeh, Mocco. Drafting the article: Waters, Dababneh, Ford. Critically revising the article: Dababneh, Hedna, Ford, Peters, Mocco. Reviewed submitted version of manuscript: Waters, Dababneh, Ford, Taimeh, Peters, Mocco. Approved the final version of the manuscript on behalf of all authors: Waters. Statistical analysis: Waters, Dababneh, Ford, Mocco. Administrative/technical/material support: Waters, Dababneh, Ford, Mocco. Study supervision: Waters, Dababneh, Hedna, Ford, Peters, Mocco.

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Manuscript submitted September 27, 2011.
Accepted November 8, 2011.
Please include this information when citing this paper: DOI: 10.3171/2011.11.FOCUS11263.

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Neurosurg Focus 32 (2):E2, 2012

Validation of frontal near-infrared spectroscopy as noninvasive bedside monitoring for regional cerebral blood flow in brain-injured patients

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Object. Near-infrared spectroscopy (NIRS) offers noninvasive bedside measurement of direct regional cerebral arteriovenous (mixed) brain oxygenation. To validate the accuracy of this monitoring technique, the authors analyzed the statistical correlation of NIRS and CT perfusion with respect to regional cerebral blood flow (CBF) measurements.

Methods. The authors retrospectively reviewed all cases in which NIRS measurements were obtained at a single, academic neurointensive care unit from February 2008 to June 2011 in which CT perfusion was performed at the same time as NIRS data was collected. Regions of interest were obtained 2.5 cm below the NIRS bifrontal scalp probe on CT perfusion with an average volume between 2 and 4 ml, with mean CBF values used for purposes of analysis. Linear regression analysis was performed for NIRS and CBF values.

Results. The study included 8 patients (2 men, 6 women), 6 of whom suffered subarachnoid hemorrhage, 1 ischemic stroke, and 1 intracerebral hemorrhage and brain edema. Mean CBF measured by CT perfusion was 61 ml/100 g/min for the left side and 60 ml/100 g/min for the right side, while mean NIRS values were 75 on the right and 74 on the left. Linear regression analysis demonstrated a statistically significant probability value ($p < 0.0001$) comparing NIRS frontal oximetry and CT perfusion–obtained CBF values.

Conclusions. The authors demonstrated a linear correlation for frontal NIRS cerebral oxygenation measurements compared with regional CBF on CT perfusion imaging. Thus, frontal NIRS cerebral oxygenation measurement may serve as a useful, noninvasive, bedside intensive care unit monitoring tool to assess brain oxygenation in a direct manner.

(http://thejns.org/doi/abs/10.3171/2011.12.FOCUS11280)

Key Words • near-infrared spectroscopy • cerebral oxygenation • computed tomography perfusion • cerebral blood flow

Early detection and correction of cerebral ischemia is an essential part of the ICU treatment of patients after traumatic brain injuries or hemorrhagic and ischemic stroke.[14,24] Current methods used to monitor cerebral hemodynamics have significant limitations. Stable xenon-enhanced CT, PET, SPECT, or perfusion-weighted MR imaging requires transportation of a critically ill patient, which is impractical for most ICU settings and carries the risk of clinical deterioration. Other bedside methods such as jugular bulb oximetry indicate changes in CBF without direct measurement of CBF.

Near-infrared spectroscopy offers the advantage of measuring brain tissue arteriovenous oxygenation via an emitted near-infrared light that penetrates the scalp and underlying brain tissue and detects the absorption of oxygenated hemoglobin compared with deoxygenated hemoglobin. As a result, NIRS provides a noninvasive, real-time, bedside monitoring tool of cerebral oximetry in critically ill brain-injured patients without exposing patients to radiation. The correlation of CBF as measured by NIRS and CT perfusion has not been studied previous-

Abbreviations used in this paper: CBF = cerebral blood flow; CBV = cerebral blood volume; ICH = intracerebral hemorrhage; MTT = mean transit time; NIRS = near-infrared spectroscopy; SAH = subarachnoid hemorrhage.

ly, and we hypothesized that there is a linear correlation between CBF as evaluated by NIRS and CT perfusion measurements, which would validate the use of NIRS as a noninvasive tool of direct CBF evaluation.

