Clinical value of intra-operative transit-time flow measurement for coronary artery bypass grafting: a prospective angiography-controlled study

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Abstract

Objective: Transit-time flow measurement (TTFM) is the most widely used method for intra-operative graft quality control in coronary artery bypass surgery. Although it may provide the opportunity for the surgeon to promptly revise the graft before the patient is discharged from the operating room, controlled clinical data on the ultimate usefulness of the TTFM are scarce. Clear cut-off values for when to revise grafts have not been set. Methods: A total of 204 consecutive grafts (left internal mammary artery (n = 46), vein graft (n = 155), and radial artery (n = 3)) underwent TTFM in 75 elective coronary artery bypass grafting (CABG) patients. The following parameters were recorded: mean graft flow (MGF), pulsatility index (PI), and insufficiency ratio (IR). After a mean follow-up of 199 ± 42 days, coronary angiography was performed for assessment of graft patency. Results: A total of 166 grafts were found to be patent (85%), and 29 (15%) were completely occluded. The median and interquartile range (IQR) of MGF for the occluded grafts at the time of surgery was 38 ml min⁻¹ (IQR, 25–49 ml min⁻¹) and for the patent grafts 45 ml min⁻¹ (IQR, 31–71 ml min⁻¹; p = ns). The corresponding PI values were 3.3 (IQR, 2.8–5.0) and 2.2 (IQR, 1.7–3.2; p = 0.003), and the IR values were 1.6 (IQR, 0.6–6.1) and 0.2 (IQR, 0–2.2; p = 0.03). By receiver operating characteristic (ROC) analysis, the highest sensitivity (72%) and specificity (70%) were associated with a PI value > 3.0. However, 49 out of 70 such grafts (70%) were found to be patent. Furthermore, 10 out of 16 (63%) grafts, that had a combination of low flow (MGF < 15 ml min⁻¹) and high PI (> 3.0), were patent at control angiography. Conclusions: TTFM predicts graft failure within the 6 months after CABG. However, specific cut-off recommendations for when to revise a graft cannot be set on the basis of TTFM. The cut-off values suggested in the literature lead to unnecessary graft revisions in the majority of cases, and, on the other hand, many technical defects probably remain unnoticed. Better methods to assess the quality of coronary artery bypass grafts are needed.

Keywords: Coronary artery bypass grafting; Transit-time flow measurement; Graft patency; Receiver operating characteristic analysis

1. Introduction

A considerable number of coronary artery bypass grafts (CABGs) fail either immediately or soon after surgery. Early graft failure is inevitably associated with serious clinical implications: myocardial ischemia or infarction, and thus potentially compromises the long-term outcome of the patients [1,2]. The causes of early graft failure are often related to technical defects in the surgical anastomoses of the proximal aortic or distal coronary arteries. For optimal operative results, good and reliable methods for assessment of the technical quality of the created bypasses are critical. Preferably, these methods should be available and used during surgery, when it is still possible to repair any graft failure immediately.

At present, transit-time flow measurement (TTFM) is the most common intra-operative method for assessment of the function of the graft. TTFM is convenient, and the measurement results are sufficiently valid, exact, and reproducible for clinical purposes [3]. Several retrospective studies have provided data to show that TTFM is useful for detecting grafts with impaired flow, and that TTFM values correlate to a satisfactory degree with simultaneous and immediate postoperative coronary angiography flow data [4–6]. However, the correct interpretation of the results of TTFM is still a matter of debate: there are no universally accepted TTFM threshold criteria as to when the graft should be judged as failing or not. Further, only very little is known about how TTFM relates to prognosis in terms of graft patency and long-term survival of the patients.

In this study, we have assessed prospectively the predictive value of the TTFM in CABG patients with regard
to short-term graft patency and long-term patient survival. The TTFM values were related to the findings at angiography.

2. Patients, materials and methods

2.1. Patient population

The study population consisted of 75 patients, who underwent primary elective CABG with no concomitant procedures at the Helsinki University Hospital between March 2001 and December 2002. The study was approved by the ethics committee of the Helsinki University Hospital and written informed consent was obtained of all patients. The demographic and clinical data of the patients are shown in Table 1.

2.2. Data collection, angiography and follow-up

Patients were recruited in conjunction with a proximal anastomotic device evaluation study. All data were collected prospectively on a specific clinical report form and, altogether, 28 variables were recorded. All pertinent clinical data within the study period were analyzed to find correlations between the flow measurement values and clinically relevant endpoints, that is, perioperative myocardial infarction (defined by either a new Q wave in the postoperative electrocardiography (ECG) or by a new wall-motion defect in the postoperative echocardiogram associated with creatine kinase-MB mass (CK-MBm) release $>75 \, \mu g \, l^{-1}$, major stroke, or cardiac death. After a mean $(\pm SD)$ follow-up period of $199 \pm 42$ days, a multiplane coronary angiography was performed by an independent senior cardiologist, who was blinded to the patient data. In the angiograms, the grafts were defined as being normal (the runoff to the coronary bed was unimpeded), stenotic (a narrowing of the graft greater than 50% either at the anastomotic site or in the graft body), or completely occluded [1]. In March 2010, after a mean follow-up of $8.4 \pm 0.2$ years, all patients were traced with respect to survival status or the cause of death from the continuously updated National Cause of Death Register (National Centre of Statistics). The follow-up data were 100% complete.

