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Intraoperative Coronary Graft Flow Determination – Does it Have a Prognostic Value for Midterm Graft Patency?

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Abstract
Objective: To characterise the prognostic value of intraoperative ultrasonic graft flow determination during CABG for mid-term patency.
Methods: From 01/2000 to 08/2003 3146 CABG procedures were performed at our institution. Graft flow was determined in all patients. Lumen diameter was given in mm and a sclerosis score was applied for the target vessel. 100 of these patients (3.2%) underwent postoperative coronary angiography at a mean time interval of 8.0 ± 0.5 months.
Results: In 100 patients, 114 LITA and 204 venous anastomoses were performed. At re-angiography 112 LITA (98%) and 174 venous (85%) anastomoses were patent. The amount of occluded LITA grafts was to low to perform statistical analyses. Mean graft flow of patent vein grafts was 48 ± 2 ml/min vs. 32 ± 4 ml/min in occluded vein grafts (p = 0.001). After multiple logistic regression analysis, only intraoperative vein graft flow was found to be a predictor for patency at mid-term (p = 0.005, odds ratio 0.97, 95% confidence interval [CI] from 0.95-0.99). No differences were found concerning sclerosis scores or vessel lumen between patent and occluded grafts.
Conclusions: Significant differences concerning intraoperative graft flow were found between vein grafts patent or occluded at re-angiography. The predictive power of intraoperative vein graft flow for mid-term patency was confirmed by multiple logistic regression analysis.

Key words: Transit time flow measurement, mid-term patency rate

Introduction

During coronary artery bypass grafting (CABG), intraoperative determination of bypass graft flow has been performed since many years. In recent years, transit time Doppler flow determination [1] has taken the place of electromagnetic graft flow determination which used to be the standard method in the past [2]. Intraoperative graft flow determination serves as acute quality control at the end of bypass surgery [1] and a certain flow value may prove functional importance of the graft. Low flow or even no flow may have direct consequences, for example revision of a graft or other measures such as performance of an additional graft to the affected coronary artery [3]. In the early postoperative period, myocardial ischemic markers such as cardiac troponin I, creatine kinase or myoglobin serve as indicators for early patency after CABG. Early graft failure has been associated with a significant early rise in serum cardiac troponin I [4]. Graft flow and patency rates were reported to be influenced by the diameter of the anastomosed coronary artery [5].

The prognostic significance of a certain intraoperative graft flow for mid- or long term patency of the graft is not clear. Early studies performed using electromagnetic flow determination showed conflicting results [6, 7]. A more recent study showed a correlation of intraoperative hemodynamic parameters, namely an increased resistance as measured in the graft, and patency of the graft [8].

In the present study, symptomatic and asymptomatic patients underwent re-angiography ad mid-term after CABG. All grafts were classified according to their patency. Intraoperative parameters such as graft flow, diameter of the anastomosed coronary artery and morphologic criteria of the grafted vessel were correlated with the patency rate.

Material and Methods

Patients

From 01/2000 to 12/2003 3146 CABG procedures were performed at our institution. In the same time interval, 460 of these patients were referred by our inhouse colleague cardiologist. In 100 of these 460 patients (22% of referrals), 80 of whom were male, coronary re-angiography was performed in 73 asymptomatic and 27 symptomatic patients. Preoperative data of these 100 patients are shown in Table 1. Mean age at the time of surgery was 63.8 ± 1 years. Previous CABG had been performed in 11.4%. In 100 patients, 97 left internal thoracic arteries (LITA) and 172 vein grafts were placed. 17 LITA and 32 vein grafts were anastomosed sequentially with at least a second anastomosis, summing up to 114 LITA and 204 venous anastomoses. Mean time interval between surgery and angiography was 8 ± 0.5 months. Patients with a postoperative troponin I activation of >30 ng/mL were excluded from the study. Elevated troponin I levels are highly indicative for early graft occlusion after CABG [4]. In the present study, we were interested in mid-term patency of grafts in patients with an uneventful early postoperative course. After surgery,

therapy with antiplatelet agents, acetyl salicylic acid and clopidogrel, was not interrupted.

