Analysis of a Multicenter Registry on Evaluation of Transit-Time Flow in Coronary Artery Disease Surgery

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Analysis of a Multicenter Registry on Evaluation of Transit-Time Flow in Coronary Artery Disease Surgery (EFCAD Study)

May 2017 - March 2021
- 1616 patients undergoing isolated CABG enrolled at 9 sites.
- 1414 patients eligible for analysis.
- 1176 patients eligible for primary end-point analysis (MACE).

Acceptance of incorrect (<15 ml/min.) graft flow on LAD was predictive of adverse outcomes.

<table>
<thead>
<tr>
<th>Multivariate analysis of predictors of MACE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Event N</td>
</tr>
<tr>
<td>Incorrect (&lt;15 ml/min.)</td>
</tr>
<tr>
<td>LAD graft flow</td>
</tr>
<tr>
<td>No</td>
</tr>
</tbody>
</table>

MACE, Major Cardiac Adverse Events. LITA, Left Internal Thoracic Artery; LAD, Left Anterior Descending Artery. PI, Pulsatility Index. DF%, Diastolic Filling %.
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Word Count: 3168

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Abbreviations and Acronyms

- CABG, coronary artery bypass grafting
- LITA, left internal thoracic artery
- RITA, right internal thoracic artery
- LAD, left anterior descending coronary artery
- OM, obtuse marginal branch
- PDA, posterior descending artery
- TTFM, transit-time flow measurement
• PI, pulsatility index
• GF, mean Graft Flow
• DF, Diastolic Filling
• MACE, major cardiac adverse events
• CPB, cardio-pulmonary bypass
• PTCA, Percutaneous Transluminal Coronary Angioplasty

Central Picture Legend

Acceptance of inadequate (≤15 ml/min.) graft flow on LAD was predictive of adverse outcomes

Central Message

According to a prospective multicenter registry focused on TTFM assessment in isolated CABG patients, acceptance of inadequate (≤15 ml/min.) graft flow on LAD was predictive of adverse outcomes.

Perspective Statement

Data from EFCAD prospective multicenter registry suggest that TTFM is a reliable tool to evaluate graft flow and we found that postoperative adverse events are significantly higher in patients with inadequate (≤15 ml/min.) graft flow on LAD. Even if interpretation of TTFM assessment depends on learning curves and surgeon’s commitment, it should be routinely adopted in CABG procedures.
ABSTRACT

Objective: EFCAD registry aims to assess the impact of Transit-Time Flow Measurement (TTFM) in daily practice.

Methods: EFCAD is a prospective, multicenter study involving nine centers performing TTFM during isolated coronary artery bypass grafting (CABG). Primary end-point was occurrence and risk factors of Major Adverse Cardiac Events, including perioperative myocardial infarction, urgent postoperative coronary angiogram and/or revascularization, and hospital mortality.

Secondary end-points were rate of graft revision during surgery and factors affecting graft flow.

We respected the limit values set by the experts: Mean Graft Flow >15 ml/min and Pulsatility Index ≤5.

Results: Between May 2017 and March 2021, 1616 patients were registered in EFCAD database. After review, 1414 were included for analyses. Of those, 1176 were eligible for primary end-point analysis. Graft revision, mainly due to inadequate TTFM values, occurred in 2% (29 patients).

Primary end-point occurred in 46 (3.9%) patients, and it was related with left anterior descending artery (LAD) Graft Flow ≤15 ml/min. (OR 3.64, p<0.001). Graft flow was related with number of grafts (3 vs 1-2, β=-1.6; 4-6 vs 1-2, β=-4.1, p<0.001, β >0: higher flow), and graft origin (Aorta vs Y, β=9.2; in situ left internal thoracic artery vs Y, β=3.2; in situ right internal thoracic artery vs Y, β=2.3, p<0.001).

Conclusions: Data from EFCAD study suggest that TTFM is reliable to evaluate graft flow, and acceptance of inadequate flow on LAD anastomosis affect postoperative outcomes. In our opinion,
TTFM assessment should be routinely used in CABG procedures, even if interpretation depends on learning curves.

