Intraoperative Validation of Left Internal Mammary Artery Graft by Flourescence Imaging Technique

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Abstract :

Background: *In coronary artery bypass surgery (CABG) left internal mammary artery (LIMA) is considered gold standard conduit of choice for myocardial revascularization. Graft failure following CABG reduces cardiac mortality and morbidity both in short and long term. Although conventional angiography is gold standard for assessing graft patency but rarely available in same operating room. So intraoperative florescence imaging could be an efficient and reliable method of assessing the patency of graft.*

Methods*: This study was conducted between July 2013 to June 2014 in the Department of Cardiac Surgery of National Institute of Cardiovascular Diseases (NICVD). Thirty six LIMA grafts were assessed by using IFI system .ICG administered through CVP line and imaging acquired during pass of the ICG through field of view graft flow. Quality of anastomosis was intra operatively to validate graft.*

Results*: Mean age of study population was 54±8.38 years. Per operative assessment of LIMA to left anterior descending artery revealed 32 (88.8%) patent anastomosis, narrowing of anastomosis was found in 2 (5.55%) patients.*

Conclusion*: Intraoperative fluorescence imaging is an effective and inexpensive way to validate patency of LIMA graft.*

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Introduction:

Coronary heart disease (CHD) is the leading cause of morbidity and mortality worldwide, accounting for an estimated 7.3 million death in 2008 according to World Health Organization (WHO) For a large number of patients with CHD, coronary artery bypass graft (CABG) surgery remains the preferred strategy for coronary revascularization.[1]

Bypass graft patency is an important factor to predict patient outcome after CABG. The internal mammary artery (IMA) offers patient survival benefit and superior graft patency compared with vein grafts. For this reason, at least one arterial graft, usually the LIMA to the LAD, is attempted in virtually every patient undergoing coronary revascularization. [2]

Intraoperative graft failure is a major cause of cardiac mortality and morbidity and occurs in at least 4% of grafts (8% of patients) during CABG. This leads to graft compromise in 5%to 20% of patients at discharge. Graft failure is the most common cause of perioperative myocardial infarction, which is evident in up to 9% of CABG patients and contributes to adverse long-term clinical outcome. Postoperative angiography, used to assess graft patency before hospital discharge, has resulted in reoperation in some patients.[3]

Consequently, several techniques have been employed to assess intraoperative graft patency. These have included electromagnetic, ultrasound flow measurement, Doppler velocity waveform, epicardial ultrasound scanning, conventional and thermal coronary angiography, Transit-Time Flowmetry (TTFM) techniques. But all these techniques have limitations and poor resolution with misinterpretation chances. Conventional coronary angiography remains the gold standard, but time consuming not possible in our situation at Operation Theater.[4]

Intraoperative fluorescence imaging (IFI) is an intraoperative angiography-like imaging modality using fluorescent indocyanine green

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(ICG) excited with laser light. Recently, assessment of graft patency using the IFI system was introduced into clinical use. The IFI system (SPYTM intra-operative imaging system Novadaq Technologies Inc., Toronto, Canada) has been developed as a means for detecting dysfunctional grafts during CABG.[5]

Methods:

It was a descriptive cross sectional study done at NICVD study between July 2013 to June 2014 in a single unit under Department of Cardiac Surgery on 36 patients where patients underwent elective first-time CABG with LIMA used as a conduit. CABG with associated other procedure (Valve replacement, correction of congenital anomalies etc.),CABG without median sternotomy, when LIMA was not graftable (injury/ short/narrow caliber/arteriopathy), diseased Subclavian artery or reduced LIMA flow anticipated on angiography, patients with allergy to iodide , patients with severe hepatic malfunction [Serum Billirubin >1.2 mg/dl, Alanine aminotransferase (ALT) >50 U/L] and patients with renal insufficiency (serum creatinine>120 mmol/L) were excluded from the study.