Anesthesia and Surgery

The operative technique has been descibed previously [3]. After systemic heparinisation the target ACT was 400 sec. All CABG-procedures were performed using CPB. Conventional CPB roller pumps (Stöckert, Munich, Germany) and a disposable membrane oxygenator (Jostra, Hirrlingen, Germany) were used. Implementation of CPB after cannulation of ascending aorta and right atrium was followed by routine cross clamping of the aorta. With a systemic flow of 2.4 L/min/m2 mean arterial pressure was adjusted to 60 mmHg by repetitive intravenous neosynephrine injections, if required. The patient was cooled (32 °C) and 1500 ml of cold Bretschneider cardioplegic solution (Custodiol® Köhler Chemie, Alsbach-Hähnlein, Germany) were infused into the aortic root after cross clamping. The lowest hematocrit accepted was 18%, with packed red cells transfused, if necessary. 5000 IU heparin (Ratiopharm, Ulm, Germany) and 2 million KIU aprotinin were added to the prime. After termination of bypass, blood remaining in the CPB circuit was retransfused.

Morphologic criterion documented by the respective surgeon at the time of surgery is a sclerosis score of 0-3 at the site of anastomosis and in the peripheral vessel (0 = no sclerosis, 1 = slight sclerosis, 2 = intermediate sclerosis, 3 = severe sclerosis). Lumen diameter was given in mm. Vessel lumen was determined using a metal probe which was intraoperatively applied after incision of the coronary artery. These data were aquired from our institutional database, defining each patient with more than 1800 items (HVMD, Heidelberger Verein zur multizentrischen Datenanalyse) [9].

In 100 patients, 97 left internal thoracic arteries (LITA) and 172 vein grafts were placed. 17 LITA and 32 vein grafts were anastomosed sequentially with at least a second anastomosis, summing up to 114 LITA and 206 venous anastomoses. In 8 patients additional procedures were performed: There were 3 concomitant aortic valve replacements, 2 concomitant endoventriculoplasties, 1 concomitant mitral valve replacement, 1 concomitant mitral valve reconstruction and 1 concomitant closure of a patent foramen ovale. In all patients, the proximal anastomoses were performed using tangential clamping. Postoperative treatment in the intensive care unit was standardized for all patients. Intravenous heparin were given 2 hours after arrival on the intensive care unit and, if there was no bleeding tendency, 500 mg of intravenous acetylsalicylic acid were applied 4 hours after arrival on the ICU. As secondary prophylaxis, all patients were treated with 100 mg acetylsalicylic acid, once a day, clopidogrel was not applied on a routine basis.

Graft Flow Determination

After termination of CPB, resting flow on all arterial and venous grafts was instantly measured using transit time measurement [3]. We did not measure flow reserve and we did not compromise flow in the native coronary artery to minimise competitive flow. In all cases, flow measurement was performed under stable hemodynamic conditions with a cardiac index of at least 2.4 L/min/kg body weight. A certain flow value was only registered when a characteristic flow pattern was present. The flow curve and the flow value were monitored on a screen and both were printed out and stored in the patient files. Dopplersonographic flow probes with a diameter of 2-4 mm (CardioMed, Oslo, Norway) were used. Usually, a 2 mm flow probe was used for measuring the IMA in a partly skeletonized segment. For venous grafts 3 or 4 mm flow probes were used. In case of sequential grafting, some graft flows could not be determined individually. In these cases, the total flow was divided by the number of grafts performed.

The pulsatility index (PI) is obtained by dividing the difference between the maximum and minimum flow by the value of the mean flow. It is supposed to be an indicator of the quality of the anastomosis with an increasing likelihood of a technical error for PI values exceeding 5 [10].

