Contrast-enhanced cardiac MRI before coronary artery bypass surgery: impact of myocardial scar extent on bypass flow

Abstract The aim of the study was to relate the extent of myocardial late gadolinium enhancement (LGE) in cardiac MRI to intraoperative graft flow in patients undergoing coronary artery bypass graft (CABG) surgery. Thirty-three CAD patients underwent LGE MRI before surgery using an inversion-recovery GRE sequence (turboFLASH). Intraoperative graft flow in Doppler ultrasonography was compared with the scar extent in each coronary vessel territory. One hundred and fourteen grafts were established supplying 86 of the 99 vessel territories. A significant negative correlation was found between scar extent and graft flow ($r=−0.4$, $p<0.0001$). Flow in grafts to territories with no or small subendocardial scar was significantly higher than in grafts to territories with broad nontransmural or transmural scar ($75±39$ vs. $38±26$ cc min$−1$; $p<0.0001$). In summary, the extent of myocardial scar as defined by contrast-enhanced MRI predicts coronary bypass graft flow. Beyond the probability of functional recovery, preoperative MRI might add value to surgery planning by predicting midterm bypass graft patency.

Keywords Cardiac MRI · Contrast-enhanced MRI · Myocardial viability · Coronary artery disease · Coronary artery bypass graft · Doppler ultrasonography

Introduction

Occlusion of coronary artery bypass grafts (CABG) is a clinically relevant problem, although improvements in patency have been achieved by using arterial instead of or in addition to venous grafts [1, 2]. Whereas long-term occlusions (>3–5 years after surgery) are mainly caused by graft degeneration influenced by atherosclerosis risk factors such as diabetes, smoking, and dyslipidemia [3], the rate of midterm occlusions (months to years) largely depends on vessel resistance which is determined by the anastomosis diameter as well as the distal runoff vessel resistance and myocardial microperfusion [4]. Intraoperative measurement of bypass flow is in this respect a reliable measure of vessel resistance and can be used as a prognosticator [5]. Different techniques have been used [6]. Intraoperative Doppler ultrasound is among these and has been proven to predict midterm graft patency [4, 7]. However, the role of Doppler graft flow measurement has not yet totally been defined, and there is still controversy regarding the cutoff values for graft flow to be accepted. Since perfusion of infarct scar is largely decreased compared with viable myocardium, it has been shown that early and late graft function is influenced by the viability of the supplied myocardial region [8].
Myocardial late gadolinium enhancement (LGE) imaging in contrast-enhanced cardiac magnetic resonance imaging (MRI) has been established as the standard of reference in myocardial viability assessment since late accumulation of gadolinium-based contrast agents in chronic myocardial infarction reflects irreversible damage [9, 10]. Studies in coronary artery disease (CAD) patients have proven MRI to be superior to standard methods [11–13]. In recent years, LGE in chronic infarction has been proven as a prognostic factor for the response to cardiac resynchronization therapy [14] as well as major cardiac events and cardiac mortality [15]. Whereas LGE does predict the outcome of regional and global left ventricular (LV) function after revascularization [16–18], no data have been available concerning the impact of LGE on the patency prognosis of coronary artery bypass grafts.

The purpose of the present study was to define the impact of myocardial LGE extent in contrast-enhanced MRI before CABG surgery on intraoperative bypass graft flow assessed by pulsed Doppler ultrasonography as a predictor of midterm graft patency.

Materials and methods

Study population

Thirty-three consecutive, unselected CAD patients (29 male, 4 female; mean age, 66±5 years) with impaired LV function were enrolled in the study. Inclusion criteria were proven CAD, indication for CAGB surgery, LV ejection fraction (EF) <40% on echocardiography, and scheduled MRI by clinical indication for viability assessment. The results of the MRI study, i.e., the extent of myocardial scar, influenced the decision on whether or not the patient was referred to surgery. The regional distribution of scar did not have an impact on which vessel territory was revascularized. Acute myocardial infarction ≤3 months before examination was an exclusion criterion. Patients' clinical characteristics are given in Table 1. All of them underwent contrast-enhanced cardiac MRI 6±4 days before scheduled CAGB surgery. During CAGB surgery, pulsed Doppler ultrasonography flow measurements of the grafts were done as part of common practice in the participating department of thoracic and cardiovascular surgery. Since preoperative MRI was clinically indicated and served as an inclusion criterion and intraoperative graft flow has been regularly done, ethics committee approval was not necessary.

