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Clinical Study

Safety, efficacy, and cost of intraoperative indocyanine green angiography compared to intraoperative catheter angiography in cerebral aneurysm surgery

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ABSTRACT

Intraoperative angiography in cerebrovascular neurosurgery can drive the repositioning or addition of aneurysm clips. Our institution has switched from a strategy of intraoperative digital subtraction angiography (DSA) universally, to a strategy of indocyanine green (ICG) videoangiography with DSA on an as-needed basis. We retrospectively evaluated whether the rates of perioperative stroke, unexpected postoperative aneurysm residual, or parent vessel stenosis differed in 100 patients from each era (2002, "DSA era"; 2007, "ICG era"). The clip repositioning rate for neck residual or parent vessel stenosis did not differ significantly between the two eras. There were no differences in the rate of perioperative stroke or rate of false-negative studies. The per-patient cost of intraoperative imaging within the DSA era was significantly higher than in the ICG era. The replacement of routine intraoperative DSA with ICG videoangiography and selective intraoperative DSA in cerebrovascular aneurysm surgery is safe and effective.

1. Introduction

Residual aneurysm filling, parent vessel stenosis, and perforating artery compromise have complicated open clipping of aneurysms since the origin of cerebrovascular neurosurgery. In the last decade, our institution and others have advocated the routine or selective use of intraoperative digital subtraction angiography (DSA) to assess aneurysm residual and vessel patency [1–7]. Some neurosurgeons have advocated selective intraoperative DSA use, such as in large or complex aneurysms only, and cited that routine DSA is not necessarily cost-effective [4]. However, our group has previously published a study of routine DSA in all aneurysm clip patients, and found that surgeons could not always predict preoperatively when intraoperative DSA would be useful, suggesting more routine use [5].

Indocyanine green (ICG) is a near-infrared (NIR) fluorescent compound utilized since the 1950s in humans for liver diagnostics and subsequently approved by the US Food and Drug Administration for ophthalmologic angiography in the 1970s. ICG is excreted unchanged via the hepatic system and the incidence of major or minor complications associated with systemic exposure is minimal. The dye is injected intravenously, is quickly plasma-protein bound, and reaches the cerebral vasculature within 30 seconds. The first report of indocyanine green angiography (ICGA) in cerebrovascular surgery utilized a separate NIR light source and NIR-sensitive video camera, but soon afterwards the technology for both the NIR light source and recording was integrated into the surgical microscope [8,9]. This allows for the real-time visualization of vessel flow and aneurysm filling within the surgical field in both arterial and venous phases. In the last decade, our group and others have successfully utilized ICGA in surgery for elective and ruptured cerebral aneurysms, intracranial–extracranial bypass, and cerebral arteriovenous malformations [9–24]. ICGA has similar rates of clip repositioning and parent vessel stenosis when compared head-to-head with either intraoperative or postoperative DSA [9,23,25]. Published studies have focused on the technical sensitivity and specificity of ICGA when compared to a "gold standard" of intraoperative or postoperative DSA in patients receiving both imaging modalities. This literature has established ICGA as a viable alternative to intraoperative DSA, but these studies are focused on technical comparisons of the imaging modalities. However, no study to our knowledge has compared patient outcomes following the replacement of intraoperative DSA with routine ICGA in a clinical practice. While ICG is a more rapid and convenient form of angiography in clinical practice, its value would be much less if its use was not associated with similar or better outcomes. Our institution now routinely employs ICGA during

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aneurysm surgery with the selective use of intraoperative DSA and micro-Doppler techniques; this practice evolved over the era of the Barrow Ruptured Aneurysm Trial (BRAT) [26,27]. Our clinical experience represents a natural comparison of the two diagnostic methods via retrospective review of two "eras": the year prior to BRAT (2002), in which the intent was for all aneurysm clipping patients to receive intraoperative DSA, and the year after BRAT (2007), in which the primary intraoperative angiographic modality for aneurysm clipping patients was to receive ICGA. We assembled the present study not to compare the previously published intraoperative utility of ICGA *versus* intraoperative DSA, but rather to assess if a paradigm shift away from routine intraoperative DSA to routine ICGA with selective intraoperative DSA would result in similar patient outcomes, such as stroke and return to the operating room for unexpected postoperative imaging findings.

2. Methods

2.1. Study population

We retrospectively identified all aneurysms treated via open microsurgical clipping in the years 2002 ("DSA era") and 2007 ("ICG era") at the Barrow Neurological Institute, AZ, USA using a departmental registry. The first 100 patients in each year with available inpatient and outpatient records were identified and analyzed. This study was approved by the St. Joseph's Hospital and Medical Center Institutional Review Board for human research.