Intraoperative Flurescence Imaging :

Novadaq Technologies SPY TM System: The technology is based on the fluorescence properties of ICG, a nontoxic dye that has been used in medicine for >40 years. When illuminated with 806 nm light, ICG fluoresces and emits light at 830nm. This fluorescent light is captured by a charged couple device video camera at 30 frames per second and displayed on a computer monitor. After analyzing the sequence, the images are saved to the computer in audio video interleave movie format. Hard copies of individual frames may also be printed on the video printer provided.[6]

Principle: Intraoperative fluorescence imaging is a novel imaging technique (SPY; Novadaq Technologies Inc, Toronto, Canada). Intraoperative fluorescence imaging is based on the fluorescent properties of indocyanine green (ICG) dye. After intravenous injection ICG binds immediately to plasma proteins and when illuminated with a monochromatic light source at 806 nm (near infrared) it emits light with a wavelength at 830 nm. This fluorescence is captured on a charged couple device video camera. The IFI system raises two potential safety issues regarding the laser light source and ICG dye. The total output of the laser is 2.7 watts, it operates at a distance of 30 cm above the heart and is spread over an area of 7.5 cm 7.5 cm. The laser light is of low intensity with a depth of tissue penetration of about 1mm to avoid myocardial thermal damage. The laser has an excellent safety profile for both the patient and operating room staff and no protective eyewear or clothing is required. Indocyanine green itself has an excellent safety profile and has been in clinical use for more than 4 decades. The incidence of allergic reaction to ICG is strongly dose dependent, being greatest with doses in excess of 0.5 mg/kg, and is reported to be approximately 1:40000, especially in patients allergic to iodine.[7]

Procedure: The camera imaging head is covered with a sterile polyethylene drape and positioned 30 cm above the heart. A green diode on its range detector gauge guides the positioning of the imaging head directly over the operative field. Indocyanine green is made up of a concentration of 2.5 mg/ml and on completion of the distal coronary anastomosis in off-pump CABG, a bolus of 1 ml of ICG dye is injected into the central venous catheter, which is rapidly flushed with 10 ml of normal saline. Alternatively the dye can be injected into the ascending aorta. For on-pump CABG the dye is injected directly into the oxygenator. Immediately after intravenous dye injection (or after a 5-second delay if the dye is injected into the oxygenator), the laser power is activated and captured images are recorded on the computer hard drive. The appearance of fluorescent ICG dye passing antegradely through the bypass grafts confirms graft patency. The visualization of dye fluorescence is better with skelitonised internal thoracic artery and radial artery conduits compared with pedicled conduits. The procedure takes approximately 3 minutes per graft, and ICG injections can be administered repeatedly.[8]

Time required for the procedure (IFI):
An average of 3 minutes and 14 seconds needed for the procedure ranging from 2 minutes to 5 minutes.

Revision/Salvage graft:
There was provision of revision of the LIMA to LAD graft or giving a salvage venous graft in LAD for the two stenosed and two narrowed grafts. Among them in only two cases a salvage graft was given.

With this system of IFI we did the study first time in Bangladesh at NICVD Dhaka. Objective of the study was to validate the use of intraoperative fluorescence imaging (IFI) system to assess patency of grafts in the peroperative setting.

Results :
Regarding Age 40-60 years were highest 69.2%, more than 60 years 29.1% and less than 40 years were only 7.7%. Male dominates 88.5% and female being 11.5%. Patent LIMA were found in all 36 patients .LAD were stenosed proximally in 26 patients (72.22%)and mid LAD were stenosed in 10 patients (27.77%).The extent of stenosis in LAD was more than 70% in 32 patients (88.89%) and less than 70% in only 4 patients (11.11%). In preoperative echocardiographic finding EF were more than 50% in 26 patients ,EF 40-50% in 8 patients and EF of less than 40% in 2 patients.

