Review Article

Techniques for intraoperative graft assessment in coronary artery bypass surgery

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Abstract: Early graft patency is a major determinant of morbidity and mortality following coronary artery bypass surgery. Long-term graft failure is caused by intimal hyperplasia and atherosclerosis, while early failure, especially in the first year, has been attributed, in part, to surgical error. The need for intraoperative graft evaluation is paramount to determine need for revision and ensure future functioning grafts. Transit time flowmetry (TTFM) is the most commonly used intraoperative modality, however, only about 20% of cardiac surgeons in North America use TTFM. When combined with high resolution epicardial ultrasonography, TTFM provides high diagnostic yield. Fluorescence imaging can provide excellent visualization of the coronary and graft vasculature; however, data on this subject is limited. We herein examine the literature and discuss the available techniques for graft assessment along with their limitations.

Keywords: Fluorescence imaging coronary artery bypass surgery; transit time flowmetry (TTFM); intraoperative imaging; intraoperative graft assessment

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Introduction

Coronary artery bypass graft (CABG) surgery, since its introduction in the 1960's, has been one of the cornerstones in the treatment of coronary artery disease. Its success over the years is attributed to a multitude of factors, in particular, advances in intraoperative and surgical techniques (1,2). Graft patency is a major factor contributing to cardiac morbidity and mortality, especially in the early follow-up period (3,4). At 1-year follow-up graft occlusion rates of 20.0% for venous and 8.0% for arterial grafts have been reported (5,6). While the cause of late graft failure is attributed to intimal hyperplasia and atherosclerosis, failure within the first year is, thought in part, to be related to technical error that could be corrected at the time of operation (7,8). The risk of graft occlusion secondary to surgical error is amplified in technically demanding cases such as off-pump CABG (8). However, the immediate assessment of grafts following anastomosis is often neglected or performed with crude evaluations such as finger palpation (4). This highlights the need for further research and examination into intraoperative graft assessment modalities that could aid the surgeon in decision making regarding graft revision. We herein review the literature and detail the most common techniques and their limits for intraoperative

graft evaluation used in CABG surgery.

Search method

In January 2017, we quarried PubMed using the terms "transit time flowmetry" (TTFM), "graft assessment", "intraoperative fluorescence", "indocyanine green" coupled, with "CABG", "imaging" and "patency." Relevant abstracts were reviewed and when found relevant the full article was examined. References from selected studies were cross-checked. The most important articles where included and in cases of disagreement an agreement was negotiated.

TTFM

TTFM is based on the principle that ultrasound waves passing from transducer to receiver will have a time delay or "transit time". A coronary graft is placed into a flow probe in a perpendicular fashion between two ultrasonic transducers, which can also act as receivers, and a single reflector. Ultrasonic signals are then transmitted from the proximal transducer to the reflector and redirected to the distal transducer. The same signal redirection occurs from the more distal transducer to the more proximal. The time delay between transducer to reflector to receiver is the transit-time and is determined by the flow velocity in the graft (9). The flowmeter then accurately and precisely calculates the flow volume in the graft based on the provided transit time (10).

When done properly, TTFM can provide invaluable information regarding graft flow; however, proper handling technique is paramount. Graft patency and flow are assessed by four variables namely: mean graft flow (MGF), pulsatility index (PI), backward flow percentage (%BF), and diastolic filling percentage (DF%) (10,11). While each variable adds its own unique piece of information, no one variable can be taken in isolation during decision making for graft revision.

MGF is represented in mL/min and is often coupled with electrocardiography. This coupling displays MGF as a flow curve with systolic (often red) and diastolic (often blue) easily displayed and recognizable.

The PI is calculated by subtracting the peak systolic flow from the peak diastolic flow and dividing by the mean flow and is represented by the equation $PI = [(Q_{max} - Q_{min})/Q_{mean}]$ (9,10). With unit cancellation the PI is represented as an absolute number and provides information on flow patterns and resistance.