Magnetic resonance imaging

All examinations were performed on a 1.5-T MR system (Magnetom Sonata, Siemens Medical Solutions, Erlangen, Germany). Patients were placed in supine position. Two

| Table 1 Patients’ characteristics and intraoperative parameters |
|----------------------------------------|------------------|
| Characteristic/parameter              | Value            |
| Age (years)                           | 66±5             |
| Male/female (n)                       | 29/4             |
| MRI ejection fraction preop (%)       | 28±17            |
| Peripheral arterial occlusive disease [n (%)] | 4 (12)          |
| Proximal bypass anastomoses (n)       | 2.0±0.5          |
| Distal bypass anastomoses (n)         | 3.5±1.0          |
| Cardiopulmonary bypass time (min)     | 106±7            |
| Aortic cross clamp time (min)         | 67±4             |
| Maximum postoperative troponin I (ng ml⁻¹) | 9.8±3.8        |
| Maximum postoperative myoglobin (ng ml⁻¹) | 645±210         |

Cardiovascular characteristics and risk factors of the study patients. Operative parameters and postoperative biomarkers
the single slice volumes (slice summation). Ejection fraction (EF) calculation was done using the equation: EF = (EDV−ESV)/EDV.

LGE image analysis and scoring

All MRI examinations were interpreted by two experienced radiologists by consensus prior to surgery. PACS monitors were used for readout of the inversion-recovery turboFLASH images regarding LGE. Based on the 17-segment model of the American Heart Association (AHA) for segmentation of the left ventricular myocardium [21], the LGE extent in each of the acquired short axis slices was assessed: in basal and midventricular slices six segments were assigned, in the apical myocardium four segments were assigned. The apical segment 17 was assessed in the horizontal long axis view. A score system was used to quantify the transmural extent of LGE: 1 = no LGE; 2 = subendocardial LGE including <50% of the wall thickness; 3 = nontransmural LGE including ≥50% of the wall thickness; 4 = transmural LGE.

According to the AHA statement, the 17 segments were then assigned to the three major epicardial coronary vessel territories: left anterior descending (LAD, 7 segments: 1, 2, 7, 8, 13, 14, and 17), left circumflex artery (LCx, 5 segments: 5, 6, 11, 12, and 16), and right coronary artery (RCA, 5 segments: 3, 4, 9, 10, and 15). Finally, a mean LGE score was calculated for each of the three vessel territories separately by calculating the mean of the segment scores from each acquired short axis slice assigned to the individual vessel territory.

Surgery and graft flow measurement

All operations were performed under cardiopulmonary bypass with cardioplegic arrest using 1,500 ml of cold Bretschneider cardioplegic solution (Custodiol®, Köhler Chemie, Alsbach-Hähnlein, Germany) after aortic cross clamping. As standard graft material, the left internal thoracic artery was used for the LAD and the greater saphenous vein was used for LCx and RCA. The radial artery has not been used as a graft. Pre-, intra-, and postoperative parameters are given in Table 1.

An 8-MHz Doppler ultrasonographic flow probe with a diameter of 2–4 mm and autocalibration (CardioMed Trace System, Medi-Stim AS, Oslo, Norway) was used to measure graft flow intraoperatively in LITA and vein grafts [22]. After termination of cardiopulmonary bypass, graft flow given as cc min⁻¹ was determined in a standardized fashion as described before [4, 23] under stable hemodynamic conditions with a cardiac index of at least 2.4 l min⁻¹ m⁻². Recording sites were in the proximal vein graft segment or the midportion of the internal thoracic artery pedicle. In the case of sequential bypass grafts to one single vessel territory (e.g., LAD and first diagonal branch), blood flow was measured proximal to the side-to-side anastomosis. In sequential bypass grafts to different vessel territories (e.g., diagonal branch and marginal branch), flow was measured proximal and distal to the side-to-side anastomosis to identify both supplies by subtracting the two values. The ultrasound pencil probe is acoustically coupled to the vessel by a small amount of sterile gel. Figure 1 shows measurement of graft flow and simultaneous recording.

Relation of LGE extent to graft flow: statistical analysis

Intraoperative graft flow as a measure of myocardial perfusion was compared with myocardial scar extent in each of the corresponding vessel territories expressed as the above-mentioned scores (Figs. 2 and 3). Results are expressed as mean ± SD. For nonparametric, non-Gaussian distributed data, differences of means between groups were evaluated using the Mann–Whitney U test for independent variables and standard software (SPSS, version 12.0.1, SPSS Inc., Chicago/IL, USA). Pearson’s correlation coefficient and the line of regression were calculated (SPSS software) to describe the correlation between raw data of
Scar extent and bypass graft flow. Differences were considered to be significant with a \( p \) value < 0.05.

**Results**

The study included 33 patients. Preoperative global LV function in the study population was considerably impaired with an MRI-measured EF of 28±17%, range, 13–47%. LV volumes were increased with EDV, 221±69 ml and ESV, 160±63 ml (corresponding normalized values were EDVI, 119±37 ml \( \text{m}^{-2} \text{BSA} \); ESVI, 86±34 ml \( \text{m}^{-2} \text{BSA} \)). NYHA heart failure class was 3.0±0.1 preoperatively.