Coronary Re-angiography

In 27 of 100 patients complaints like angina or dyspnoea were the indication for re-angiography, 73 of 100 patients underwent re-angiography for a routine follow up, and were not symptomatic at the time of re-angiography. Informed patient consent was obtained in all cases. Repeat catheterization was performed within 1 month of operation in 2 patients and later in 98 patients (mean 8.0 ± 0.5 months; range 1 to 25 months).

Coronary angiography was performed in a biplane or monoplane catheterization laboratory (Hicor, Siemens Medical Systems). All patients gave informed consent to re-angiography and study of their coronary conduits. Vascular access was obtained using the femoral approach, and 6F sheaths and catheters were used [11]. Coronary angiography was done with a minimum of 3 views of the left native coronary system and 2 views of the right coronary artery and bypass grafts. Only Fitzgibbon grafts A&B were considered patent [12]. Accordingly, patients with patent grafts belonged to group A and patients with at least one occluded graft belonged to group B. Narrowing ≥ 50% of the lumen diameter of native vessels or bypass grafts was defined as obstructive stenosis and documented for each of the major coronary arteries. Catheter intervention was carried out when considered to be necessary.

Statistical Analysis

Results are expressed as means ± standard error of the mean (SEM). Differences of means between groups were evaluated using Student's t-test for numerical data (Standard Excel Software). For categorical data, the Fischer's exact test was applied (Sigma Stat Software, SPSS Inc. Chicago, Illinois, USA). An a priori null hypothesis was rejected with an a-error p of less than 0.05. A multiple logistic regression analysis was performed to investigate a possible correlation between preoperative ejection fraction, preoperative serum creatinine level, cardiopulmonary bypass time, aortic cross clamp time, intraoperative graft flow, pul-

sation index and mid-term patency (Sigma stat 2.0). Receiver operating characteristics curve was applied using SPSS for windows 10.0 (SPSS Inc. Chicago, Illinois, USA). A p value <0.05 was considered to indicate statistical significance.

Results

Re-Angiography

At re-angiography, 112 (98%) of 114 LITA anastomoses and 174 (85%) of 204 venous anastomoses were patent. The 2 occluded LITA grafts were found in asymptomatic patients. 85 ITA belonged to asymptomatic and 29 ITA grafts belonged to symptomatic patients. Of the 30 occluded venous grafts, 18 were found in asymptomatic patients and 12 were found in symptomatic patients. On the whole, 148 venous grafts belonged to asymptomatic patients and 50 venous grafts belonged to symptomatic patients. Accordingly, the patency rate of venous grafts at 8 months after CABG was 88% in asymptomatic patients and 76% in symptomatic patients. Of the 30 occluded venous anastomoses, 2 were placed on intermediate branches, 4 on diagonal branches, 14 on marginal branches and 10 on branches of the right coronary artery.

Intraoperative Data

Intraoperative data of all patients are shown in Table 1. Mean intraoperative graft flow was 41.6 ± 2.3 ml/min in LITA grafts and 45.8 ± 2 ml/min in vein grafts. Intraoperative ITA flow in grafts that were patent at re-angiography (group A) was higher than ITA flow in grafts that were occluded at re-angiography (group B). A statistic comparison could not be performed because of low n-number (Fig. 1). Intraoperative flow in vein grafts patent at re-angiography (group A) was sig-

Table 1. Pre- intra and postoperative patient data.

Age [years]	63 ± 1
Male [n]	80
Coronary 1 VD [n]	11
Coronary 2 VD [n]	13
Coronary 3 VD [n]	76
Main stem stenosis [n]	31
Previous myocardial infarction [n]	38
EF [%]	63 ± 2
Serum creatinine [mg/dl]	1.3 ± 0.2
Conventional CPB [n]	94
Previous CABG [n]	11
OPCAB [n]	6
Aortic cross clamp time [min]	68 ± 2
Bypass time [min]	104 ± 3
Stay on ICU [d]	1.6 ± 0.2
Time of intubation [h]	13.4 ± 2.3
Troponin I max [ng/ml]	12.6 ± 2.6
CK max [U/l]	443 ± 71
Myoglobin max [U/l]	926 ± 164

Data are means ± SEM; VD: vessel disease; EF: Ejection fraction; CPB: Cardiopulmonary Bypass; CABG: Coronary Artery Bypass Grafting; OPCAB: Off-Pump Coronary Artery bypass grafting, ICU: Intensive Care Unit; CK: Serum creatinekinase.