Regarding procedure of CABG surgery among all the 36 patients the percentage of conventional CABG in arrest heart was 69.45% (in 25 patients) and OPCAB was 30.55% (in 11 patients). However none of these patients underwent on pump beating heart CABG surgery. So it was clear that 69.45% of CABG patients required (in 25 patients) use of CPB while 30.55% (in 11 patients) of them not required any use of CPB.

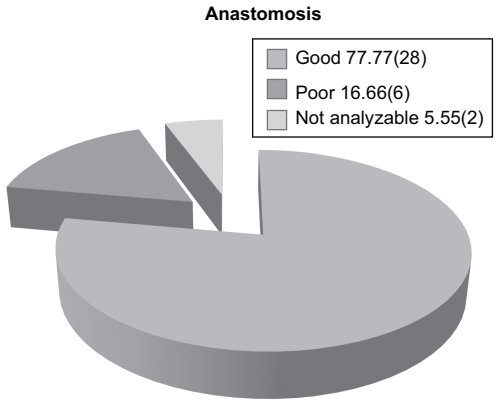

Fig.-1: *Optical Quality of graft anastomosis.*

Table-I
Quality of Dye flow in grafts and coronaries.

Quality of flow	No of anastomosis	Percentage
Good	33	91.66
Poor	02	05.55
Not analyzable	01	02.77

Table-II
ICG washout in the grafts and coronaries.

ICG washout	No of cases	Percentage
Fast	33	91.66
slow	02	05.55
Not analyzable	01	02.77

The washout of ICG was visually defined as follows:

- Fast washout: d+15 heartbeats required for ICG washout.
- Slow washout: >15 heartbeats required for ICG washout.
- Fast washout was observed in 33 cases and
- Poor washout found in 2 cases among 36 cases.

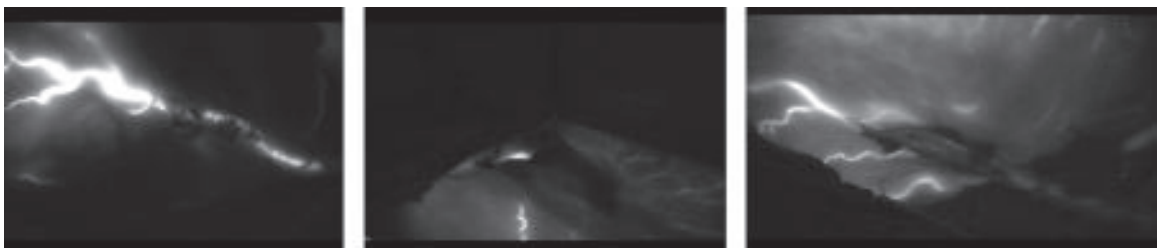

Fig 2: *IFI imaging showed LIMA to LAD. A- Excellent anastomosis; B -Stenosed anastomosis and C- Narrowing of anastomosis*

Discussion:

Despite tremendous improvements in the quality of processes of care in cardiac surgery over the past decade, there is still no well-accepted or broadly used technique to assess the quality of the bypass graft itself. Indeed, until recently and in the absence of suitable devices for assessment of graft patency. The current natural incidence of intraoperative graft failure has been poorly documented, which can contribute to early morbidity and mortality and adversely affect long-term outcomes. After promising clinical investigations with IFI technique, human studies were performed first in 2002. Subsequently, a rigorous systematic approach was embarked to intraoperative graft patency assessment using ICG angiography. The technique showed perfect inter-rater reliability for graft patency among two surgeons, one with significant experience in the technique and one with no previous experience with the technique, suggesting that interpretation of images does not require significant training or a learning curve. There was poor inter-rater reliability for graft TIMI flow grade. Because most free grafts in the series were hand injected, the subjective interpretation of TIMI flow grade was dependent on the rate of injection by the surgeon or assistant, which were not standardized.[9]