Abstract Word Count: 250

**KEYWORDS**

Multicenter Registry; Coronary Artery Surgery; Transit-Time Flow Measurement
INTRODUCTION

In the context of coronary artery bypass surgery, graft patency seems to play an important role in early and late postoperative outcomes. Technical errors could be one of the factors, in addition to various factors affecting graft patency, and although rare, objective assessment of graft and anastomosis quality by intraoperative measurement of graft flow should be welcomed. Although several studies have led Transit Time Flow Measurement (TTFM) to enter the guidelines, it has not yet routinely adopted by surgical community as a standard of care, with an estimated usage rate of only 30% of procedures. To be Time-consuming and the need for a learning curve to interpret the results have generally been put forward to explain the reluctance to use it, as well as the lack of results concerning its clinical impact, which remains controversial. This study aims to describe the impact of routine use of TTFM in our daily practice and to find any relationship between TTFM values and clinical outcomes.

PATIENTS AND METHODS

Study Design

The EFCAD registry is a multi-institutional, prospective registry involving nine French centers routinely performing CABG. The registry was originally designed to assess the association between postoperative outcomes and TTFM parameters measured with MiraQ device or VeriQ C devices (Medistim ASA, Oslo, Norway). Preoperative patient’s data and outcomes were prospectively collected in on-line database (EFCAD database), which received a CNIL (French Commission of
Information Technology and Freedom, *Commission Nationale de l'Informatique et des Libertés*)

approval: 2060635 v 0 (May 3, 2017). An Institutional Review Board grant was released by the ethical committee of the French Society of Thoracic and Cardiovascular Surgery (CERC-SFCTCV-2023-06-27_29236_Mojgan Laali), and the study received a research grant from Medistim ASA (Oslo, Norway).

**Study Population**

Between May 2017 and March 2021, 1616 patients undergoing primary isolated CABG were enrolled. Inclusion criteria was the need for isolated CABG and exclusion criteria were combined surgery, redo surgery, emergency surgery, and patients with very low EF (≤ 20%) for whom a temporary circulatory assist device was planned.

**Definitions and Outcomes**

Primary end-point of interest was the occurrence and the risk factors of Major Adverse Cardiac Events (MACE) at 30 postoperative days, including perioperative myocardial infarction, urgent postoperative coronary angiogram and/or revascularization, and hospital mortality. Secondary end-points were rate of graft revision and factors affecting graft flow (GF). Incomplete TTFM assessment, which means at least one graft not tested per patient, was also described. In case of revised graft, only TTFM values after revision were applied for analyses of graft flow and primary end-point occurrence.

**TTFM Assessment**

TTFM measurements were performed with the MiraQ or VeriQ C devices (Medistim ASA, Surgitech, France), after cross-clamp release, on partial cardio-pulmonary bypass (CPB). The systolic blood pressure at the time of the measurements was at least 100 mmHg. In case of off-pump procedures, assessment was carried out before protamine administration. The measurements
were taken after all grafts were completed. The 2 or 3-mm probe was most commonly used. In order to obtain homogenous results, TTFM was assessed by respecting the following instructions: the acoustic coupling index must be above 40% (displayed in green or yellow on the screen), indicating the accuracy of the ultrasonic conductivity; and the flow measurement was registered when mean flow, indicated by the red line, was constant and horizontal. The patency of the grafts was assessed using three variables: diastolic flow curve, mean flow, and PI. Normally the flow curve will show a small backflow during early systole and a predominantly forward flow during diastole.

Cut-off values of TTFM assessment were mean Graft Flow (GF) >15 ml / min, Pulsatility Index (PI) < 5, and Diastolic Flow (DF) > 70% for left coronary bed, and > 50% for the right one.