Again, once TTFM is coupled with electrocardiography %BF can be calculated. The %BF is measured during one complete cardiac cycle and is the percent backward blood flow across the anastomosis. When displayed on a graph it is the area below the zero point.

The DF% is calculated from the following equation $DF\% = [(Q_{diastole}/Q_{Systole} + Q_{diastole})]$ and as with MGF and %BF requires the use of electrocardiography. It is a measure of the diastolic flow within the graft and optimally should be >50% of the MGF (10).

Each one of these variables provides specific information regarding the state of the graft and distal coronary bed and is influenced by similar and differing factors. MGF can be influenced by blood viscosity, graft and native coronary artery size, outflow bed quality, in cases of arterial grafts, spasm, and anastomosis quality (10,12). As a measure of flow, PI is altered by the level of native coronary stenosis, graft spasm or stenosis, and quality of the distal anastomosis. The %BF is influenced by competitive flow and this gives information regarding the severity of distal native coronary stenosis (13). DF% varies depending on probe location and which coronary circulation is being investigated. For example, while diastolic flow prevails in all grafts it varies depending on graft length and whether the graft is on the right or left coronary system, with the former having lower transmyocardial pressure gradients and thus more systolic flow (9,10).

Cutoff values

With varying cut off values and limited data, the parameters for TTFM have had limited wide spread acceptance. Currently the ESC/EACTS guidelines for TTFM graft assessment recommend cutoff values for MGF of >20 mL/min and <5 for the PI. However, most of this data is based on small cohorts and studies with differing cutoff values for predicting graft failure.

Di Giammarco and colleges examined 157 patients undergoing myocardial revascularization (304 total grafts) and found that MGF of ≤15 mL/min (OR: 21.2, P<0.001), PI of ≥3.0 (OR: 3.5, P<0.001), and %BF values of ≥3.0% (OR: 3.5, P<0.001) were all independent variables for predicting increased incidence of graft failure (12). This lead the authors to suggest a MGF cutoff value of ≤15 mL/min. Subsequent reports suggest similar values in particular a PI <5, DF% >50%, and MGF >15 mL/min (14,15).

In a recent study Amin and colleagues, in an effort to provide more coherent cutoff values for TTFM, reviewed and consolidated the available data on the subject (10). The

authors found that MGF values varied depending on the type of conduit with venous graft values of 40 mL/min and arterial graft values of 20 mL/min being suggested. PI has a high association with graft failure especially when above 5. The recommended PI values range from 3–5 with below 3 being ideal. A %BF of 3% or greater is associated with graft failure and thus a 3% or less cutoff is advocated. DF% has not been shown to be predictive of graft patency. However, since the predominate flow in bypass grafts should be diastolic flow the DF% is recommended to be >50%.

Predictability and adjuncts

The diagnostic accuracy of TTFM has been brought into question due to a wide range of reported sensitivities and specificities (4,11,12). This has likely been amplified by the fact that no single cutoff values are agreed upon leading to varying values being used in studies.

In one study, Kim and coauthors examined 58 patients who underwent total arterial off-pump CABG with intraoperative TTFM assessment. They found that when their institutional criteria [(I) systolic dominant or balanced flow curve in the left coronary system; systolic dominant flow curve in the right coronary system; (II) mean flow <15 mL/min; (III) PI >3 in the left coronary system and >5 in the right coronary system; (IV) insufficiency ratio >2%] for detecting abnormal flow were applied the sensitivity and specificity of TTFM was 96.2% and 76.9%, respectively (16). Adjuncts to TTFM have also been studied. The addition of high-resolution epicardial ultrasonography (HR-ECUS) to TTFM was theorized by Di Giammarco and coauthors to increase the diagnostic yield of TTFM as compared to TTFM alone (17). After examining 717 grafts, Di Giammarco and colleagues found that the positive predictive value of TTFM rose from 10% to 100% when HR-ECUS was added to the intra-operative assessment.

