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A New and Simplified Method for Coronary and Graft Imaging During CABG

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ABSTRACT

Background: Improvements in percutaneous catheter interventions and new technical demands in the practice of coronary surgery have increased the need for an accurate and easy-to-use imaging modality for validating the quality of bypass grafts in the operating room. This report examines the initial clinical use of fluorescent cardiac imaging, a technology that uses indocyanine green (ICG) with a portable imaging device to visualize coronary anatomy and grafts intraoperatively.

Methods: The modality was evaluated at two institutions in 20 patients undergoing non-emergent CABG or MIDCAB with respect to safety, feasibility of use, and image quality. Images were generated and acquired with a portable laser diode/infrared camera device after injection of 0.5 ml of ICG (0.5–5.0 mg/ml) either intravenously, via the antegrade cardioplegia cannula, or via the cardiopulmonary bypass circuit.

Results: There were no ICG- or imaging device-related complications. The technology was easy-to-use during conventional CABG as well as MIDCAB and adequately demonstrated coronary anatomy, filling of the grafts, and graft patency in all but two patients. In one patient, the use of the modality resulted in the intraoperative recognition and revision of a non-functioning graft.

Conclusion: This technology is user-friendly in the operating room, appears to be safe, provides good-quality images of coronary anatomy and grafts, and holds promise as an intraoperative graft validation tool for conventional and minimally invasive CABG.

INTRODUCTION

With the improvement of alternatives for the treatment of coronary artery disease, conventional and new techniques of coronary artery bypass grafting (CABG) have come under scrutiny due to their perceived lack of quality assurance. Accurate identification of target vessels and determination of optimal anastomotic sites can occasionally be difficult, particularly in patients with diffuse coronary disease, those who have undergone previous CABG, or those operated upon through minimally invasive approaches. Furthermore, intraoperative confirmation of technical success with imaging is not routinely performed, potentially contributing to early occlusion rates of up to 20% for vein grafts [Grondin 1989]. While interventional cardiologists are in an ideal position to immediately assess and address the success or failure of their interventions, procedural logistics, costs, and risks continue to make routine coronary angiography impractical during CABG. Consequently, there is an increasing need for an easy-to-use imaging modality that would immediately validate the quality of coronary bypass grafts after their construction in the operating theatre.

This report examines the initial clinical use of fluorescent cardiac imaging (FCI), a technology that uses indocyanine green (ICG) in combination with a portable laser diode/infrared camera unit to visualize coronary anatomy and grafts intraoperatively. The study was undertaken to assess the safety and feasibility of this modality as well as to evaluate its usefulness for the intraoperative identification of target coronary segments and the validation of graft patency.

METHODS

Patient Selection

The study was conducted at two Canadian institutions, the University of Ottawa Heart Institute in Ottawa, Ontario, and the Sunnybrook and Women's Health Sciences Center in Toronto, Ontario between January and June of 2001 and included patients undergoing non-emergent CABG. Exclusion criteria were renal insufficiency (serum creatinine >120 μmol/L) or a history of allergy to ICG or contrast dye. The study was approved by the Research Ethics Committees at both institutions, and informed consent was obtained from each patient before participation.

Intraoperative Fluorescent Cardiac Imaging

ICG is a fluorescent molecule that is 98% plasma protein-bound and temporarily confined to the vasculature after systemic injection. It emits near-infrared light at a wavelength of 830 nm when exposed to light at 806 nm. The

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delivery routes and dosing ranges of ICG and the imaging device configurations were determined in large-animal experiments prior to the study. To generate fluorescent images in CABG patients, a volume of 0.5 ml of ICG solution (Akorn Pharmaceuticals, Decatur, Illinois) was injected either through a central venous catheter, through the aortic cardioplegia cannula, or through the cardiopulmonary bypass circuit. The following ICG concentrations were used: 0.25, 0.5, 2.5, 5.0 and 12.5 mg/ml. The performance of the study did not lead to a modification of operative strategy in any patient, with the exception of the actual conduct of the fluorescent imaging procedure.