Methods

We retrospectively reviewed all patients admitted to the Mayo Clinic in Jacksonville, Florida, from February 2008 through June 2011 with SAH, ischemic stroke, or ICH who underwent CT perfusion studies. Computed tomography perfusion was performed at the same time as NIRS data were collected. The CT perfusion method uses an iodinated contrast agent administered intravenously with subsequent acquisition of repeated high temporal resolution images. An increase in Hounsefield units can be measured in the intravascular and tissue beds. The transient increase in radiation attenuation is proportional to the amount of contrast in a given region and the speed at which the agent passes from arterial to venous circuits through the tissue bed.[9] The CT perfusion technique is based on the central volume principle, which relates CBF, CBV, and MTT in the following equation: CBF = CBV/MTT. Contrast agent time-concentration curves are generated in arterial and venous regions of interest and in each pixel. Deconvolution of arterial and tissue enhancement curves provides the MTT. Cerebral blood volume is calculated as the area under the curve in a parenchymal pixel divided by the area under the curve in an arterial pixel. The central volume equation can then be solved for CBF.[9]

The CT perfusion images were analyzed on a Siemens Leonardo postprocessing workstation. The CT perfusion regions of interest were obtained 2.5 cm below the NIRS frontal scalp probes with an average region of interest volume of 2–4 ml. The CT perfusion data parameters reviewed included CBF, CBV, time to drain, and MTT. Mean values and average SD were established for all CT perfusion parameters.

Bifrontal NIRS optodes (Casmed) were placed on the scalp per the manufacturer's recommendations, separated by an interoptode distance of 4–5 cm. The NIRS retrieved cerebral oximetry values 2.5 cm from the level of the scalp for bifrontal hemispheres. The data received were compared with the CT perfusion data. Both CT perfusion and NIRS were used within as close a time frame as possible (≤ 2 hours apart or ideally ≤ 32 minutes) to ensure comparable study data. The NIRS cerebral oximetry data recorded closest in time to the complete CT perfusion examination were analyzed.

Comparative data analysis was performed using the GraphPad Prism statistics software. A linear regression analysis was performed for a "best fit" standard 95% CI analysis. Statistical significance was defined as $p < 0.05$.

Results

Of 1287 patients admitted to the neuroscience ICU or hospital during the study period with SAH, ICH, or stroke-related diagnosis, we identified 16 data sets from 8 paired examinations of CT perfusion versus NIRS cerebral oximetry that met study criteria. Patient demographic data included 2 men and 6 women with a mean age of 68.4 years (range 47–86 years). Six patients suffered SAH, 1 had ischemic stroke, and 1 had ICH and brain edema. Mean values established for CBF in the CT perfusion study were 61.2 ± 21.28 ml/100 g/min (range 43.6–76.4 ml/100 g/min) for the left hemisphere and 60.2 ± 21.21 ml/100 g/min (range 43.4–77.4 ml/100 g/min) for the right hemisphere. Mean CBVs were 3.25 ± 1.04 ml (range 2.34–3.93 ml) for the left and 3.27 ± 1.00 ml (range 2.29–4.48 ml) for the right. The mean of MTT was 3.32 ± 0.709 seconds (range 3.01–3.78 seconds) for the left and 3.45 ± 0.837 seconds (range 3.01–4.22 seconds) for the right. The mean time to drain was 3.96 ± 0.694 seconds (range 2.65–4.99 seconds) for the left and 4.07 ± 0.942 seconds (range 2.57–5.15 seconds) for the right. The data collected by the NIRS device were as follows: mean value for left frontal oximetry was 74.5 ± 9.02 oximetry units (range 60–87 oximetry units) and 75.2 ± 10.7 oximetry units (range 56–84 oximetry units) for the right. Analysis of the linear regression revealed a p value < 0.0001 comparing NIRS frontal oximetry and CT perfusion–obtained CBF values (Fig. 1).