2.3. Surgical technique and flow measurement

All CABGs were performed through a median sternotomy during cardiopulmonary bypass. Full heparinization with an initial dose of $3 \, mg \, kg^{-1}$ was given. The distal anastomoses were sutured with continuous 7/0 or 8/0 polypropylene sutures, and the proximal anastomoses in the ascending aorta either with continuous 6/0 polypropylene sutures or the CorLink$^R$ proximal anastomotic device before opening of the aortic cross-clamp. The TTFM values of all grafts were recorded intra-operatively in a standardized fashion thus: 5 min after the patient was weaned from cardiopulmonary bypass and the hemodynamic condition was assessed as being stable (systolic blood pressure between 100 and 120 mmHg), the TTFM flow measurement values and respective flow curves were obtained by using the VeriQ system TTFM device (MediStim Inc., Oslo, Norway). To guarantee that a proper size of the TTFM probe was used, the probe was fitted precisely around the mid-portion of the left internal mammary artery (LIMA) graft and proximally around the greater saphenous vein (VSM) or radial artery (RA) grafts, whichever had been used. To achieve the best possible ultrasonic coupling, skeletonization of a small segment of the pedicled LIMA graft was generally necessary. Aqueous gel was used to improve probe contact. The following variables were recorded and evaluated: (1) mean graft flow volume (MGF; ml min$^{-1}$), (2) pulsatility index (PI: maximum flow volume – minimum flow volume)/mean flow volume), and (3) insufficiency ratio (IR; percentage of backward flow).

2.4. Statistics

Altogether, 75 CABG-operated patients served as subjects, consisting of the sample size of 204 consecutively measured grafts. Qualitative data are expressed as frequencies and percentages. Normally distributed quantitative data are expressed as mean $\pm$ standard deviations and skewed data are presented as median with its interquartile range (IQR, 1st quartile–3rd quartile), as appropriate, and analyzed using the non-parametric Mann–Whitney U-test. Late survival was assessed by Kaplan–Meier’s survival analysis, and the log-rank test was used to determine the difference in mortality. Receiver operating characteristic (ROC) curves of sensitivity and specificity were used to assess...
particular cut-off values for the flow parameters with regard to graft patency. Spearman’s rank correlation test was used and the appropriate correlation coefficient was calculated to describe the correlation between the measured flow values and graft patency. Differences with a *p* value <0.05 were considered statistically significant, and all tests were two sided. The Statistical Package for Social Sciences (SPSS) version 15.0 was used for the statistical calculations (SPSS Inc., Chicago, IL, USA).

### 3. Results

#### 3.1. TTFM measurements

TTFM data of 204 consecutive grafts were recorded and analyzed prospectively. These included 46 (23%) LIMA, 155 (76%) VSM, and three (1%) RA grafts. Forty (20%) VSM grafts and one (0.5%) RA graft had more than one distal anastomosis. Detailed TTFM values by target coronary arteries are shown in Table 2. The variability of the measurements was generally rather wide, which may have affected the occurrence of statistically significant differences. However, the PI of the left anterior descendent (LAD) artery was 1.9 (IQR, 1.7—3.2) and of the right coronary artery (RCA), 3.0 (IQR, 2.0—4.3; *p* = 0.007).

#### 3.2. Coronary angiography

To assess short-term graft patency, 73 patients underwent control coronary angiography at 6 months (199±42 days) after CABG. Altogether, 195 grafts were visualized. Of these, a total of 166 grafts were patent (85%; 166/195), and 29 (15%; 29/195) were completely occluded. Of these, 43 were LIMA grafts, 149 VSM grafts, and three RA grafts, which yields an occlusion rate of 5% (2/43), 17% (26/149), and 33% (1/3), respectively. In addition, 5% (7/149) of the VSM grafts were significantly stenosed, that is, they had a >50% narrowing of the lumen diameter. The degree of CK-MBm release within 24 h after CABG predicted graft patency 6 months later: CK-MBm release was significantly higher among the patients who presented with one or more occluded grafts compared with the patients whose grafts were patent (89±95 μg l⁻¹ vs 35±48 μg l⁻¹, respectively; *p* = 0.019). The patency rate did not differ between the VSM grafts in which the proximal anastomosis was performed with an anastomotic device and those in which conventional suturing had been used (*p* = 0.547).