**Statistical Analyses**

Categorical variables were described as number (%) and continuous variables as median (interquartile range [IQR]). Risk factors of MACE and factors associated with an incomplete test were assessed using logistic regression model. Univariate analysis (p<0.2) was first performed to select potential explanatory variables (patient’s characteristics, surgical technique and TTFM parameters) that were subsequently tested in multivariate model (backward variable selection based on p-values) and presented as odds ratio (OR) with their 95% CI. Factors associated with graft flow were assessed using linear mixed model with a random effect patient (several measurements for each patient). Univariate analysis (p<0.2) was first performed to select potential explanatory variables (patient’s characteristics, surgical technique and other TTFM parameters) that were subsequently tested in multivariate model (backward variable selection based on p-values) and presented as beta coefficients with their 95% CI. Statistical analyses were performed using R Statistical Software version 4.1.0.

**RESULTS**
Patients

One hundred eighty-two patients were excluded for missing data and 20 patients because they did not undergo left anterior descending artery (LAD) artery revascularization: after review, 1414 patients were eligible for analysis. Of those, 238 patients were excluded from primary end-point analysis because of incomplete TTFM assessment (n=234, 17%) or because they received a conduit other than an internal thoracic artery (ITA) on the LAD (n=4, 0.3%). Therefore, 1176 patients were eligible for primary end-point analysis. As we can see in figure 5, the graphical abstract of the study. Fig. 1 shows a flow-chart with details of inclusions and eligibility of patients. Preoperative characteristics and operative data are summarized in Table 1a,b.

TTFM graft assessment

TTFM was assessed for 3827 of 4211 (91%) grafts realized. Details of operative characteristics and TTFM parameters assessed by graft localization are resumed in supplementary appendix (Section 1a,b). It is important to mention that as interpretation of the results in not easy, the surgeons were free to decide whether to revise the anastomosis or not based on the results of the measurements. There is no doubt that if any MACE occurred, it was then recorded in the database. In our series, thirty-three grafts were intraoperatively revised in 29 patients (2%). Twenty-three grafts were revised for inadequate GF and PI values at the same time, 4 grafts for just inadequate GF and one graft for inadequate PI; five grafts were revised despite correct values of both GF and PI. Eight hundred ninety-two grafts were not revised despite inadequate either GF and/or PI values. Revision was associated with significant GF improvement (4.0, [2.0;8.0] vs. 28.0, [10.8;38.5], p<0.001) and PI reduction (12.0, [4.5;25.0] vs. 2.5, [2.05;4.23], p<0.001, Fig. 2 a,b). Effectives of revised grafts according to inadequate flow and PI are resumed in supplementary appendix (Section 2a,b).

Primary End-point Outcome
Primary end-point outcome occurred in 46 out of 1176 patients (3.9%, 95% C.I. 2.9.5.2).

Postoperative outcomes are detailed in table 1c. Primary end-point occurred in 3 patients after revision:

- A LITA to LAD graft was revised because of low flow (8 ml/min.) and high PI (10). After revision, PI decreased to 2.9, but graft flow remained inadequate (2.4 ml/min.).
- A RITA to Obtuse Marginal graft was revised because of low flow (-1 ml/min.) and high PI (33). After revision, both graft flow and PI improved, but they remained inadequate (graft flow 10 ml/min., PI 10).
- A LITA to Obtuse Marginal graft was revised because of low flow (3 ml/min.). After revision, graft flow improved to an adequate value of 48 ml/min.

We observed an increased occurrence of primary end-point in patients needing graft revision, but this association did not reach a statistical significance (OR 2.96, 95% C.I. 0.69, 8.84 p=0.13).

MACE occurrence was higher in case of inadequate (≤15 ml/min.) flow on the LAD graft (OR 3.21, 95% C.I. 1.67, 5.95, p<0.001, Fig. 3). In multivariate analysis, again acceptance of an inadequate flow (≤15 ml/min.) on the LAD graft was associated with adverse outcomes (OR 3.64, 95% C.I. 1.87, 6.90, p<0.001, showed in Central Picture). Other predictive factors of primary end-point occurrence were off-pump surgery (OR 3.13, 95% C.I. 1.61, 5.87, p=0.001) and use of RITA as conduit for LAD graft (OR 2.74, 95% C.I. 1.38, 5.22, p=0.005). Analyses of risk factors for primary end-point occurrence are detailed in supplementary appendix (Section 3 a,b).