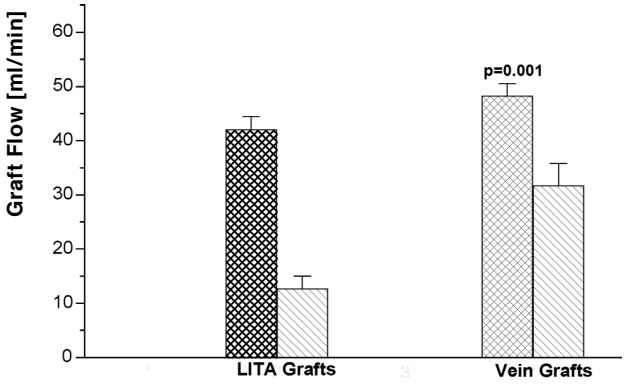

Fig. 1. Intraoperative graft flow of LiTA and vein grafts patent or occluded at the time of re-angiography. Cross-hatched bars: patent grafts; hatched bars: occluded grafts. Values are mean ± SEM.

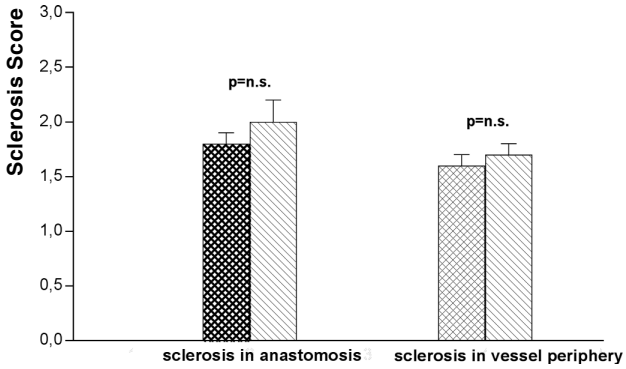

Fig. 2a. Intraoperative sclerosis score of vein grafts patent or occluded at the time of re-angiography. For definition of score see Methods section. Cross-hatched bars: patent grafts; hatched bars: occluded grafts. Values are mean ± SEM.

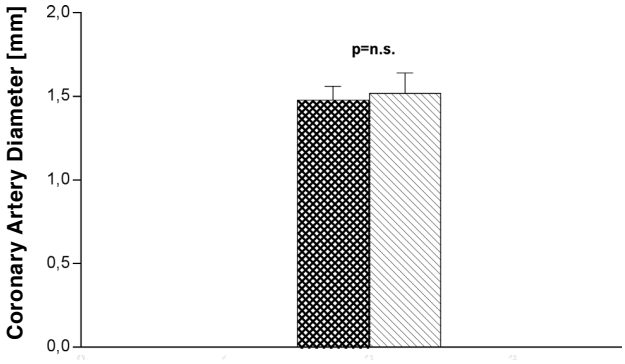

Fig. 2b. Intraoperative coronary artery vessel lumen belonging vein grafts patent or occluded at the time of re-angiography. Cross-hatched bars: patent grafts; hatched bars: occluded grafts. Values are mean ± SEM.

nificantly higher than intraoperative flow in venous grafts that were occluded (group B) at re-angiography (Fig. 1).

Morphologic criteria of vein grafts are shown in Figures 2a and b. No significant differences were found concerning sclerosis scores or vessel lumen between vein grafts patent (group A) or occluded (group B) at re-angiography. Because of low n-numbers, patent and occluded LITA grafts were not tested.