Discussion

We found a linear correlation between the use of frontal NIRS cerebral oxygenation and frontal CBF as measured by the CT perfusion method. This association has not been reported in any prior human studies that we could find and validates the accuracy of CBF measurement by NIRS.

Near-infrared spectroscopy oximetry has been evaluated in the use of vasospasm,[10] but not directly with CT perfusion CBF. These previous evaluations were animal studies using NIRS with indocyanine green in piglets[2,16] and other experiments.[1,5,6,10,19] We believe that our data, although small in number, may validate the use of NIRS as an important noninvasive real-time bedside application for NIRS in critically ill brain-injured patients who are too unstable to transport to a CT scanner for the CT perfusion-derived method. Near-infrared spectroscopy has the additional advantage of not exposing patients to radiation, a concern that is significant in patients undergoing numerous CT perfusion scans during prolonged ICU stays.

Some inherent technical limitations of NIRS need to be addressed. Cerebral blood flow measurements are of a regional nature, in contrast to CT perfusion and xenon-enhanced CT, which allow a more global assessment of brain perfusion. Also, NIRS measured approximately 2.5 cm down from the skin level, which was directly compared with regions of interest on the CT perfusion-derived regional CBF.[3] This information must be regarded with caution by clinicians. Regional information such as invasive brain tissue oxygenation (for example), Licox probes, and cerebral microdialysis probes do not always correlate with global cerebral metabolic states or even hemispheric states and are sometimes very specific to the region of injured brain. In Fig. 2, for example, in the upper left image, the posterior right hemisphere shows a hemorrhage with surrounding edema and low CBF, which would be missed by a left frontal NIRS oxygenation measurement.

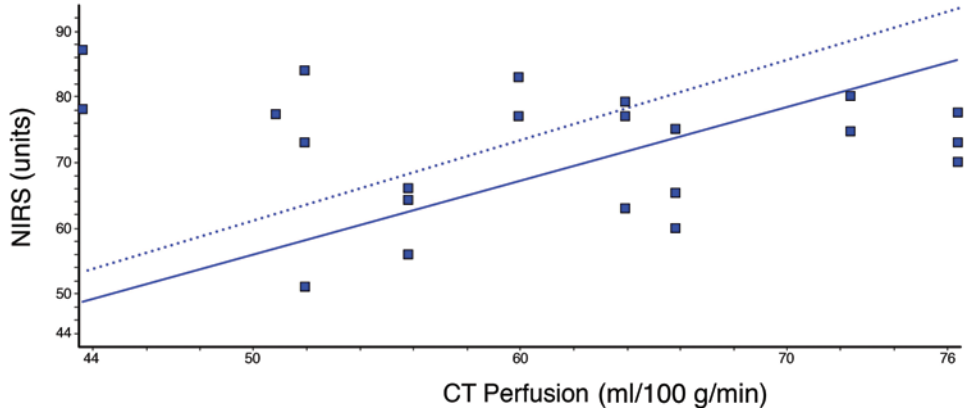

Fig. 1. Linear regression analysis comparing NIRS frontal oximetry and CT perfusion–obtained CBF values ($p < 0.0001$). The *solid line* represents the linear regression line and the *dashed line* represents the 95% CI. Twenty-two data points are shown because 3 patients underwent 2 CT perfusions with NIRS correlation.