In the 33 patients, 86 of 99 coronary vessel territories were grafted meaning 2.6±0.6 vessel territories per patient. The left internal thoracic artery (LITA) was used to graft the LAD territory in 32 patients. Sixty-six additional proximal aortic anastomoses were established in vein grafts (2.0±0.5 per patient). In total, 114 distal anastomoses (3.5±1.0 per patient) of the 98 vessels, were done to the following territories: LAD, 54; LCx, 33; RCA, 27. Among them were 16 sequential bypasses: LAD, 8; LCx, 7; RCA, 1.

In MRI, 1,802 short axis segments were evaluated in the 33 patients resulting in 55±6 segments per patient (range, 45–61) depending on the long axis diameter. Each of the 1,802 segment scores was individually assigned to one of the three major coronary vessel territories. Mean scar score in the LAD-supplied territory was 1.70±0.72, in the LCx territory 1.97±0.82, and in the RCA territory 1.66±0.60. No statistically significant difference could be found between these groups.

Mean intraoperative graft flow to the LAD and its branches was 56±34 cc min\(^{-1}\), 60±41 cc min\(^{-1}\) to the LCx territory, and 80±42 cc min\(^{-1}\) to the territory of the RCA. Flow in grafts to the RCA and its branches was significantly higher compared with LAD grafts (\( p < 0.01 \)). No gender differences existed.

**Correlation between scar extent and graft flow**

A significant negative correlation could be found between scar score and intraoperative graft flow (Pearson’s correlation coefficient, \( r = -0.4; p < 0.0001 \)), irrespective of the supplied vessel territory. Figure 4 shows a scatter plot of the data.

Graft flow in the group of vessel territories with a mean scar score 1–1.49 was significantly higher than in the group with score 2.5–3.49 (\( p < 0.001 \), Fig. 5) and in score group
3.5–4 (p<0.05). Flow in score group 1.5–2.49 was higher than in group 3.5–4 (p<0.05): 1–1.49, 75±41 cc min⁻¹; 1.5–2.49, 61±36 cc min⁻¹; 2.5–3.49, 35±21 cc min⁻¹; 3.5–4, 24±8 cc min⁻¹.

Graft flow to territories with a scar score of ≤2, meaning 50% or less of transmural LGE extent, was significantly higher than flow in grafts to vessel territories with a score >2 (75±39 vs. 38±26 cc min⁻¹; p<0.0001; Fig. 6). There was no difference in flow between LITA and vein grafts to the LAD territory (55±36 vs. 57±31, Fig. 7).

**Discussion**

The present study shows that the extent of myocardial scar in chronic myocardial infarction as presented by contrast-enhanced cardiac MRI influences the flow in both arterial and venous coronary bypass grafts supplying the corresponding myocardial territory: Those grafts supplying normal, viable myocardium provide higher flows than those to nonviable, i.e., scarred, myocardial territories. Since graft flow, as measured intraoperatively by Doppler ultrasonography, has been shown to determine midterm graft patency [4, 7], this statement carries an important
message: It is well-established knowledge that contrast-enhanced MRI reliably predicts myocardial function recovery after coronary revascularization. By evaluating the viability status of the myocardial territory belonging to a specific coronary artery to be supplied by a bypass graft, MRI may also predict the graft’s midterm patency. This, on the other hand, should have an impact on surgery planning reflecting three different situations:

1. Large extent of transmural scar in MRI and ventricular dysfunction: The scar-supplying coronary vessel does not seem to be suited for grafting for the above-mentioned reasons: no functional recovery can be expected, initial bypass graft flow will rather be low, and, thus, high midterm probability of graft occlusion is present.

2. No scar in MRI but ventricular dysfunction: Because of the high probability of functional improvement, these segments should be grafted. High bypass flow can be expected and the probability of midterm patency is high.

3. Large extent of subendocardial or smaller areas of transmural scar: Sufficiently high graft flow with respect to midterm prognosis is possible under optimal circumstances.

Following the ACC/AHA guidelines, CABG is indicated both for the relief of symptoms and for improvement of prognosis in a couple of clinical scenarios of obstructive CAD, mainly involving angina pectoris, poor LV function, and ventricular arrhythmia [24]. That leads to CABG being
among the most common operations worldwide and accounting for more costs in cardiovascular medicine than any other single procedure [24, 25]. One of the major problems in CABG patients is graft occlusion leading to new onset of symptoms. By optimizing postoperative treatment and surgical technique, the patency of bypasses has been improved during the last decade. But still, vein graft occlusion rates range from 17 to 30% and 31% compared with LITA occlusion rates of up to 10% and 15% after 5 and 10 years, respectively [1, 2, 26]. With that, it would be desirable in the preoperative workup to get information on which of the planned grafts is likely to occlude. In this context, contrast-enhanced MRI might play a role in surgery planning.