**Graft Flow**

At multivariate analysis, graft flow was related to surgical technique, other TTFM parameters, and patient’s profile. Graft flow was significantly lower in case of revascularization with multiple sequential arterial grafts for each anastomosis, even if it remained in the normal range. A free-graft with a proximal anastomosis on the Aorta showed the highest flow in comparison with a Y-
configuration, followed by in-situ ITA grafts: Aorta vs Y, $\beta=9.2$ ($\beta>0$: higher flow); in situ left ITA vs Y, $\beta=3.2$; in situ RITA vs Y, $\beta=2.3$, $p<0.001$. Patients’ characteristics associated with high graft flow were male gender ($\beta=3.4$, $p=0.009$) and smoking status ($\beta=3.8$, $p<0.001$). The other TTFM parameters, as Pulsatility Index ($\beta=-0.62$, $p<0.001$) and Diastolic Filling% ($\beta=0.31$, $p<0.001$), showed a significant association with graft flow. Data’s concerning factors associated with graft flow are detailed in supplementary appendix (Section 4 a,b).

**Incomplete TTFM Assessment**

Complete assessment (all bypass tested vs at least one bypass not tested) of all grafts was achieved in 1180 (83%) patients. Exhaustiveness of doppler measures was related, in multivariate analysis, to patient’s characteristics and surgical technique. For example, revascularization with multiple sequential arterial grafts, especially in Y or T configuration, is more challenging because great care must be taken when handling the grafts to avoid inadvertent traction on the grafts and anastomotic tears, especially when doing measurements after cross clamp release, while resumption of heart beating.

An issue was also related to the design of the Doppler probe we used at the start of the study, which was solved with the handle less model. Our study confirm that the number of distal anastomoses (NDA) (3 vs 1-2, OR 2.86; 4-6 vs 1-2, OR 3.03, $p<0.001$) and NDA with RITA (2-4 vs 0-1, OR 1.87, $p=0.017$) were associated with a higher probability incomplete assessment, while NDA with saphenous vein (1-2 vs 0, OR 0.25, $p<0.001$), age (OR 0.98, $p=0.007$) and smoking status (OR 0.43, $p<0.001$) were associated with a lower probability of being not completely tested. The factors associated with incomplete testing are detailed in supplementary appendix (Section 5 a,b).

**DISCUSSION**
The EFCAD study is a prospective, multicenter registry involving nine academic centers in France, with the aim of verifying the impact of the systematic use of Transit Time Measurement (TTFM) in our daily practice, in order to find any relationship between TTFM values and clinical outcomes.

Clinical Impact of TTFM

Nevertheless ESC guidelines on myocardial revascularization highly recommend perioperative graft evaluation by Doppler control, which is also advocated by a recent expert consensus. TTFM has not yet routinely adopted by surgical community as a standard of care. Reluctance against routine TTFM use rely upon controversies on real need and clinical benefit of the technique. In comparative studies, Becit et al. and Bauer et al. reported significant encouraging results using TTFM; in the REQUEST registry, 25% of patients required a change in surgical strategy guided by TTFM and ultrasonic imaging of Aorta, conduits and grafts, resulting in reduction of in-hospital mortality and morbidity. However, the GRIIP RCT trial and a sub-analysis of ROOBY trial failed to demonstrate any impact of TTFM on one and 5-years clinical outcomes. These discrepancies concerning clinical evidence could be explained by several factors. First, occurrence of acute adverse events in contemporary coronary surgery is rare, ranging between 2 and 7% post-operative period and and 12% at 5 years. In EFCAD registry, the overall occurrence of MACE was 3.9%. A direct link between inadequate TTFM values and adverse postoperative outcome may be difficult to show because an impaired graft may have no immediate clinical impact, resulting in a silent postoperative course. As noted by Gaudino et al., the relationship between graft patency and clinical outcomes is a complex process, which could be affected by competitive flow, persistent collateral flow, diabetes, quality of target vessels.
and other factors. However, even if small series reported no clinical impact of graft occlusion, a large number of studies found a correlation between graft patency and patients outcomes. As we recently published in a series with total arterial revascularization with ITAs, MACE occurrence was significantly reduced by half, from 6.9% to 3.3%, by adopting TTFM. Moreover, every adverse event was reduced, even without reaching statistical significance.

