Fractional flow reserve–guided coronary artery bypass grafting: Can intraoperative physiologic imaging guide decision making?

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Objectives: Fractional flow reserve–guided coronary artery bypass grafting is emerging in cardiac surgery, in which the nature (anatomic and functional characteristics) of the target vessel epicardial coronary artery stenosis is important in graft site selection. The nature of the stenosis might determine a different physiologic response to bypass grafting. We report our recent experience using near infrared fluorescence complex angiography and perfusion analysis to identify the nature of stenoses in the target vessel by imaging the physiologic response to grafting.

Methods: In 167 patients who underwent consecutive multivessel coronary artery bypass grafting cases (63% off-pump coronary artery bypass grafting) with traditional anatomy-based revascularization, we imaged and analyzed 359 grafts (53% arterial). This platform provides angiographic data of both the target vessel epicardial coronary artery and graft simultaneously (to assess the imaged competitive flow); and because a change in fluorescence intensity is proportional to the change in blood flow and perfusion, the quantified change (if any) in regional myocardial perfusion surrounding the grafted target vessel epicardial coronary artery.

Results: The patient outcomes in our series were excellent. All 359 grafts were widely patent by angiography, and 24% of the arterial and 22% of the saphenous vein grafts showed no regional myocardial perfusion change in response to bypass grafting. In 165 in situ internal mammary artery grafts to the left anterior descending artery (>70% stenosis), 40 had no change in regional myocardial perfusion, and 32 of the 40 had competitive flow imaged.

Conclusions: An important number of angiographically patent bypass grafts demonstrated no change in regional myocardial perfusion, suggesting anatomic, but nonfunctional, stenoses in those target vessel epicardial coronary arteries. In in situ arterial grafts, imaged competitive flow is associated with nonfunctional stenoses in the target vessel epicardial coronary artery. Imaging these physiologic responses to target vessel revascularization might be useful in the emerging fractional flow reserve–guided era. (J Thorac Cardiovasc Surg 2013;146:824-35)

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JTCS VIDEO CLIP Video clip is available online.

Supplemental material is available online.

For 50 years, the conceptual and practical basis of surgical revascularization with coronary artery bypass grafting (CABG) has been the underlying coronary anatomy[1] and the accompanying stenotic[2] atherosclerotic plaque and/or thrombotic occlusion in the target vessel epicardial coronary artery (TVECA). Early on, incomplete revascularization within this anatomy-based construct was associated with a 15% reduction in 5-year survival,[3] and the principle of complete anatomic revascularization became linked to these anatomic stenotic triggers.

Using this approach, the outcomes from isolated CABG have improved dramatically, despite the significant increase in preoperative risk of patients undergoing CABG.[4,5] The 5-year results from the Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery[6] (SYNTAX) and Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease[7] (FREEDOM) trials, along with observational database analyses, have documented that in certain patient populations, CABG is a preferable treatment alternative to multivessel percutaneous coronary intervention (PCI), because a long-term mortality benefit is conveyed with CABG.[8]

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Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
CAPA	= complex angiography and perfusion analysis
COURAGE	= Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation
CPB	= cardiopulmonary bypass
FAME	= Fractional Flow Reserve Versus Angiography for Multivessel Disease
FFR	= fractional flow reserve
FREEDOM	= Future Revascularization Evaluation in Patients with Diabetes Mellitus: Otpimal Management of Multivessel Disease
ICF	= image-described competitive flow
ICG	= indocyanine green
IDAP	= image data acquisition protocol
IDS	= image data sequence (34 seconds)
IMA	= internal mammary artery
NIRF	= near-infrared fluorescence
OPCAB	= off-pump CABG
PCI	= percutaneous coronary intervention
PREVENT-IV	= Project of Ex-vivo Vein Graft Engineering via Transfection IV
RA	= radial artery
RMP	= regional myocardial perfusion
SVG	= saphenous vein graft
SYNTAX	= Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery
TVECA	= target vessel epicardial coronary artery