Early clinical outcome after surgery is not influenced by graft flow [5]. However, it has been shown that midterm graft patency is influenced by the flow features of bypass grafts [4, 7]. This holds true for both arterial and venous grafts, even though occlusion rates of arterial grafts are lower as mentioned above. These findings justify intraoperative flow measurement in bypass grafts for two reasons: First, to estimate the patency prognosis of a well-perfused graft. Second, to immediately react and improve the coronary supply in case of impaired graft flow in a vessel territory where higher graft flows may be expected [22]. In our study population, none of the bypass vessels has been revised due to low flow measurement. The idea that, based on LGE in MRI, preoperative estimation of maximal graft flow may be possible, is promising—particularly in patients with severely impaired left ventricular function. Vessel territories with mostly scar tissue of the corresponding left ventricular region may not be worth grafting which would be predicted by the extent of LGE in MRI.

Obviously, the type of graft vessel, i.e., LITA/RITA, radial artery, vein, is one determinant of graft patency. However, the runoff features of the coronary bed distal to the bypass graft anastomosis also play an utmost important role in the determination of coronary flow. Coronary flow and flow reserve are influenced by both the patency of the epicardial parts of the coronary tree and myocardial perfusion as a surrogate of the microvasculature [27, 28]. In postinfarction scar tissue, perfusion is decreased compared with normal, viable myocardium. The mechanism by which scarred myocardium, even in the territory of a nonobstructed epicardial coronary artery, causes a reduction of flow and flow reserve is obvious: Destruction of the morphologic integrity and scar formation of the myocardium as caused by myocardial infarction negatively affect the coronary microcirculation [29]. Using MRI, Spies et al. described that flow reserve after adenosine-induced hyperemia is not only influenced by the lumen of the bypass graft and the degree of stenosis, but strongly depends on whether the bypass supplies normal myocardium or scar [30]. These findings very much match our results.

In our study, we found no significant difference in flow between LITA and vein grafts. This is consistent with the findings of Kjaergard et al. [31] in a study comparing LITA and vein grafts in on- and off-pump patients with the transit time method. In a Japanese study, flow in LITA and vein grafts was also equal with higher flow velocities in LITA grafts compensating for smaller lumen diameters [32]. Other groups found lower flows in LITA grafts compared with veins. This might be caused by the higher resistance in arterial grafts [33]. Another theory is that arterial spasm as well as edema of the arterial wall through manipulation at the site of distal bypass anastomosis during operation might cause lower flows. Therefore, intraoperatively measured graft flow is not necessarily representative of the subsequent flow conditions. However, based on our data, one might suggest that absolute flow measurement without knowledge of the supplied myocardium is not reliable.

In this context, it is remarkable that graft flow in the RCA territory was found higher than in the LAD territory. This is most probably due to the high percentage of sequential LITA grafts supplying the LAD territory. The combination of smaller vessel diameter of the LITA compared with vein grafts with multiple runoff anastomoses might lead to lower flows in the distal branches through impaired central LITA flow.

Several limitations of the present study have to be mentioned. A midterm follow-up of the study patients, particularly of bypass graft patency, was not performed. The hypothesis that preoperative MRI assessment of regional myocardial viability may predict graft patency at midterm is, thus, based on the earlier observation that bypass graft vessels which are patent at midterm have a higher intraoperative graft flow [7]. This may distort the results since a direct correlation between intraoperative graft flow and midterm patency is not possible in the present study. Second, not all hearts follow the coronary arterial topography as described by the AHA segmentation model for the most common distribution type [21]. This has not been taken into account during evaluation. Third, intraoperative flow measurement may be prone to user error and this may distort the data. Flow has only been measured by one surgeon without interindividual control under study conditions. Fourth, measurement of flow in sequential bypasses is not as reliable as in normal bypass vessels since the flow in the distal vessel parts depends on many circumstances like diameter in the several anastomoses and resistance in the different myocardial regions. Fifth, the intraoperative determination of bypass graft flow is only a “snapshot” which not only depends on parameters like arterial pressure and cardiac output which are highly variable, but also on coronary artery vessel resistance, bypass graft lumen, and others. Sixth, myocardial scar extent was only evaluated in a semiquantitative, visual manner ("eye balling"). This may also have led to measurement imprecision; however, the method seems to be justified in clinical routine.

In conclusion, bypass flow is influenced by the extent of myocardial scar in the respective area of the left ventricular wall as assessed by contrast-enhanced MRI. Since it has
been shown earlier that bypass flow determines the midterm patency of bypass vessels and we demonstrate here that bypass graft flow to left ventricular areas with a large extent of scar tissue is lower than to normal myocardium, it may be postulated that preoperative MRI predictions for MRI in patients with CAD before they undergo CAGB surgery.

References