Postoperative Data

Postoperative data of all patients are shown in Table 1. A comparison of the data of patients with patent grafts at re-angiography (group A) and with at least one occluded graft at re-angiography (group B) is made in Table 2. No significant differences were found between group A and group B patients.

Table 2. Pre-, intra- and postoperative data of group A and group B patients.

	Group A	Group B	p
Preoperative EF [%]	65 ± 2	61 ± 3	P = 0.17
Aortic cross clamp time [min]	69 ± 3	66 ± 4	P = 0.32
Bypass time [min]	104 ± 4	104 ± 6	P = 0.49
Troponin I max [ng/mL]	12.0 ± 2.6	12.5 ± 2.9	P = 0.47
CK max [U/L]	477 ± 76	357 ± 38	P = 0.22
Myoglobin max [U/L]	999 ± 174	746 ± 128	P = 0.25

Data are means ± SEM. Group A: patients with patent grafts at angiography; Group B: patients with at least one occluded graft at angiography. EF: left ventricular ejection fraction; CK: serum creatinkinase. No significant differences between the groups were found.

Predictive Value of Intraoperative Graft Flow

In a multiple logistic regression analysis, preoperative left ventricular ejection fraction and serum creatinine, cardiopulmonary bypass time and aortic cross clamp time and intraoperative vein graft flow and the respective pulsation index were investigated for a possible correlation with venous graft patency rate at midterm. Only Intraoperative vein graft flow was significantly associated with vein graft patency at 8 months after surgery (p = 0.004, odds ratio 0.97, 95% confidence interval [CI] from 0.95-0.99). In order to find an optimal cut-off value of intraoperative graft flow concerning the power of discrimination of patency at midterm, a receiver operating characteristics (ROC) curve was performed (Fig. 3). The area under curve was 0.64 ± 0.06. An intraoperative vein graft flow of 41.5 ml/min was found to have an optimum sensitivity of 61% and an optimum specificity of 60% in this setting.

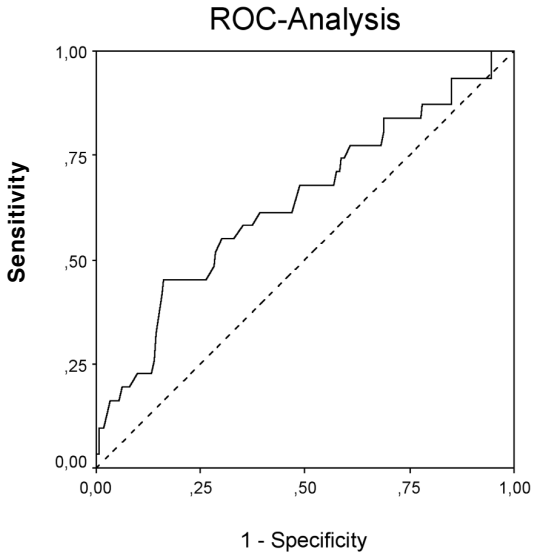

Fig. 3. Receiver operating characteristics (ROC) analysis curve indicating area under curve, sensitivity and specificity of respective intraoperative graft flow values concerning midterm patency.

Table 3. Multiple logistic regression analysis data.

	Odds ratio	Confidence intervals	p
Pre-op EF	1.022	0.985-1.060	P = 0.253
Pre-op serum creatinine	1.664	0.828-3.344	P = 0.153
Bypass time	1.015	0.981-1.050	P = 0.383
Cross clamp time	0.978	0.931-1.028	P = 0.384
Vein graft flow	0.971	0.948-0.994	P = 0.015
Pulsation index	0.987	0.943-1.032	P = 0.555

Data are means ± SEM. Group A: patients with patent grafts at angiography; Group B: patients with at least one occluded graft at angiography. Pre-op: Preoperative; EF: left ventricular ejection fraction; CK: serum creatinkinase. No significant differences between the groups were found.

Only venous graft flow could be tested because the incidence of LITA graft occlusion at the time of re-angiography was to low to perform a statistic analysis.