The imaging device (SPY™, Novadaq Technologies, Toronto, ON) consists of a laser diode and driver that produces light at a wavelength of 806 nm and at a maximum output of 2.7 W. This laser output is decollimated to provide illumination spread homogeneously over a 7.5 × 7.5 cm field of view at a working distance of 30 cm. Images are acquired at a rate of 30 images/second by means of a charge-coupled device (CCD) camera sensitive to near-infrared light and equipped with an optical filter for the selective transmission of light at 830 nm. The laser, optics, camera, and filter are integrated into an imaging head supported by a mobile arm and connected to a wheeled cart, which allows for it to be moved close to the surgical table at a correct focal distance above the area of interest (Figure 1,). The imaging head and extension arm are covered with a customized sterile drape that preserves optical quality (Novadrape™, Novadaq Technologies). As ICG is injected, the device is activated by means of a foot switch that powers up the laser and allows images to be instantaneously captured by the CCD camera, viewed in real-time on a video monitor, and automatically recorded onto a VCR tape (see Movie,).

End-Points

The study evaluated the clinical safety and feasibility of the use of this modality as well as the quality of acquired images. *Safety* end-points included assessment of the effects of the fluorescent imaging procedure on renal and cardiac function. To this end, daily serum creatinine levels were obtained for a minimum of three days postoperatively. Patients were kept on telemetry for 24 hours after discharge from the intensive care unit. Electrocardiograms were obtained preoperatively, four hours postoperatively, and then daily for three days. Troponin-T levels were measured four hours after surgery, the next morning, and on each subsequent day if elevated values were observed. Perioperative myocardial infarction was defined by the appearance of new Q-waves or the loss of R-wave progression on ECG, or by a peak serum troponin-T level of 1.5 μg/L or higher.

Feasibility assessment included an evaluation by staff and surgeons of the simplicity of use of this modality in the operating room, as well as the time required for device positioning and image acquisition. The *quality of acquired images* was subjectively evaluated with respect to: (1) the localization of coronary vessels, (2) the identification of stenotic coronary lesions, and (3) the validation of graft patency. The following variables were modified in attempting to optimize image quality: the site of ICG injection, the ICG concentration, and the timing of device actuation with respect to the injection.

RESULTS

Patient Characteristics and Safety

Twenty patients (18 men and 2 women) were enrolled in the study. Mean age was 65.8 ± 8.9 years. Eighteen patients underwent standard CABG on cardiopulmonary bypass, and two underwent a standard MIDCAB procedure performed through a left anterior thoracotomy without cardiopulmonary bypass. It was noted that ICG injections temporarily interfered with peripheral O_2 saturation readings, but this effect lasted less than 30 seconds after each bolus and was completely reversible. There was no postoperative occurrence of ventricular arrhythmia or myocardial infarction. One patient experienced atrial fibrillation, one was re-explored for chest wall bleeding, and one had an episode of postoperative delirium. One patient with severe preoperative left ventricular dysfunction developed temporary renal insufficiency, which resolved spontaneously without the need for dialysis.

Imaging Results

A total of 110 images were acquired. The number of good quality images, defined as the adequate demonstration of target anatomy or flow through the graft, was 50. No satisfactory image could be obtained in two patients during the initial part of the study for technical reasons related to a particular iteration of the device. The average total time required for positioning the device was two minutes, and the time that the heart was illuminated with laser light was 30 seconds per image sequence.

In the first 10 patients, trial-and-error adjustments in imaging parameters were necessary to overcome the effects of variable epicardial fat deposition on image quality. Upon completion of this phase of the study, a standard procedure for optimal image acquisition on the non-arrested heart had been established: 0.5 ml of a 2.5 mg/ml solution of ICG was injected as a rapid bolus into the central venous line, the imaging head was activated, real-time images were displayed and recorded, and the imaging device was automatically shut off 30 seconds later, at which time ICG was seen clearing in the coronary venous system.