Other methods of CBF measurement exist and their relative advantages and disadvantages are noted in Table 1. The CT perfusion method is a commonly used method in the neurointensive care unit, using iodinated contrast to measure CBF, due to its ease of use, speed of imaging, and wide availability.[6,21,22] However, acquiring measurements by means of CT perfusion requires transportation of critically ill patients, which poses patient safety risks of invasive catheter dislodgement (central venous lines or invasive brain catheters/probes), lowering the head of the bed during transport (increasing the risk of ventilator-associated pneumonia or raised intracranial pressure in patients with borderline intracranial compliance), exposure to ionizing radiation, and risk of possible allergic or anaphylactic reaction due to iodinated contrast material, or even contrast-induced nephropathy.[15,23] The peak dose from ionizing radiation in CT perfusion is approximately 325–435 mGy and depends on many factors including acquisition technique and type of scanner.[21] Early transient erythema may occur in some patients at a skin dose of 2000 mGy.[7] It is apparent that several CT perfusion scans in a short period of time could cause transient erythema and even "stripe alopecia."[7] There has been increasing scrutiny by the public of radiation dosing within the hospital.[7] Xenon-enhanced CT is another method used to measure CBF and is regarded as a potential gold standard for regional CBF measurement due to its superior spatial resolution, accuracy, and reproducibility.[6,17] However, xenon-derived CBF or xenon-enhanced CT is not widely available in many ICUs. Also, xenon has been known to be a vasodilator and may increase CBF (up to 100%).[8] One key advantage of the use of NIRS is its availability to be performed at the bedside, even in unstable patients who cannot be transported to the CT suite.[12]

Another method of measuring cerebral O_2 metabolism is the jugular venous catheter and jugular venous O_2 saturation by placement of a venous catheter into the internal jugular vein in the patient's neck. Jugular venous O_2 saturation estimates jugular venous oxygenation via a jugular vein catheter oximeter within the internal jugular vein and typically requires recalibration every 8–12 hours.[21] Jugular venous O_2 saturation can provide an indirect measurement of CBF by "supply and demand physiology" similar to NIRS, albeit with some differences explained below. When jugular venous O_2 saturation is low (< 50% for > 10 minutes in duration), it generally indicates decreased "supply physiology" such as very low hemoglobin defined by the delivery of O_2 equation: de-

TABLE 1: Different methods of CBF measurement

Method of CBF Measurement	Advantages	Disadvantages
Kety-Schmidt model	reliable measurement of global CBF[25]	inhalation mixture of O_2 & N_2O[25]
xenon-enhanced CT	accurate, high spatial quality, extensively researched[4]	not widely available, xenon known as a vasodilator[19]
CT perfusion	perhaps more widely used than xenon-enhanced CT, quantifies CBF, CBV, MTT, & time to peak[26]	x-ray exposure, bolus injection of iodine dye (dye allergy & anaphylactic risks), risk of contrast nephropathy, & transportation of critically ill[4]
PET	standardized, quantitative measurements of CBF & CBV, excellent spatial resolution[26]	not widely available to most ICUs, radioactive components[26]
MRI w/ perfusion-weighted imaging	can demonstrate structural brain changes as well as perfusion, & does not require use of ionizing radiation; measures CBF, CBV, MTT, & time to peak[13,26]	Gd intravenous contrast agent administration, may be problematic in renal failure, longer scan time vs CT[26]
NIRS w/ indocyanine green dye (animals)	noninvasive, no major side effects reported w/ use[5]	not standardized in humans, complex distortion by skin tissue[2]