#### 3.3. Morbidity, early mortality and long-term survival

In terms of morbidity, five patients sustained a perioperative myocardial infarction (7%). The early mortality rate (within 30 days after surgery) was 3% (2/75). The causes of early deaths were postoperative bleeding leading to fatal cardiac tamponade on the first postoperative day and fatal type A aortic dissection on the 15 postoperative day. The overall survival and cardiac survival in the long term (8.4±0.2 years) were 79% (59/75) and 85% (64/75), respectively (Fig. 1). In terms of mortality, 69% (11/16) of the deaths were categorized as cardiac and 31% (5/16) as non-cardiac (malignancy in three patients and degenerative brain disease in two patients). The causes of deaths were determined by clinical examination in 63% (10/16) and by autopsy in 37% (6/16) of the cases. The presence of occluded grafts at 6-month control angiography did not predict long-term cardiac survival.

#### 3.4. TTFM in relation to angiography and outcome

The MGF volume measured with TTFM was 38 ml min⁻¹ (IQR, 25—49 ml min⁻¹) for the completely occluded grafts and 45 ml min⁻¹ (IQR, 31—71 ml min⁻¹) for the patent grafts.
Discussion

Perioperatively, coronary grafts become occluded in 4–12% of the patients [7,8], with a postoperative increase in graft occlusion amounting to a total occurrence of 5–20% at the time of patient discharge [9], and no less than 30% by 1 year [10]. Clearly, quality control of coronary grafts should be a standard practice at the time of coronary artery bypass surgery, if these figures are to be reduced. The rationale for routine intra-operative graft assessment stems from the fact that graft failure usually results from poor surgical technique, and should thus be a potentially avoidable complication. Undiagnosed early graft failure results in increased cardiac surgical morbidity, that is, myocardial infarction, which occurs in 9% of the patients during short-term follow-up [11], and jeopardizes long-term outcome [12].

There are a number of techniques available for direct intra-operative assessment of graft function, in addition to the traditional methods: inspection, palpation, electrocardiography (ECG), and echocardiography [13]. The three most commonly used methods are TTFM, conventional coronary angiography, and intra-operative fluorescence imaging (IFI). Of these, coronary angiography is the most accurate technique for the evaluation of graft patency, and it should be considered as the gold standard against which all techniques should be compared [14]. It provides direct visualization of the flow of blood within the graft and of the quality of the anastomotic site, and it also enables evaluation of blood flow into the coronary bed and the myocardial territory supplied by the graft. However, its intra-operative use is limited by the availability of a fully equipped hybrid laboratory, and by the potential complications related to the invasive technique and use of nephrotoxic contrast agents [15,16]. In addition, some studies indicate that intra-operative echocardiography can accurately visualize coronary artery bypass graft anastomosis, and it is feasible for the intra-operative detection of technical errors and inadequacies of coronary anastomosis. However, intra-operative echocardiography has not reached popularity equal to TTFM, probably due to operator dependency and its subjectivity, and higher costs compared with TTFM, albeit it is more inexpensive than IFI and safer in terms of potential complications than coronary angiography [17].

The most common method for intra-operative graft patency assessment is TTFM, which is based on the principle of transit-time ultrasound technology. TTFM provides an integrated summary of the various measurements and allows assessment of graft quality: TTFM provides both quantitative data of average blood flow volume and several calculated derivatives as the flow of blood in the graft is displayed in waveform. TTFM is simple, rapid, safe, and cost effective [13,14,18]. However, TTFM values relate not only to the technical quality of the surgical anastomosis, but also to physiological conditions at the time of measurement, for example, blood pressure, peripheral resistance, and competitive flow [14]. Thus, the cause of poor blood flow in the graft is not always straightforward; the accuracy of TTFM is high under good hemodynamic and graft-flow conditions, but may be biased when hemodynamics is poor and the blood flow is low [13,14,18].

IFI is a recent method for graft-quality assessment, and it is based on the fluorescent properties of the dye indocyanine green (ICG). When a laser light strikes ICG, light is emitted, and then captured and analyzed with a charge-coupled device near-infrared video camera. The technique is semi-quantitative and involves injecting 1 ml of ICG into the patient’s circulation, which carries a risk of hypersensitivity. Some studies have stated that IFI may not visualize the entire graft or that the anastomotic sites are often not well defined [14,19,20]. On the other hand, a randomized prospective study with 106 patients found that IFI provides better diagnostic accuracy for detecting clinically significant graft errors than TTFM [21].

