EXHIBIT 1007
Intraoperative Angiography to Assess Graft Patency After Minimally Invasive Coronary Bypass

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Background. Intraoperative angiography was performed to confirm graft patency immediately after minimally invasive coronary bypass operations.

Methods. In 26 patients who had internal mammary artery grafting, intraoperative coronary angiography was performed with a portable digital fluoroscope.

Results. High-resolution angiograms were obtained in all cases. Angiography documented vasospasm of the graft or native vessel in 9 patients (graft in 3, native in 2, graft and native in 4 others), which responded promptly to intracoronary vasodilators in all. Angiography identified technically unsuspected and clinically silent fixed stenoses (>50%) in 11 patients, attributable to graft kinking in 2, anastomotic obstruction in 6 (total occlusion in 4), and stenosis of the left anterior descending artery just distal to the anastomosis in three cases (total occlusion in one). In 9 of 11 patients, fixed stenoses were sufficiently severe to warrant intraoperative intervention by surgical revision (n = 5) or angioplasty via the graft (n = 4).

Conclusions. Intraoperative angiography after minimally invasive coronary artery bypass operations can immediately identify dynamic and fixed obstructions and facilitate their prompt treatment, thereby ensuring that each patient leaves the operating room with an optimal surgical result.

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Minimally invasive coronary artery bypass grafting (MINICAB) performed on the beating heart potentially allows patients to avoid sternotomy and eliminates complications associated with heart-lung bypass, advantages that could translate into less morbidity, more rapid recovery, and reduced costs [1-18]. However, compared with coronary revascularization on the arrested heart, operations on the beating heart are technically more challenging. Not surprisingly, postoperative angiographic studies show graft compromise in 5% to 20% of patients [3, 5, 6, 9, 11-17], in some cases necessitating reoperation. In fact, graft compromise is of sufficient concern to warrant testing to confirm procedural results, including performance of routine early postoperative coronary angiography in some institutions [11, 14, 19-21].

At present, early angiography after MINICAB is performed in a standard fixed cardiac catheterization laboratory either immediately [11], or 1 to 3 days postoperatively [14]. We reasoned that intraoperative angiography would provide instantaneous documentation of graft patency and facilitate prompt surgical or percutaneous revision of compromised grafts. This strategy would also avoid the logistic burdens and time delays inherent in transferring patients from the operating room to the catheterization laboratory and potentially preclude the need for reoperation. Equipping an operating room with a standard fixed cardiac imaging system facilitates performance of intraoperative angiography [22], but this approach is relatively expensive and might impose substantial equipment space demands. We recently demonstrated the feasibility of performing high-resolution coronary angiography using an inexpensive commercially available portable digital fluoroscopic system [23, 24]. The present study was designed to demonstrate the feasibility of performing intraoperative angiography with a high-resolution mobile imaging system, to assess graft patency immediately after MINICAB.

Methods

Operative Procedure

Patients scheduled for MINICAB were screened to exclude excessive risk for contrast dye toxicity, including renal insufficiency, congestive heart failure, and allergies to contrast media. Informed consent was obtained from all patients. All patients were treated preoperatively with aspirin (325 mg four times daily). The goal of anesthetic management was early extubation. Short-acting narcotics supplemented by propofol or isoflurane were used. Subarachnoid morphine was administered preoperatively to minimize postoperative pain. Short-acting narcotics supplemented by propofol or isoflurane were used. Subarachnoid morphine was administered preoperatively to minimize postoperative pain. Patients were monitored by measurement of radial artery pressure and by electrocardiographic limb leads. An 8- to 10-cm thoracotomy incision was made over the third or fourth costal cartilage, and the entire costal cartilage was excised. The internal mammary artery (IMA) and its bundle...
were identified, the pleura opened, and the pericardium incised longitudinally. The native target coronary artery was identified and explored for accessibility and quality. The IMA was then dissected from the second costal cartilage to the fifth intercostal space, and heparin was administered intravenously (1.5 mg per kilogram of body mass). The IMA was clamped, ligated, divided, and tested for flow. Verapamil (250 μg/mL) was applied externally or injected into the IMA. The target vessel was encircled with tapes on either side of the planned anastomotic site and stabilized with either a two-prong instrument or stabilizing platform retractor (Cardiothoracic Systems, Cupertino, CA, or US Surgical Systems, Norwalk, CT). After slowing the heart rate to 38 to 45 beats per minute by intravenous beta-blockers, an end-to-side anastomosis was done using continuous sutures of 8-0 or 7-0 Prolene (Ethicon, Somerville, NJ). A dry operative field was maintained by continuous insufflation of carbon dioxide. After the anastomosis was completed, the tapes and IMA clamp were removed.