2.2. Data collection

Hospital and clinical records were reviewed, as were pre and postoperative imaging studies. Each patient was treated by an experienced cerebrovascular neurosurgeon (R.F.S., P.N., or J.M.Z.). Intraoperative DSA was performed by an endovascular neurosurgeon or a diagnostic neuroradiologist. Patient characteristics identified included age at surgery, sex, aneurysm size and location, the form of intraoperative imaging used, and pre and postoperative neurological deficits. Each patient was assessed for perioperative stroke, defined here as a new permanent or transient neurological deficit within 72 hours of surgery with an appropriate imaging correlate on MRI or CT scan. Technical difficulties with either imaging modality were noted, as were residual aneurysm filling and parent vessel occlusion on independent postoperative imaging such as follow-up DSA, computed tomography angiography (CTA), or magnetic resonance angiography (MRA).

2.3. Statistical analysis

Univariate analysis to compare categorical variables was performed using Fisher's exact test with a probability value of <0.05 considered statistically significant. Univariate analysis to compare continuous variables was performed using Student's *t*-test with a probability value of <0.05 considered statistically significant. All analyses were conducted using GraphPad QuickCalcs (GraphPad Software Inc., La Jolla, CA, USA).

3. Results

3.1. Patient demographics

We identified the first 100 consecutive patients undergoing 100 craniotomies for the treatment of 119 aneurysms in the year 2002 ("DSA era," Table 1), and the first 100 consecutive patients undergoing 100 craniotomies for the treatment of 122 aneurysms in the year 2007 ("ICG era," Table 1). The average age between patients in each era did not differ significantly (52.2 years in DSA era, 54.0 years in ICG era, p = not significant [NS]). A female predominance was seen in both study periods. More patients presented with aneurysm rupture and subarachnoid hemorrhage (aSAH) in the DSA era than in the ICG era (49% *versus* 30%, $p = 0.008$, Fisher's exact test). Furthermore, more middle cerebral artery (MCA) aneurysms and fewer posterior communicating artery (PCoA) aneurysms were treated in the ICG era than DSA era (30% *versus* 11% and 3% *versus* 18%, respectively, $p < 0.05$, Fisher's exact test). Regardless of the modality used intraoperatively, all patients at our institution underwent CTA, MRA, and/or DSA postoperatively within 24 hours of surgery as a control.

Table 1
Patient demographics

	DSA era	ICG era
Patients	100	100
Treated aneurysms	119	122
Mean age, years	52.2	54.0
Sex, M:F	26:74	34:66
Presentation		
Elective	46*	64*
Acute SAH	49*	30*
Remote SAH	5	6
Location, n (%)		
Anterior circulation	97 (82%)	108 (89%)
ACoA	19 (16%)	30 (25%)
ACA	9 (8%)	2 (2%)
ICA	24 (20%)	20 (16%)
MCA	13 (11%)*	36 (30%)*
OphthA	10 (8%)	16 (13%)
PCoA	22 (18%)*	4 (3%)*
Posterior circulation	22 (18%)	14 (11%)
AICA	3 (3%)	0 (0%)
BasilarA	8 (7%)	6 (5%)
PCA	2 (2%)	0 (0%)
PICA	7 (6%)	5 (4%)
SCA	2 (2%)	3 (2%)
Intraop DSA	81%*	13%*
Intraop ICG	0%*	79%*
Periop stroke	4%	3%
Clip repositioning	6%	4%
False-neg rate	1%	1%
Routine postop DSA	12%	8%

ACA = anterior cerebral artery, ACoA = anterior communicating artery, AICA = anterior inferior cerebellar artery, BasilarA = basilar artery, DSA = digital subtraction angiography, F = female, False-neg = false-negative study, ICA = internal carotid artery, ICG = indocyanine green, Intraop = intraoperative, M = male, MCA = middle cerebral artery, OphthA = ophthalmic artery, PCA = posterior cerebral artery, PCoA = posterior communicating artery, Periop = perioperative (within 72 hrs), PICA = posterior inferior cerebellar artery, postop = postoperative, SAH = subarachnoid hemorrhage, SCA = superior cerebellar artery.
* $p < 0.05$ comparing DSA era to ICG era.

3.2. Utilization of intraoperative modalities

In the DSA era, 81% of patients underwent intraoperative DSA; none underwent ICGA as it had not yet been introduced at our institution. In the ICG era, 79% of patients underwent ICGA, and 13% of patients underwent intraoperative DSA either in conjunction with (2%) or as a substitution of (11%) ICG. Patients who underwent intraoperative DSA within the ICG era did not differ from patients who underwent ICGA alone in any variable examined (Table 2). In one patient treated with ICGA, the parent vessel could not be adequately visualized and so intraoperative DSA was utilized. Otherwise, there were no cases of intraoperative technical failure using either technique. No patient suffered an allergic reaction to either injected iodinated contrast or ICG. No pseudoaneurysms or

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