Long-term predictability

The predictive power of TTFM to determine long-term graft patency is also variable. In a mid-term angiographic follow-up of 16.5±7.6 months, Tokuda and colleagues found that a lower mean flow (OR: 0.96, 95% CI: 0.93–0.98; P<0.01) and a higher %BF (OR: 1.08, 95% CI: 1.01–1.17; P<0.05) were predictors for mid-term graft failure (11). In a later study by Kieser and colleagues, patients undergoing arterial revascularization were all submitted to intraoperative TTFM and the followed up for occurrence of mortality and major adverse cardiac events (MACE) (4). The authors found that a PI >5 was significantly associated with occurrence of MACE (17% *vs.* 5%, P=0.005) and mortality (32% *vs.* 12%; P=0.011). Mean flow values of <15 mL/min and a DF% cutoff of <45% were no predictive of MACE or mortality. However, when the 32 emergent cases were excluded from the analysis DF% was predictive of mortality (10% *vs.* 3%, P=0.043).

Limitations

A number of factors have to be taken into consideration leading to a complex assessment algorithm and the tendency to rely too heavily on one variable over another. The inability of TTFM to locate an obstruction within the graft, anastomosis, or coronary vessel leads to a more binary reading of patent *vs.* non-patent (7). Also the MGF is influenced by a number of other systemic factors such as mean arterial pressure and distal coronary flow that value range is often wide.

In conclusion, TTFM is the most commonly used intraoperative tool for graft assessment (10). Its variables can be influenced by a number of systemic factors making standardization of values difficult; however, its diagnostic accuracy can be increased with the addition of adjuncts such as HR-ECUS. Its predictability for long-term outcomes is variable and inconclusive with more research needed to clarify this point.

Intraoperative fluorescence coronary angiography

Intraoperative fluorescence imaging (IFI) is based on the properties of indocyanine green dye (ICG). The two properties of ICG that make it useful for IFI are its light emitting fluorescence properties when excited, and that the ICG molecule binds to intravascular proteins securing its location in the vascular system (7,18). When ICG is stimulated by laser energy at a wavelength of 806 nm the molecule emits a fluorescence wavelength of 830 nm. This excited fluorescence light is then captured by a charged couple device camera at a rate of 30 frames/sec as it moves through the graft. A series of images is then compiled to create a video documenting graft flow.

The procedure begins after the distal anastomosis has been completed. The laser source is positioned over the heart at a distance of approximately 30 cm and activated just prior to the first ICG bolus. ICG is injected into the central venous

system either via a central line or injection into the inferior vena cava in the cases of off-pump CABG. For on-pump CABG administration is through the cardiopulmonary bypass oxygenator or into the ascending aorta. The area of analysis is a 7.5 cm × 7.5 cm square (7,18). Both the laser and ICG are safe with the laser having a tissue penetration depth of only 1-mm and the ICG having rare allergic reaction unless used at high doses (0.5 mg/kg) (7,19).

Early use

Since its introduction by Detter and colleagues as a feasible means for intraoperative assessment of coronary blood flow in pigs, ICG has been employed with increasing frequency in humans as a method for coronary graft assessment (20). One of the earliest studies examining intraoperative use of ICG was done by Taggart and coauthors (18). They described their preliminary experience using ICG in 213 bypass grafts done both on- and off-pump. IFI confirmed graft patency was seen in all but four conduits which required graft revision. The authors concluded that IFI was simple, safe, non-invasive, and reproducible. Of note, the authors mention that in a majority of cases the image quality was similar to that of angiography. These findings have been confirmed in other studies demonstrating the feasibility and high quality imaging obtained from IFI (21,22).