In parallel, relentless advancement in our understanding of patients with chronic stable angina in need of revascularization continues. The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation[9] (COURAGE) trial established the importance of optimal medical therapy for these patients, and a substudy identified the requirement of a significant (>10%) degree of myocardial ischemia for revascularization strategies to have clinical benefit.[10] In a paradigm shift, fractional flow reserve (FFR) analysis of anatomic lesions has transformed an anatomic stenosis to a "functional stenosis" classification.[11] In such cases, the anatomic lesion is presumptively linked to regional ischemia and/or a perfusion deficit in the surrounding myocardium supplied by the TVECA. In the Fractional Flow Reserve Versus Angiography for Multivessel Disease (FAME) trial,[12] 20% of the anatomic lesions with 71% to 90% stenosis and 60% of lesions with 51% to 70% had no measured functionality. In the FAME 2 trial,[13] many patients with more severe 3-vessel anatomic disease were reclassified as having 2- or 1-vessel functional disease.

Thus, surgical revascularization is at the point at which anatomy as the sole criterion for the revascularization strategy needs to be reconsidered. We report a unique, real-time intraoperative imaging technology to identify differences in the physiologic (angiographic and functional) response to revascularization, on a per graft basis. These physiologic findings could be critically important in a FFR-guided revascularization strategy adapted for CABG.

METHODS

Imaging Technology Developments

Near-infrared fluorescence (NIRF) angiography in CABG has been previously described, with mixed results.[14-18] The fidelity of NIRF versus conventional angiography was inferior, but the technique was better at identifying potential anastomotic technical issues than transit-time flowmetry.[19]

NIRF uses the nontoxic fluorophore indocyanine green (ICG) dye, administered as a bolus injection into the blood stream.[20,21] The pharmacokinetics of its binding to endothelial cells and circulating proteins, its metabolism by the liver, and excretion by the kidneys is well-understood, with a half-time of approximately 90 seconds. The fluorophore is excited by a low-energy NIR laser, and the fluorescence image data are collected as a 34-second image data sequence (IDS) of 1020 images at a camera speed of 30 frames/s. Because no radiation is involved, this full 34-second image data set can be safely captured with each ICG injection. ICG fluorescence behavior in the heart has been studied in nearly 1000 patients, and we have confirmed clinically the experimental data validating that the ICG behavior is consistent on the first pass through the coronary arteries; the fluorescence intensity is proportional to the concentration of dye and dose administered and to the circulating blood volume; and under certain conditions, the regional fluorescence intensity is directly proportional to the myocardial blood flow and myocardial perfusion.[22] Therefore, a change in fluorescence intensity will be a direct indicator of a corresponding change in myocardial perfusion.

Early on, we recognized that the 34-second image data sequence contained considerably more information about the myocardial blood flow and perfusion than did angiography alone. We developed, tested, and implemented a complex angiography and perfusion analysis (CAPA) platform into the NIRF system for real-time intraoperative analysis.

Clinical Experience With NIRF-CAPA

From May 2009 (when the image data acquisition protocol [IDAP] for the post- versus pregrafting comparison with the CAPA platform was validated) through March 2013 (to allow for full 30-day follow-up), we performed 167 consecutive isolated CABG procedures with ≥2 grafts placed. All patients underwent CABG by 1 of us (T.B.F., Jr), using predetermined revascularization strategy-based anatomy, with a revascularization trigger of ≥70% for TVECAs and >50% for left main disease.

We attempted to image all the grafts in all patients using this standardized IDAP and platform. Technical reasons were the cause for nonimaged patients and/or grafts; this diminished with accrued experience. All patient clinical characteristics were captured in a combined American College of Cardiology/Society of Thoracic Surgeons clinical database for analysis.

The raw IDS and the NIRF-CAPA analysis data were stored in a unique data construct that directly combined the imaging data with the clinical data; thus, access to the raw imaging data files was always available for

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