This positive effect could be explained by the fact that a technical problem concerning the conduit or graft anastomosis in a multiple sequential arterial technique can be more dramatic, given that blood perfusion of a large part of the myocardium often depends on the flow in a single conduit.

Studies have shown that, among TTFM parameters, PI was significantly associated with postoperative outcomes, either alone or in association with other clinical parameters. In EFCAD registry, tolerance of an inadequate graft flow on LAD is strongly associated with adverse outcomes, probably because the aforementioned mechanisms are less likely to compensate an impaired LITA to LAD graft in presence of a severe proximal stenosis of the native coronary artery. Figure 4 shows TTFM recording before and after revision of a malfunctioning LITA to LAD graft. Even if pulsatility index is in a normal threshold, both graft flow value and waveform testify for an impaired graft (Fig. 4a). After revision, graft flow value increases and waveform recovers a normal shape (Fig. 4b).

Adoption of TTFM

The surgeons who do not adopt TTFM assessment, believing on the one hand that the error rate is low, on the other hand, that doing the measurements is time-consuming, and interpreting the results is not easy. It is right that TTFM assessment was associated with longer CPB times, but median extra-time needed for measurement was only three minutes in our recently published study (76.0 min. [62.0;91.2] vs. 79.0 min. [65.0;94.0], p=0.042). Several studies confirm that graft revision is an infrequent event, reported to be undertaken in 3.3% to 5.7% of patients with abnormal TTFM values. In REQUEST study, among 25% of patients requiring a change in
surgical strategy guided by TTFM and epicardial ultrasonography (HR-ECUS), only 7.8% were solely related to the grafts. In EFCAD registry graft revision rate was even lower, 2% (per patient rate) with only 33 grafts revised out of a total of 3827 grafts tested, and 28 grafts revised out of 920 grafts with abnormal TTFM values. EFCAD study showed that in two patients, after revision, improvement of TTFM values remained under adequate thresholds. Obviously, it is possible, and even probable, that anastomosis revision causes greater trauma to the anastomotic site and therefore higher risk of graft failure. Of course, we can understand that surgeons are reluctant to revise the grafts.

We confirm that interpretation of TTFM results is not easy and we know that, even if the threshold values and curves were defined for different types of grafts and revascularized vessels, standardization of TTFM findings is difficult because of large biologic variability among different patients, as well as within the same patient. The ability to correctly interpret TTFM findings develops with experience. On the other hand, we have to keep in mind that TTFM values are only useful and do not dictate the decision.

We emphasize that great care must be taken when handling the grafts to make the measurements to avoid inadvertent traction on the grafts and anastomotic tears, and this is another reason that restraint the surgeons from using this technique. As underscored by Kieser, assessment of a graft on the posterior or lateral wall could be not possible off-pump; in case of revascularization with multiple arterial sequential grafts, TTFM assessment could be difficult even while on partial CPB, which could also explain the 17% incomplete testing rate in EFCAD patients. Indeed, as reported in supplementary appendix (Section 1a), while frequency of lateral or posterior grafts not tested ranged between 14% and 24%, only 4% of LAD grafts was not tested. We believe that, even with all these limitations, by gaining experience with this device, we can prevent a large number of unpleasant events, but surgeons who have not been exposed to TTFM technology cannot easily accord it the proper level of importance.
Another consideration about the adoption of TTFM concerns training of residents in coronary surgery.

A recent analysis \(^{19}\) showed that, by using TTFM with "appropriate supervision... residents can perform CABG with appropriate results, without compromising patient outcome."

**, Graft Flow**

Recent meta-analysis confirmed that graft flow is lower in arterial than in venous grafts, \(^ {20}\) which was also found in EFCAD univariate analysis (supplementary appendix, Section 4a).