Images from representative cases are shown in Figures 2 to 5. The round bright spot seen on these images is due to an infrared light source employed as part of a range sensor system for the automatic verification of focal distance. This was a safety feature of the device used in this study that has been abolished during image acquisition in subsequent iterations.

Imaging of a MIDCAB Procedure

Figure 2A ( ) shows an image acquired during a MIDCAB procedure, prior to construction of a left internal thoracic artery (LITA) anastomosis to the left anterior descending artery (LAD). The image demonstrates the location of the LAD. Figure 2B ( ) shows an image acquired immediately following construction of the graft, demonstrating flow through the graft pedicle to the LAD.

Imaging of a Graft While on Bypass: Systemic Injection and Injection Through the Cardioplegia Line

Flow from the LITA was selectively imaged by injecting ICG systemically via the CPB circuit and by acquiring images prior to the release of the aortic cross-clamp. Figure 3A ( ) shows a LITA to LAD graft in which the pedicle had not been skeletonized, while Figure 3B ( ) shows a similar graft in which the sequential arterial pedicle had been skeletonized.

ICG injected through the cardioplegia line while the aortic cross-clamp was in place also provided good-quality images. Figure 4 shows a vein graft through which very poor flow was initially demonstrated (Figure 4A,) and the same graft after correction of its orientation prior to revision of the proximal anastomosis (Figure 4B,).

Imaging of Proximal Anastomoses

Images semi-quantitatively indicating the rate of filling and the fluorescence intensity of bypass grafts coming off the ascending aorta were also obtained (Figure 5,). There was rapid, intense ICG filling of all three grafts followed by rapid emptying.

DISCUSSION

Main Findings

Improvements in the outcome of catheter-based interventions and new technical demands in the field of coronary surgery have increased the need for an accurate and easy-to-use modality that would validate graft quality in the operating room. This preliminary report suggests that intraoperative fluorescent cardiac imaging is clinically safe and can accomplish those aims. Native coronary vessels and target segments were easily seen following intravenous ICG injection during conventional CABG, and optimal anastomotic sites on the LAD were clearly identified through a 7 cm left anterior thoracotomy during MIDCAB cases. Good-quality visualization of grafts was also obtained, using ICG that was injected either intravenously through the central line or into the ascending aorta through the cardioplegia line or bypass circuit. Optimal ICG concentrations were determined to be 2.5 mg/ml for intravenous administration and delivery through the cardiopulmonary bypass circuit, and 0.5 mg/ml for injection through the cardioplegia line. For patients with a body weight >100 kg, an IV concentration of 5.0 mg/ml of ICG was found to improve image quality. An ICG bolus volume of 0.5 ml was used for all images.

Intraoperative fluorescent cardiac imaging was also employed to assess proximal and distal anastomoses. In this regard, rapid and simultaneous graft filling was observed in all grafts except one, which showed severe diminution of flow. This graft was revised and normal flow was demonstrated with fluorescent imaging (Figure 4,).

Safety of Indocyanine Green

ICG is a non-toxic agent that has been widely used in humans for other medical indications such as retinal angiography. The incidence of adverse reactions related to the clinical use of ICG is very low, with most reactions being mild and usually consisting of sore throat or a feeling of warmth. The initial four reports of adverse reactions to ICG occurred over a time interval during which 240,000 doses had been given [Carski 1978]. A literature review published 34 years after the clinical introduction of ICG compiled only 17 adverse reactions, including two deaths. Both deaths occurred in patients undergoing cardiac catheterization (in one patient the autopsy findings suggested multi-systemic contributing pathologies). Seven of the 17 reactions were encountered in hemodialysis patients, and as a consequence ICG should be avoided in patients with severe renal insufficiency [Benya 1989]. One additional death reported in Japan [Nanikawa 1978], as well as three other case reports prompted a second literature review which concluded that the incidence of complications is very low and that there is no data linking reactions to pre-existing allergies [Speich 1988]. Subsequently, a prospective cohort study involving 1,923 consecutive retinal angiograms using ICG in 1,226 patients recorded only eight reactions of varying intensity, one of which was judged to be severe [Hope-Ross 1994]. Adverse reactions to ICG were also reported in this study to occur less frequently than those secondary to the use of fluorescein.