Although TTFM does not produce an image or depict the nature of any technical graft-related problems, it certainly
fulfills most of the requirements of a good intra-operative tool for quality assessment of coronary artery bypass grafts. Critical questions and problems do remain, however: how should the recorded flow values be interpreted and how are they to be put into their correct clinical context; that is, what to do at operation if the flow and pulsatility parameters are poor [22]? The current proof of the clinical merits of TTFM is based either on circumstantial evidence of improved flow parameters after revision of the grafts believed to be in a failing state or on retrospective angiography-controlled series of selected cases. These studies have typically included patients with symptom-driven angiograms, which cause significant selection bias. D’Ancona and colleagues [4] evaluated prospectively 409 patients who underwent off-pump CABG: a total of 1145 grafts were tested with TTFM and 37 (3.2%) grafts were revised in 33 patients (7.6%). Twenty-nine of these grafts (78%) were revised for abnormal flow patterns, high PIs (>5), and low flow values (<15 ml min⁻¹), and 34 (92%) were revised for both low flow and abnormal flow curve patterns. Although three grafts (8%) were revised for low flow (<7 ml min⁻¹) despite normal flow patterns, there were no findings at revision, and flow values and curves remained unchanged after revision. The authors concluded that TTFM is reliable for detecting technical errors, but the decision to revise should be based on a comprehensive interpretation of this technique. Particular importance when interpreting TTFM data should be placed on analysis of the flow pattern, rather than on relying on any single numeric value. In another study by Hol and colleagues [23], TTFM and angiography findings were compared in 72 CABG patients with 124 grafts. They reported that TTFM did not reliably detect graft abnormalities that were angiographically significant, and concluded that the use of TTFM alone may underestimate graft failure [23].

Clear cut-off values for graft revision in terms of MGF, PI, and IR have not been set. Tokuda and colleagues found that for grafts to the left coronary system, a mean flow <15 ml min⁻¹, and for grafts to the right coronary system, a mean flow <20 ml min⁻¹ were predictive of graft failure [24]. They also stated that PI > 5.0 and IR > 4.7, and PI > 4.7 and IR > 4.6% were predictive of graft failure in the left and right coronary system, respectively, within the 1 year of follow-up [24].

In our prospective angiography-controlled study, we found that the best predictor of early (<6 months) graft patency was the PI value: PI > 3.0 resulted in highest sensitivity (72%) and specificity (70%) in ROC analysis, and predicted graft patency better than MGF or IR alone or in combination. The correlation between PI and IR was strong and significant, indicating that the combination of these two variables does not improve the specificity of TTFM. Similarly, the combination of a low flow volume (<15 ml min⁻¹) with a PI > 3.0 did not improve the sensitivity or specificity of the model. The average PI in the RCA was statistically significantly higher than in the LAD artery (3.0; IQR, 2.0–4.3 vs 1.9; IQR, 1.7–3.2; p = 0.007). In our clinical experience, PI has proved to be the most reliable and applicable tool in day-to-day practice.

In the current study, the 6-month graft occlusion rate verified by coronary angiography was 15%. This finding is in quite good agreement with the other current publications [9,10], although the most recent and important study of Kieser and colleagues reported that a high PI > 5.0 predicts technically inadequate arterial grafts during CABG, and it also predicts early postoperative adverse events, especially operative mortality — even if all other intra-operative assessments indicate good graft quality [25]. In our study, the only clinically relevant predictor of early graft occlusion was a high CK-MBm release within 24 h after surgery (89 µg l⁻¹ vs 35 µg l⁻¹, p = 0.019). In contrast to the findings of Kieser and colleagues [25], we were not able to show any correlation with the TTFM parameters and clinically relevant post-operative end points, that is, myocardial infarction, stroke, or death. In our study, cardiac survival was 85% after an average of 8.4 ± 0.2 years of follow-up, which appears to be quite an acceptable result.

This study is limited by a relatively small sample size, and these findings need to be confirmed in a large-scale study. As no immediately imaging studies were performed, the proportion of graft failure that took place in the early perioperative period, that is, before discharge from hospital, is not known, which makes the precise fraction of technical defects missed by TTFM difficult to assess. In addition, TTFM values may vary due to fluctuation of physiological conditions within the intra-operative phase in the same patient, but because our study protocol was to record TTFM parameters only at one time point, we are not able show the effect of alternating physiological conditions on TTFM measurements.

In conclusion, TTFM predicts graft failure within 6 months after CABG, but it does not predict long-term outcome. Clinically useful recommendations when to endeavor to revise a graft cannot be set on the basis of the TTFM result alone. If the cut-off values suggested in the literature are applied clinically, they are likely to lead to numerous unnecessary graft revisions. On the other hand, many technical defects will probably remain unnoticed, if only TTFM is relied upon. In some borderline cases, the surgeon’s expectation of flow measurements with the actual measurements may have a value in deciding whether or not to revise the graft. However, this decision should be taken only by an experienced surgeon, and it should be based on thorough analysis of the target vessel, coronary bed, and an expected runoff. Among the several parameters offered by TTFM, PI is probably the most applicable tool for day-to-day clinical practice.

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References