Nevertheless, these results were irrespective of the graft origin, in situ or free-graft. Data from EFCAD registry showed that highest flow is associated with free-grafts implanted on the Aorta, followed by in situ ITA grafts and free-grafts implanted on a Y- configuration. These results are difficult to translate in a clinical setting: in EFCAD registry, 79% of patients underwent a bilateral ITA revascularization and 64% received a total arterial revascularization with only ITAs (Table 1b). Since graft flow was inversely related to the number of anastomoses, total arterial revascularization with multiple sequential grafts could be associated with lower flow per graft. So far, there is no evidence that anastomosis with more flow, when within the normal range, works better. By the way, TTFM is not here to verify the flow patterns which depends to several factors, it is here to give us an objective assessment for the quality of grafts and anastomosis.

As reported by Krasopoulou, \(^ {21}\) we also found a positive correlation between graft flow and male gender, probably because of larger diameter of coronary arteries and grafts; this may also explain the correlation between graft flow and smoking status, being more frequent in male patients.

**LIMITS**
Nevertheless its prospective design, the EFCAD study carries all the limits that implies a non-randomized controlled trial (RCT), meaning lack of a control arm for comparison the results with or without Doppler control during CABG. Even if has often been advocated, we believe that a randomized trial to check the effectiveness of doppler graft control is no more ethically possible and even desirable: an increasing amount of evidences is now available to confirm the association between TTFM values and graft patency, and more recently also between TTFM and clinical outcome.

CONCLUSION

Transit-time flow measurement gives important and accurate intraoperative information about the status and patency of each individual graft. It enables technical problems such as kinked, twisted, or stenotic grafts to be diagnosed accurately, thereby allowing prompt revision of the constructed grafts before the patient leaves the operating room. Our data suggest that TTFM is a reliable intraoperative tool to evaluate graft flow and we found that postoperative adverse events are significantly higher in patients with an inadequate (≤15 ml/min.) flow on LAD graft (Figure 5). We have also noticed that this technology could be useful in university hospitals for residency training programs. Based on this study, we suggest that TTFM assessment should be routinely used in CABG procedures.

Acknowledgment

A complete list of Investigators and affiliated Institutions is available in the Supplementary Appendix.
REFERENCES


Table 1. Preoperative Characteristics, Operative Data and Postoperative Outcomes

A. Preoperative characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N = 1,414¹</th>
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<tbody>
<tr>
<td><strong>Age</strong> Median (IQR)</td>
<td>67.82 (61.02, 73.33)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td><strong>F</strong></td>
<td>205 (14.50%)</td>
</tr>
<tr>
<td><strong>M</strong></td>
<td>1,209 (85.50%)</td>
</tr>
<tr>
<td><strong>Smoking (active or history of)</strong></td>
<td>596 (42.15%)</td>
</tr>
<tr>
<td><strong>History of smoking</strong></td>
<td>421 (29.77%)</td>
</tr>
<tr>
<td><strong>Active smoking</strong></td>
<td>175 (12.38%)</td>
</tr>
<tr>
<td><strong>Insulin Dependent Diabetes</strong></td>
<td>228 (16.12%)</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>1,007 (71.22%)</td>
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</table>

B. Operative Data

<table>
<thead>
<tr>
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</tr>
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<tbody>
<tr>
<td><strong>Off pump surgery</strong></td>
<td>180 (12.73%)</td>
</tr>
<tr>
<td><strong>Nb of distal anastomoses (with data)</strong></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>143 (10.11%)</td>
</tr>
<tr>
<td>2</td>
<td>357 (25.25%)</td>
</tr>
<tr>
<td>3</td>
<td>432 (30.55%)</td>
</tr>
<tr>
<td>4</td>
<td>369 (26.10%)</td>
</tr>
<tr>
<td>Characteristic</td>
<td>( N = 1,414^1 )</td>
</tr>
<tr>
<td>--------------------------------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>5</td>
<td>96 (6.79%)</td>
</tr>
<tr>
<td>6</td>
<td>17 (1.20%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>4211 (100%)</strong></td>
</tr>
</tbody>
</table>