Discussion

The prognostic value of intraoperative graft flow determination for mid- and longterm patency of the graft has not yet been determined. In the present study, CABG patients underwent coronary re-angiography for various reasons at a mean follow-up of 8 months. In patients with patent vein grafts at the time of re-angiography, intraoperative graft flow had been significantly higher than in patients in whom vein grafts were found to be occluded at the time of re-angiography. Moreover, in a logistic regression analysis,

intraoperative vein graft flow was significantly associated with graft patency at mid-term.

On the other hand, the pulsatility index, reported to be a good indicator of the quality of the anastomosis [10], did not differ between the groups. Accordingly, the levels of postoperative activation of markers for myocardial ischemia, such as cardiac troponin I, creatine kinase and myoglobin were not different between patients with grafts patent or occluded at the time re-angiography. Increased levels of the above mentioned markers for cardiac ischemia in the early phase after CABG indicate early graft failure [4]. Thus, in the patients described here, graft failure must have occurred at a later time point.

Both graft flow and patency rate were reported to be influenced by the diameter of the anastomosed coronary artery [5]. In the respective study, absolute flow values were not reported, but 40% of venous grafts had a flow value of >100 mL/min and only 18% had a flow value of <50 mL/min, as determined electromagnetically. This method has been shown to be associated with significantly higher flow values compared with ultrasonic determination. However, it is less reliable [13], and has, therefore, been abandoned in clinical practice in most cardiac surgical centers.

In the present study, no differences were found concerning lumen diameter between patent or occluded vessels. Sclerosis scores at the site of the anastomosis and in the periphery of the coronary artery, as documented by the individual surgeon, were not different either.

The patency rates observed in the present study have to be interpreted with caution. More than 25% of our patients undergoing re-angiography were symptomatic. In an earlier study, performed at a mean follow-up of 1000 days, patency of venous grafts was observed in 62% of symptomatic patients [14]. In another study, 13% of LITA grafts to the LAD were occluded at a median follow-up of 39 months in symptomatic patients [15]. In another large study, 3174 saphenous vein grafts were studied at a mean follow-up of 105 months after CABG in symptomatic patients, with an overall patency of vein grafts of 61% [16].

Limitations of the study

Although intraoperative ultrasonic flow determination was performed only under stable hemodynamic conditions with a cardiac index of at least 2.4 L/min/kg body weight, pre- and afterloads and patient support with catecholamines varied individually.

Distal run off in an individual native coronary artery was not described in the present study. However, the combined consideration of vessel lumen, sclerosis at the site of the anastomosis and in the periphery of the coronary artery may help to characterise distal run off, as well as the general condition of the grafted coronary artery. Another parameter, that was no described in the present study, is competitive flow. However, it is our policy only to graft coronary arteries with significant narrowing (grade of stenosis >70%). Therefore, competitive flow did probably not play a considerable role.

Our study population is inhomogenous. It consists of 75% asymptomatic and 25% symptomatic patients. However, the presence or absence of symptoms did not disturb our investigation, because it was our aim to study the prognostic value of any specific intraoperative graft flow for mid-term patency of bypass grafts, no matter whether angiography was performed for symptoms or not.

In all patients, only resting flow was determined which is the usual clinical practice. Hyperaemic coronary flow reserve [17] may better characterise. However, in all patients, postischemic hearts were in a hyperaemic state, therefore mimicking the application of vasodilating drugs such as adenosine which provoke a hyperaemic flow velocity reserve.

The optimal cut-off value of 41.5 mL/min, revealed by ROC analysis had only a relatively low positive and negative predictive value, which could possibly be improved by the implementation of the respective flow reserve values, which will be matter of future investigation.

Conclusion

Our study shows that, in venous grafts, occluded at the time of re-angiography, intraoperative graft flow had been lower than in venous grafts, patent at the time of re-angiography. The predictive value of intraoperative vein graft flow for mid-term patency is confirmed by multiple logistic regression analysis.

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