Conventional angiography vs. IFI

Angiography continues to be the gold standard for visualization of coronary anatomy, however, routine intraoperative use is hindered by its highly invasive nature, need for cumbersome equipment, increased operative time, and potential nephrotoxicity. Reuthebuch and Taggart both examined IFI for graft assessment and found that it provides high quality images comparable to angiography without the need for radiation or catheters (18,21).

Clinical outcomes

Series based on IFI report a graft revision rate between 1.4% and 5.0% (18,21-25). In a randomized trial, Desai and coworkers compared TTFM and IFI to conventional angiography in 106 CABG patients (26). Of the entire cohort 46 patients were evaluated with all three techniques comprising a total of 139 grafts. Angiography detected 12 (8.2%) of grafts to have ≥50% stenosis or be completely occluded. IFI was able to detect 83.3% of theses abnormal grafts while TTFM only detected 25.0%. This lead to a calculated sensitivity and specificity for detecting a 50% stenosis of 83.3% and 100% for IFI and 25.0% and 98.4% for TTFM, respectively. The overall comparison of sensitivity and specificity for IFI and TTFM gave a significant P value of 0.011. In a similar prospective study Balacumaraswami and colleagues compared IFI with TTFM in 100 CABG patients totaling 266 grafts (27). Both TTFM and IFI demonstrated poor flow in 3.0% of grafts that requiring revision. However, in another 3.8% of grafts TTFM indicated poor flow based on MGF and PI values, while IFI demonstrated adequate flow. These grafts where not revised and the authors concluded that TTFM alone may increase the incidence of unnecessary graft revision.

In a later study by Hatada and coworkers TTFM was compared to IFI in ten saphenous vein grafts (15). Intraoperative data for both TTFM and IFI were compared to post-operative angiography. One graft was found to have 75% stenosis on angiography. Intraoperative IFI showed this graft to be patient with no difference between the other grafts. Only the harmonic distortion of TTFM was significantly different between the stenosed and remaining grafts.

Limitations

IFI visualization of the graft gives only a "semi-quantitative assessment" (7) of graft patency and gives very little information on competitive flow, the distal coronary bed, and transit times. Each graft has to be evaluated and requires 3–4 minutes(18) which prolongs operative time. Pedicled conduits have poorer visualization when compared to skeletonized conduits making IFI of limited value in the former case. For adequate imaging the heart has to be adjusted and is not in its native positioning meaning graft flow could be altered due to graft crimping.

In conclusion, while IFI has been used for years in other surgical subspecialties (18), its use in determining coronary bypass patency has not been definitively proven. While several studies have shown promising results, continued research with long-term follow-up will help delineate IFI's role in coronary surgery.

Alternative techniques for intraoperative graft assessment

While TTFM and IFI are the predominate methods

for intraoperative graft assessment in coronary surgery, other techniques have been described. Thermal coronary angiography was investigated by Iwahashi and colleagues in 107 coronary grafts (28). The technique uses either warm or cold solutions that are injected into the bypass grafts. This creates a temperature differential between the graft and the epicardial surface that can be visualized by an infrared camera. The authors were able to identify 3.7% of grafts as not patent. Similar to IFI, this technique had poor visualization on pedicled conduits. HR-ECUS has been examined in isolation but never used as such as it is operator dependent and while anterior conduits are easy to assess, lateral, inferior and posterior conduits are harder. Its best utilization seems to be in combination with TTFM.

Newer technologies are being continually developed to better understand and predict graft patency. A recent technology, iCertainty^{TM} uses multispectral physiologic visualization in hopes of better imaging graft flow (29).

Conclusions

TTFM, although limited as a single adjunct, when combined with HR-ECUS has a high diagnostic utility for determining need for graft revision. The data on long-term predictability is limited and further research is needed. We recommend the use of TTFM especially in the setting of technically difficult cases such as off-pump multivessel sequential CABG. IFI appears to be a promising modality for graft evaluation, however, limited data exists and we do not recommend its wide spread adoption at this time. More research is needed to delineate its diagnostic capacity.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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