Intraoperative Angiography

The portable imaging system (Digital Mobile C-Arm, Series 9600; OEC Medical Systems, Salt Lake City, UT) is a commercially available digital x-ray imaging system specifically modified for coronary imaging [23, 24]. The pulsed fluoroscopic system is capable of 30 frames per second dynamic acquisition and playback. Digital images can be viewed in real time or as still images, and can be permanently copied onto 3.5-inch high-density computer disks or ½-inch videotape for long-term storage. Modifications that facilitate coronary angiography include a big C configuration of the C-arm (characterized by additional 7-inch depth over conventional portable C-arms), to allow easier positioning of the x-ray table and greater range of angiographic angles. To optimize image quality and facilitate obtaining angulated views, a low-attenuation (high-resolution) carbon fiber topped fluoroscopic surgical table was used (Stille-Beta Medical Systems, Akron, OH).

Angiography of the Internal Mammary Artery

After anastomosis was completed but before closure of the thoracotomy incision, graft angiography was performed using femoral or radial arterial access. The IMA was selectively engaged with a preformed 5- or 6Fr IMA catheter, and angiography was performed in right and left anterior oblique and lateral projections. Angiography was performed before and after administration of intracoronary nitroglycerin (200 mg/mL), verapamil (250 mg/mL), or both. If the IMA graft and native vessel were patent with excellent flow, the catheter was removed and protamine was given. If angiography showed a stenosis of greater than 90% unresponsive to vasodilators, then surgical revision or intraoperative percutaneous transluminal coronary angioplasty was performed, using a 6Fr left IMA guiding catheter, a 0.014-inch high-torque floppy wire, and appropriate balloon dilation catheters. In all such cases, repeat angiography was performed to ensure that each patient left the operating room with an optimal surgical result.

Data Analyses

Adverse clinical events included intraoperative or postoperative revascularization (surgical revision, percutaneous transluminal coronary angioplasty, or conversion to routine bypass), in-hospital ischemia, myocardial infarction, congestive heart failure, stroke, or death. Time to extubation and length of stay were recorded. Angiograms were analyzed by two experienced reviewers according to previous techniques [23, 24]. The IMA graft, anastomoses, and native vessel were analyzed for patency and flow. Spasm was defined as a stenosis greater than 50% of that improved after administration of intracoronary vasodilators. Fixed lesions were defined as stenoses greater than 50% unresponsive to intracoronary vasodilators analyzed by quantitative angiography using electronic calipers. Continuous variables are expressed as mean ± standard deviation, and dichotomous variables are reported as frequency.

Results

We performed MINICAB in 26 patients between October 1996 and November 1997. Left internal mammary artery grafts were placed to the left anterior descending artery in 24 patients, and right internal mammary artery to the right coronary artery in 2 others. One patient underwent combined (hybrid) intraoperative revascularization in which successful MINICAB of the left internal mammary artery and left anterior descending artery was confirmed by angiography and followed by successful percutaneous stenting of a stenosis in the right coronary artery using the portable imaging system. In all cases, the surgeon considered the anastomosis to be successful and the graft patent by visual inspection. No patient had electrocardiographic changes suggesting ischemia or hemodynamic instability.

Angiographic Findings

The IMA graft, anastomosis, and native distal target vessel were visualized with excellent angiographic resolution in all cases (Figs 1–4). Arterial spasm (Fig 2) was identified in 9 patients (35%), including IMA spasm alone in 3 (compromised flow in 1), native vessel spasm alone in 2 patients (1 with impaired flow), and spasm involving the IMA and native vessel in 4 patients (1 with diminished flow). Spasm was completely relieved by nitroglycerin (Fig 2) in 5 patients, but required additional verapamil in 4 others. Fixed stenoses were documented in 11 patients (42%) (Figs 3–5). Kinking of the IMA graft (Fig 3) was identified in 2 of 11 pts. Anastomotic obstruction (Fig 4) was documented in 6 patients, with total obstruction in 4 patients and impaired flow in 5 of 6 patients. Obstruction of the native left anterior descending artery just distal to the anastomosis was documented in 3 patients, with impaired flow in 1.
Intraoperative Angiography During MINICAB

Intraoperative Graft Revision
The two cases of IMA kinking were relieved by simple surgical graft repositioning (Fig 3). Surgical revision was performed in 2 patients with severe anastomotic obstruction, resulting in a widely patent graft and native vessel on repeat angiography. Intraoperative percutaneous transluminal coronary angioplasty (Fig 4) was attempted in 5 other patients with obstruction at the anastomotic site ($n = 3$) or left anterior descending artery just distal to the anastomosis ($n = 1$). In four of five cases, coronary angioplasty led to prompt relief of stenosis (99% ± 2% to 10% ± 8%, $p < 0.05$), with restoration of TIMI 3 flow in all cases. Angioplasty failed to cross a total anastomotic obstruction in 1 patient, who required surgical revision. In 2 patients with 40% to 70% hazy stenoses, no intervention was performed.