ICG has been used during CABG procedures as a tracer to document changes in lung water content and assess changes in regional blood flow. There are 16 reports in the literature on the use of ICG under these conditions, with no occurrence of adverse effects [Boldt 1990, Boldt 1991, Boer 1994]. Moreover, the total amount of ICG per patient used in the present study is several times less than the dosage administered in those reports due to the sensitive nature of fluorescent imaging compared with other techniques that involve ICG.

Safety of the Laser Diode

Light of the wavelength used in the present study is not transmitted through tissues, does not damage them, and presents no known hazard to the patient. The light source was a laser (to provide a discrete wavelength of illumination) that was decollimated to encompass an area of 7.5 cm × 7.5 cm at an operating distance of 30cm. The maximum laser output was 2.7 W, with a final output of 2.25 W post-decollimation with optical lenses. This resulted in a power density of 40m W/cm^2 on the epicardial surface, considerably below the allowable 200 mW/cm^2 minimum exposure limit for light densities in this range of the spectrum (American National Standards for Safe Use of Lasers ANSI Z136.1). The low power and decollimation of the laser minimizes the potential hazard to the operating room staff and makes safety eyewear unnecessary during operation of the system. Preliminary studies with swine also indicated that prolonged illumination of the heart with this device does not significantly effect myocardial temperature (J. Docherty, unpublished data—National Research Council of Canada).

Other Alternatives to Contrast Angiography

Several assessment modalities have been introduced over the years as an alternative to intraoperative angiography, which remains cumbersome, invasive, and subject to the risk of additional radiation exposure or potential dye toxicity

when used in an intraoperative setting. The most commonly used of these modalities, transit-time flow measurement, imposes significant limitations. Transit-time flow measurements cannot be used for native coronary vessel assessment due to the need to encircle the target vessel. It is also unreliable in detecting less than critical stenosis [Jaber 1998], despite the recent addition of spectral analysis [Koenig 1999]. Thermal imaging is a non-invasive modality that does not involve contrast material or radiation exposure [Mohr 1997], but it has very limited image resolution and is potentially unsuitable for off-pump or minimally invasive surgery, due to the need for surface cooling of the heart before restoring flow through the bypass graft. Furthermore, thermal imaging, like transit-time flow measurements, cannot be used for the intraoperative confirmation of coronary anatomy, which is desirable for minimal access surgery.

Limitations

This study involved a small number of patients and its safety data would benefit from further clinical experience with this modality. There are also some restrictions to the technology used in this study. Overlying fat or muscle can artifactually obscure the penetration and detection of ICG fluorescence. The modality also works best with skeletonized arterial grafts and saphenous vein grafts; it appears less accurate with non-skeletonized arterial grafts unless the segment of interest (such as an anastomotic site) is skeletonized. Finally, difficulty was encountered in accurately profiling distal coronary anastomoses, a limitation which may be obviated by improvements in the design of the device.

CONCLUSION

In spite of the above limitations, this series provides preliminary insight into the safety and clinical feasibility of intraoperative fluorescent cardiac imaging for visualization of coronary anatomy and grafts through either a median sternotomy or a left anterior thoracotomy. Images were successfully acquired on the beating heart as well as on the arrested heart. The technical details of ICG administration have been further elucidated, and the procedure resulted in the acquisition of video images confirming graft patency. We believe that further work should concentrate on the use of this technology to gain better insight into anastomotic morphology and on evaluating whether its use may ultimately improve the outcome of CABG operations.

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