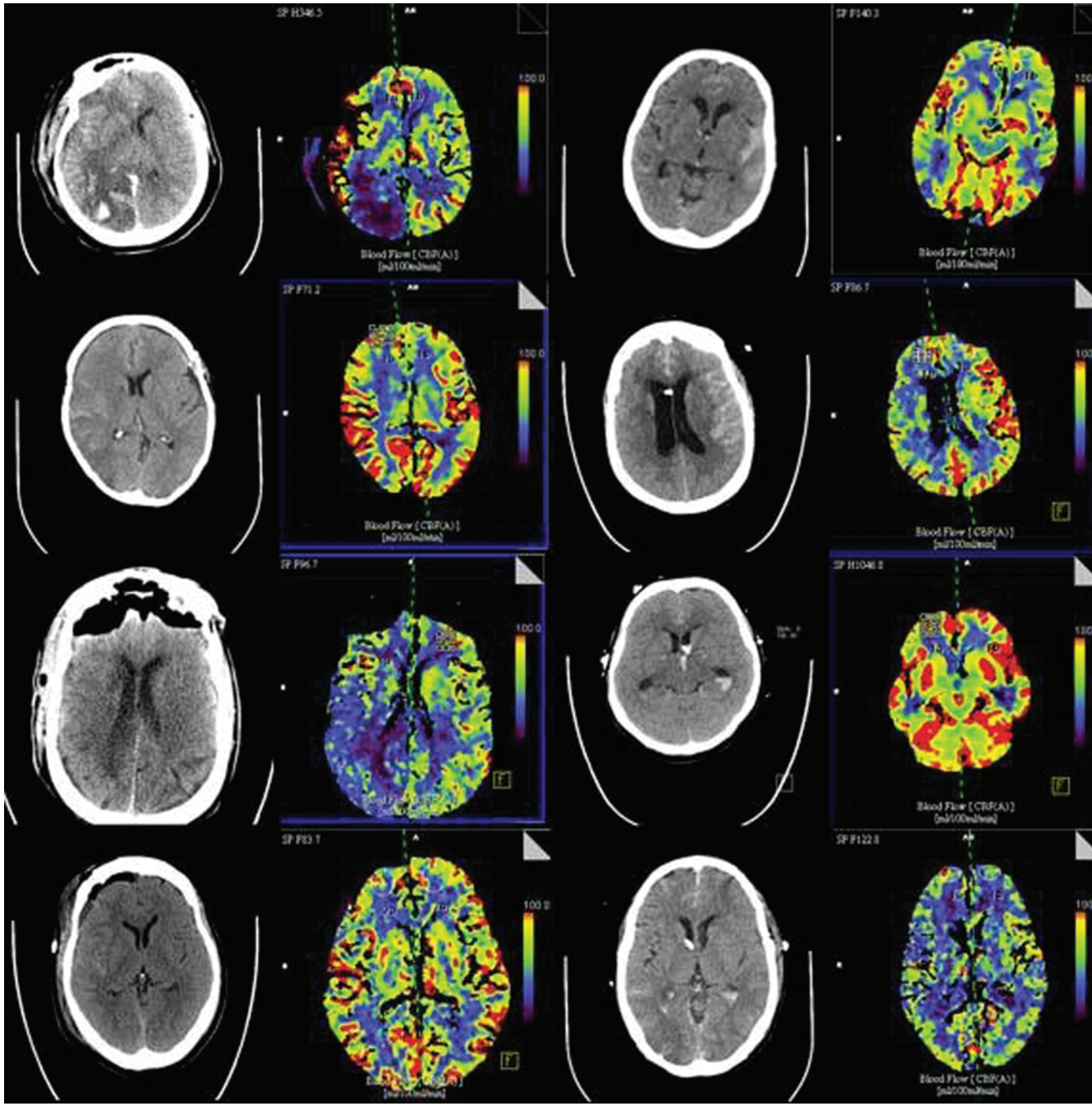

Fig. 2. Axial CT head and CT perfusion images of all 8 patients included in the study.

livery of O_2 = cardiac output × carrying capacity of O_2. The carrying capacity of O_2 is further defined as follows: (hemoglobin × 1.36 × saturation of O_2) + (partial pressure of O_2 × 0.0031). Other low "supply" physiological considerations include low cardiac output or poor oxygenation via the variables partial pressure of O_2, low hemoglobin, or saturation of O_2. Conversely, an increase in cerebral metabolism (increased demand) can similarly change the jugular venous O_2 saturation (or NIRS) by increased cerebral consumption of O_2 or increased O_2 extraction fraction. In fact, the arteriovenous O_2 content difference (carrying capacity of O_2 – the venous O_2 content of the blood) multiplied by the cardiac output is defined as O_2 demand by the Fick Principle.[21] Downsides to jugular venous O_2 saturation monitoring include invasive venous puncture and risks of central bloodstream-related infection (which is a national benchmark of inpatient quality), jugular vein thrombosis, and potential raised intracranial pressure from jugular venous outflow obstruction.[13]