**Graft tests**

- Completely tested: 1,180 (83.45%)
- Incompletely tested: 234 (16.55%)

**Total arterial revascularization**: 926 (65.49%)

**Total arterial revascularization with only ITAs**: 902 (63.79%)

**Grafts distribution**

- **Number of SV**
  - 0: 926 (65.49%)
  - 1: 424 (29.99%)
  - 2: 64 (4.53%)

- **Number of RA**
  - 0: 1,387 (98.09%)
  - 1: 24 (1.70%)
  - 2: 3 (0.21%)

- **Number of LITA**
  - 0: 12 (0.85%)
  - 1: 889 (62.87%)
  - 2: 487 (34.44%)
  - 3: 26 (1.84%)

- **Number of RITA**
  - 0: 287 (20.30%)
  - 1: 678 (47.95%)
  - 2: 343 (24.26%)
  - 3: 99 (7.00%)
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>( N = 1,414 )</th>
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<tbody>
<tr>
<td>4</td>
<td>7 (0.50%)</td>
</tr>
</tbody>
</table>

**Graft BITA**  
1,115 (78.85%)

**Graft origin distribution**

- **Number of In situ LITA**

<table>
<thead>
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<th>Number</th>
<th>Count</th>
<th>Percentage</th>
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<td>30</td>
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<td>899</td>
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<td>2</td>
<td>464</td>
<td>32.81%</td>
</tr>
<tr>
<td>3</td>
<td>21</td>
<td>1.49%</td>
</tr>
</tbody>
</table>

- **Number of Y-graft configuration**

<table>
<thead>
<tr>
<th>Number</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>607</td>
<td>42.93%</td>
</tr>
<tr>
<td>1</td>
<td>390</td>
<td>27.58%</td>
</tr>
<tr>
<td>2</td>
<td>315</td>
<td>22.28%</td>
</tr>
<tr>
<td>3</td>
<td>95</td>
<td>6.72%</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>0.50%</td>
</tr>
</tbody>
</table>

- **Number of In situ RITA**

<table>
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<th>Count</th>
<th>Percentage</th>
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<tr>
<td>0</td>
<td>1,056</td>
<td>74.68%</td>
</tr>
<tr>
<td>1</td>
<td>328</td>
<td>23.20%</td>
</tr>
<tr>
<td>2</td>
<td>26</td>
<td>1.84%</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>0.28%</td>
</tr>
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</table>

- **Number of AO**

<table>
<thead>
<tr>
<th>Number</th>
<th>Count</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>905</td>
<td>64.00%</td>
</tr>
<tr>
<td>1</td>
<td>428</td>
<td>30.27%</td>
</tr>
<tr>
<td>2</td>
<td>78</td>
<td>5.52%</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>0.14%</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>0.07%</td>
</tr>
</tbody>
</table>

**Intraoperative graft revision**  
29 (2.05%)

**Number of intraoperative graft revision**

<table>
<thead>
<tr>
<th>Number</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1,385</td>
<td>97.95%</td>
</tr>
<tr>
<td>Characteristic</td>
<td>( N = 1,414 )</td>
<td></td>
</tr>
<tr>
<td>---------------</td>
<td>----------------</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>25 (1.77%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4 (0.28%)</td>
<td></td>
</tr>
</tbody>
</table>

ITAs, internal thoracic arteries; SV, saphenous vein; RA, radial artery; LITA, left internal thoracic artery; RITA, right internal thoracic artery; BITA, bilateral internal thoracic arteries; AO, Ascending Aorta.

**FIGURE LEGENDS**

Central Picture: At multivariate analysis, acceptance of inadequate (<15 ml/min.) flow on the LAD graft is a risk factor for Primary End-point (MACE) occurrence (OR 3.64, 95% C.I. 1.87, 6.90, \( p<0.001 \)).

CABG, coronary artery bypass grafting; LITA, Left Internal Thoracic Artery; LAD, left anterior descending coronary artery; TTFM, transit-time flow measurement; MACE, major adverse cardiac events.