Detter and colleagues reported their experience with IFI imaging in 348 grafts in 120 patients and confirmed the value of IFI in the clinical setting. They found an inter observer agreement of 100% for graft occlusion between two surgeons, one experienced and another inexperienced with the interpretation of IFI images and 100% sensitivity and 100% specificity when compared with postoperative angiography to detect graft occlusion or a graft narrowing greater than 50%.[10]

Set-up and clinical usage of the ICG-based imaging system is simple. No further IV lines or catheters are necessary in order to acquire images. The chest remains open when graft patency is confirmed and so there is no reopening necessary in case of irregularities. Draping and adjustment of the articulating arm supporting the laser/camera unit is simple. Thirty-second sequences are long enough to analyze graft flow, anastomotic site and run-off of ICG. However, quantitative flow measurement and curve analysis is not yet available but is under development.[11]

In the present study, like previous studies we did not observe any adverse reaction either intraoperatively or postoperatively. In addition to the intrinsic safety of ICG, the present application may benefit from the very low dose of ICG (1.25 to 5 mg per patient per injection), which we had to inject, compared to 0.5 mg/kg of body weight administered in liver function tests. We did not observe any liver enzyme elevation (SGPT), nor did we encounter any renal dysfunction expressed as elevated serum creatinine or urea.

In this study, we determined that in an academic practice, nearly 5.5% of left internal mammary artery grafts required graft revision and 5.5% required minor correction when completion ICG angiography was performed for intraoperative quality assessment and validation of the grafts. These results are almost identical to those of other groups (approximately 5%) who have used this technology.[12] In all cases, the lesions would have otherwise been missed by the operating room team. The clinical consequences of early graft failure are not benign. A report suggests that the perioperative mortality in patients with unrecognized graft problems is over 9%.[13]

All the angiography by IFI done in our study was fully analyzable except one case. Reuthebuch and colleagues found 107 of 124 grafts analyzable in their study. They found that 18 grafts were not analyzable due to posterior location As we imaged LIMA to LAD graft which is located anteriorly, we have not faced such problem. In our study the quality of visualization of the coronary artery was excellent. The native arteries were visualized very well.[14]

Compared with slow washout, fast washout of the ICG is associated with a higher preoperative ejection fraction, use of internal mammary artery grafts, anterior anastomosis location and collaterals. The semi quantitative analysis of the contrast dye washout showed that more rapid elimination of ICG was associated with higher ejection fraction. Although angiography requires

forced contrast medium injection through the coronary arteries, the IFI system observes natural flow of both native vessels and grafts in off-pump CABG. The IFI washout analysis can potentially provide additional functional information that is different from frame counts by angiography. In our cases, there were virtually no cases of severe graft stenosis except for total occlusion. Thus, we are unable to assess the possible relationship of graft stenosis and ICG washout. Waseda and colleagues also had same experience as ours.[12] Further analysis may be necessary to clarify the clinical implications of this IFI finding.

For an average the total extra time needed to perform intraoperative patency assessment was approximately 3 minutes for each graft whereas conventional angiography takes about 30 minutes. In other studies 2 to 3 minutes required for each image-sequence acquisition. So assessment of the graft by IFI was not very difficult for the surgeon to implement. Conventional angiography is done after closure of the chest whereas IFI is done while the chest is still open. There is great opportunity to validate the grafts by this fluoresce angiography and if any stenosis found in the anastomosis there is provision to revise the graft or put a salvage graft although the decision solely depends on the operating surgeon.[9,13,14]

Conclusion

The ICG-based imaging system is a convincing tool for peroperative assessment of graft patency. The device has the great advantages of non-invasiveness and safety and the quality of images. Intraoperative fluorescence imaging provides critical information to surgeons to detect non-patent grafts, allowing them to be revised while the patient is still on the operating table. Using the IFI system, technical failures could be completely resolved during surgery. We conclude that the use of the IFI system for intra-operative graft validation during CABG may become the gold standard for surgical management in the near future.

Conflict of Interest - None.

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