The NIRS method is an emerging technology for measuring O_2 content via near-infrared light (approximately 600–900 nm) originally described by Jobsis,[11] in which near-infrared light emitted light through a cat's head. Neural activity is ultimately fueled by glucose-

oxidative metabolism and is dependent upon delivery of oxygenated hemoglobin transported from the blood to the tissue and results in exchange of oxygenated hemoglobin to the deoxygenated hemoglobin form.[21] In mammals, hemoglobin is a strong "chromophore" or light-absorbing molecule. Oxygenated and deoxygenated hemoglobin consist of different optical absorbing properties, which allows for its detection by NIRS; the maximum absorption of oxygenated hemoglobin is approximately 900 nm of near-infrared light and is approximately 760 nm in deoxygenated hemoglobin.[3] Lambert-Beer described a relationship that is a ratio of oxygenated hemoglobin versus deoxygenated hemoglobin via NIRS technology and is used in commercial and patent-specific NIRS measurement algorithms.[20]

Aoyagi described the NIRS method for isolating arterial O_2 saturation, which was described in 1985.[18] This noninvasive technology has emerged as a fairly ubiquitous tool for anesthesia and intraoperative, noninvasive, O_2 saturation monitoring to detect desaturation events in a real-time fashion. Therefore, cerebral NIRS measures combined arteriovenous oxygenated hemoglobin saturation (1/3 arterial and 2/3 venous), which has values that are higher than jugular venous O_2 saturation data and trend up and down depending on supply and demand cerebral physiology. The NIRS light is emitted at the level of the scalp, but measures deeper cerebral brain oxygenation via a "spatially resolved optode technique." Two optodes are separated by a finite distance from the light emitter, and the closer optode measures the superficial scalp tissues' contribution to tissue oxygenation, which is then subtracted from the distal optode measurement, which receives deeper cortical-subcortical brain tissue information.[3,4,21]

Therefore, NIRS indirectly measures CBF via supply and demand cerebral O_2 consumption and O_2 delivery, but not actual CBF directly. However, NIRS oximetry can indirectly assess CBF via a surrogate technique, which can provide some assessment of cerebral ischemia and physiology. To date, the isolation of the pure brain arterial oxygenation saturation via the noninvasive NIRS method remains difficult due to contamination of scalp, bone, and tissues external to underlying brain tissue. The cerebral oximetry devices have difficulty isolating the pulsatile arterial waveform that is distinct from extracerebral tissue compared with the "finger arterial saturation devices" that are commercially available and originally derived from Aoyagi's invention.[13] The NIRS cerebral oximetry technology nonetheless provides clinicians with a potentially useful method of indirectly assessing regional CBF that is noninvasive and provides some insight into neurometabolic states.

This study demonstrates that CT perfusion CBF has a significant linear correlation with NIRS measurement ($p > 0.0001$), although with several limitations. These limitations include the small sample size, a retrospective study design, and lack of a baseline comparative study between CT perfusion and NIRS methodology. Near-infrared spectroscopy is also limited by the thickness of the skull or frontal scalp swelling after craniotomy, which increases the distance from the light emitter and deeper tissues and can be further distorted if large amounts of CSF are present between skin and brain tissue or underlying severe brain atrophy.[12] Also, NIRS sensors are placed in the frontal head location only, which could complicate the estimation of the exact region of interest in CT perfusion imaging based on the depth from the optodes and penetration of NIRS light.

Disclosure

Dr. Hanel serves as a consultant to NeuroVasx and Codman.

Author contributions to the study and manuscript preparation include the following. Conception and design: Taussky, Daugherty, Pooley, Evans, Hanel, Freeman. Acquisition of data: Taussky, O'Neal, Luke, Thorpe, Pooley, Freeman. Analysis and interpretation of data: Taussky, O'Neal, Thorpe, Freeman. Drafting the article: Taussky, O'Neal, Freeman. Critically revising the article: Taussky, O'Neal, Hanel, Freeman. Reviewed submitted version of manuscript: Taussky, O'Neal, Luke, Thorpe, Pooley, Evans, Hanel, Freeman. Approved the final version of the manuscript on behalf of all authors: Taussky. Statistical analysis: Taussky, Luke. Administrative/technical/material support: Thorpe.

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Manuscript submitted October 17, 2011.
Accepted December 2, 2011.
Please include this information when citing this paper: DOI: 10.3171/2011.12.FOCUS11280.
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