Postoperative Course
In the immediate postoperative period, all patients were hemodynamically stable without electrocardiographic changes. There were no access site or other complications related to cardiac catheterization. Postoperative ischemic complications occurred in 1 patient in whom the intraoperative angiogram revealed a 70% stenosis with intraluminal haziness. Acute myocardial infarction, pulmonary edema, and cardiogenic shock developed on day 3, and emergency angiography in the cardiac catheterization laboratory documented total occlusion at the distal anastomosis. Despite successful coronary angioplasty, the patient died on day 7. There were no postoperative complications in 25 patients. In 1 patient with a 40% stenosis and luminal haziness in the left anterior descending artery on intraoperative angiogram, repeat angiography on day 3 was normal. Patients were discharged 6.3 ± 3.2 days (range, 3 to 13 days) postoperatively. All were alive, free of angina, and hemodynamically stable.

Comment
Findings from the present study demonstrated that intraoperative coronary angiography using a portable digital fluoroscopic system documents the immediate results of MINICAB, avoids the logistic burdens of transporting patients from the operating room to the catheterization laboratory, and provides timely data that could influence intraoperative treatment and patient outcome.

Although MINICAB offers potential benefits in the form of reduced complications and costs [1–18], its success must be measured ultimately in terms of graft patency [14, 20, 21]. Compared with coronary revascularization on the arrested heart, operations on the beating heart are technically more challenging, undoubtedly contributing to the incidence of early graft compromise.
previously reported [3, 5, 6, 9, 11-17, 19-21]. Although increasing operator experience and use of newer motion stabilization techniques [7, 14, 15, 25, 26] will likely improve surgical results, graft compromise is of sufficient concern to warrant early confirmation of procedural results [11, 14, 19-21]. Most patients who have elective surgical revascularization have adequate resting antegrade or collateral flow to the target vessel and do not manifest resting ischemia. Therefore, it should not be surprising that electrocardiographic, hemodynamic, direct visualization, and Doppler graft flow measurements have not been sufficiently predictive of graft patency [16]. Accordingly, the need for routine postoperative angiography to assess graft patency has been emphasized [11, 14, 19-21].

Findings from the present study confirm and extend those of previous reports documenting graft compromise by postoperative angiography in a significant number of patients early after MINICAB [3, 5, 6, 9, 11-17, 19-21]. In the present study, intraoperative graft imaging was safe, easy to perform, and immediately identified patients with flow-limiting lesions that were neither technically suspected nor clinically apparent. Furthermore, intraoperative identification of graft compromise facilitated timely graft revision by surgical or catheter-based interventions, thereby ensuring a widely patent graft and excellent flow before chest closure. Findings from the present study also demonstrate the feasibility of per-
forming hybrid revascularization in the operating room using the portable imaging system, which in selected patients, might preclude the need to stage such procedures [27].

Results from this observational study of our early MINICAB experience must be interpreted with caution, particularly with regard to overall patency results. We studied a consecutive series of patients from initial procedures using early stabilization techniques to later experience using more sophisticated operating platforms. The incidence of angiographic abnormalities observed in this intraoperative study is consistent with that of previous reports of postoperative angiography, and most compromised grafts occurred earliest in the learning curve of our operative experience. However, clinically silent obstructions were observed even with later cases. We can only speculate as to the precise pathophysiologic mechanisms responsible for the angiographic abnormalities observed in the present study and their natural history if left untreated. With the greater mechanical manipulation associated with operating on the beating heart, there is potential for vascular trauma that could induce vasoconstriction, intramural edema or hemorrhage, intimal thrombosis, or native vessel plaque disruption. However, the presence of early intraoperative angiographic abnormalities does not necessarily presage coronary compromise. Further studies will be necessary to delineate the natural history and optimal treatment of these lesions. The present study was not designed to compare the graft patency rates or costs of surgical revascularization by MINICAB with those of conventional arrested-heart bypass procedures. Further studies will be necessary to compare the outcomes, benefits, and costs of these two operations.

In summary, intraoperative angiography using a portable digital fluoroscopic system is easy to perform and provides immediate confirmation of graft patency after MINICAB. Intraoperative imaging identifies dynamic and fixed obstructions in the graft and native vessel and facilitates their prompt resolution by catheter-based or surgical interventions.

References