Fig.1 Flow-chart with details of inclusions and eligibility of patients.

Fig.2a Graft Flow before (median 4.0 ml/min., IQR 2.0; 8.0) and after Revision (median 28.0 ml/min. IQR 10.8; 38.5) (\( n=32, p<0.001 \)). Data are presented as box and whisker dot plots with the upper and lower borders of the box representing the 25% and 75% percentile (upper and lower quartiles). The middle horizontal line represents the median, and diamond dot the mean. The lower and upper whiskers represent the minimum and maximum values of non-outliers. Extra dots represent outliers.

Fig.2b Pulsatility Index (PI, median 12.0, IQR 4.5; 25) before and after Revision (median 2.5, IQR 2.05; 4.23) (\( n=33, p<0.001 \)). Data are presented as box and whisker dot plots with the upper and lower borders of the box representing the 25% and 75% percentile (upper and lower quartiles). The middle horizontal line represents the median, and diamond dot the mean. The lower and upper
whiskers represent the minimum and maximum values of non-outliers. Extra dots represent outliers.

Fig. 3 At univariate analysis, Primary End-point (MACE) occurrence was higher in case of inadequate (≤15 ml/min.) flow on the LAD graft (OR 3.21, 95% C.I. 1.67, 5.95, p<0.001).

Fig. 4a TTFM Assessment of a malfunctioning LITA to LAD Graft before Revision

Fig. 4b TTFM Assessment of a malfunctioning LITA to LAD Graft after Revision

Fig. 5 Graphical Abstract
EFCAD Study: Registry in 1176 CABG patients at 9 sites

Univariate analyses for prediction of MACE

<table>
<thead>
<tr>
<th>Event</th>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,176</td>
<td>46</td>
<td>3.21</td>
<td>1.67, 5.95</td>
</tr>
</tbody>
</table>

Incorrect (≤15 ml/min.) LAD graft flow

Multivariate analysis of predictors of MACE

<table>
<thead>
<tr>
<th>Event</th>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>46</td>
<td>3.64</td>
<td>1.87, 6.90</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Incorrect (≤15 ml/min.) LAD graft flow on LAD was predictive of adverse outcomes.
Patients
\( N_{\text{patients}} = 1616 \)

Exclusion of patients:
- Missing data

Patients
\( N_{\text{patients}} = 1434 \)

Exclusion of patients:
- Without LAD graft

Patients
\( N_{\text{patients,LAD}} = 1414 \)

Bypasses
\( N_{\text{bypasses}} = 4211 \)

Exclusion of patients:
- With SV or RA graft on LAD
- Incompletely tested

Tested Bypasses eligible for graft-flow study
\( N_{\text{bypasses, tested}} = 3827 \)

Fully tested patients
\( N_{\text{patients, tested}} = 1180 \)

Revised bypasses
\( N_{\text{bypasses, revised}} = 33 \)

Patients eligible for MACE study
\( N_{\text{patients, eligible}} = 1176 \)
Analysis of a Multicenter Registry on Evaluation of Transit-Time Flow in Coronary Artery Disease Surgery (EFCAD Study)

May 2017 - March 2021
- 1615 patients undergoing isolated CABG enrolled at 9 sites.
- 1414 patients eligible for analysis.
- 1176 patients eligible for primary end-point analysis (MACE).

Acceptance of incorrect (<15 ml/min.) graft flow on LAD was predictive of adverse outcomes.

Multivariate analysis of predictors of MACE

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Event N</th>
<th>OR^1</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incorrect (&lt;15 ml/min.)</td>
<td>46</td>
<td>3.21</td>
<td>1.67, 5.95</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LAD graft flow</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td>3.64</td>
<td>1.87, 6.90</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

^OR = Odds Ratio, CI = Confidence Interval

MACE, Major Cardiac Adverse Events; LITA, Left Internal Thoracic Artery; LAD, Left Anterior Descending Artery; PI, Pulsatility Index; DF%, Diastolic Filling%.