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ORIGINAL CONTRIBUTION

Outcomes After Early Postoperative Myocardial Infarction Due to Graft Failure in Patients Undergoing Coronary Artery Bypass Grafting

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Abstract

Background. Early graft failure (EGF) after coronary artery bypass grafting (CABG) occurs in up to 12% of grafts, but is often clinically unapparent. EGF may result in perioperative myocardial infarction with consequently increased mortality. The aim of the present study was to analyze the incidence of clinically apparent EGF in patients undergoing CABG and the influence on mortality. **Methods.** We analyzed outcomes of consecutive patients undergoing CABG from January 2015 to December 2018 with respect to postoperative emergency coronary angiography (CAG) due to suspected EGF and 30-day mortality. Patients with CAG-documented EGF were matched to patients without EGF to examine predictors of mortality. **Results.** The analysis included 5638 patients undergoing CABG. Eighty-six patients (1.5%) underwent emergency CAG due to suspected EGF. Clinically apparent EGF was observed in 61 of these patients (70.9%), whereas 14 (16.3%) had a culprit lesion in a native coronary artery. The majority of patients (n = 45; 52.3%) were treated with percutaneous coronary intervention and 31 (36%) underwent re-do CABG. The remaining patients were treated conservatively. The 30-day mortality rate of suspected EGF patients undergoing CAG was 22.4% (n = 19), which was higher than the mortality rate of 2.8% overall (P<.001); this remained higher after matching the EGF patients with the control group (11 [20.4%] vs 2 [4.0%]; P=.02). **Conclusion.** Emergency CAG after CABG is rare and is primarily carried out in patients with EGF. The 30-day mortality rate of these patients is high, and EGF is an independent predictor of mortality. Perioperative CAG with subsequent treatment is mandatory in these patients.

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Key words: coronary artery bypass grafting, early graft failure, perioperative mortality, perioperative myocardial infarction

Postoperative early graft failure (EGF) following coronary artery bypass grafting (CABG) may result in acute postoperative myocardial infarction (PMI). The incidence of EGF is thought to be as high as 12%, but only up to 3% are clinically apparent.[1-3] PMI is associated with increased in-hospital mortality in patients undergoing isolated CABG.[1,4,5] Published data demonstrate that expeditious management of EGF results in mid-term survival similar to that of non-ischemic patients in hospital survivors.[5] In this context, re-revascularization with emergency percutaneous coronary intervention (PCI) may limit the extent of myocardial cellular damage compared with a surgical treatment strategy in patients with acute PMI due to EGF.[3]

The major challenge is to identify patients with EGF and patients at risk of EGF. Given the low specificity of changes on the electrocardiogram (ECG) and echocardiographic wall-motion abnormalities during the postoperative course, the overall clinical picture, including hemodynamical stability and changes in biomarker levels, influences whether EGF is suspected and whether the decision for emergency coronary angiography (CAG) should be made.

There are different definitions of PMI based on changes in CABG-related biomarker.[6,7] Overall, cardiac troponin (cTn) is a more sensitive and specific biomarker for myocardial necrosis than creatine kinase MB fragment (CK-MB).[8,9] However, cTn-based PMI definitions are arbitrary, and the relationship between biomarker elevations after revascularization and mortality is still unclear. Studies suggest that only large increases in myocardial biomarker levels after CABG are clinically important,[10-12] whereas other data demonstrate that even modest CK-MB elevations after CABG are associated with increased mortality.[13] The 30-day mortality is increased in patients with a post-CABG level of CK-MB >5 times the upper limit of normal (ULN) and there is an exponential rise in mortality with a >40-fold increase in the CK-MB ULN.[14]

Independent of the biomarker-based definition of PMI, several procedural aspects, such as myocardial mass, subvalvular myectomy in patients with concomitant aortic valve replacement, or the duration of cross-clamping and use of the heart-lung machine, might contribute to biomarker changes. These confounders make it even more difficult to interpret postoperative biomarker changes. Therefore, the aim of the present study was to examine potential predictors of EGF after CABG and the incidence and outcomes of patients with EGF compared with those of patients without EGF.

Methods

General Information. All major cardiac procedures performed in Germany are legally required to be registered at the Institute for Quality Assurance and Transparency in Healthcare (IQTIG), an independent governmental organization, as part of a mandatory quality-control program. The data are routinely transferred to the IQTIG using standardized electronic data entry. The data quality is controlled at different levels, including on-site visits and structured interviews at the institutions. The underlying control mechanisms comprise testing for plausibility, completeness, concordance, and accuracy using a well-validated system. The data-validation procedures are documented in the yearly publication of the Federal Joint Committee (Gemeinsamer Bundesausschuss) in charge of quality control of healthcare in cooperation with the health insurance companies in Germany. The dataset includes parameters such as baseline clinical characteristics, comorbidities, procedural and postprocedural complications, and 30-day outcome.

Study population. From January 2015 until December 2018, a total of 5638 consecutive patients undergoing CABG at the Kerckhoff Heart and Thorax Center, Bad Nauheim, and at the University Hospital of the Wolfgang-von-Goethe University, Frankfurt am Main, Germany, were included into the study. Patients undergoing urgent CAG with suspected perioperative EGF based on biomarker changes, ECG changes, suspected echocardiographic wall-motion abnormalities, and/or hemodynamic instability were compared with patients without postoperative CAG. To analyze the impact of EGF on mortality, patients with documented EGF during CAG were matched to a control derived from the all-comers dataset. The ethics boards of the Justus Liebig University of Giessen (affiliated with the Kerckhoff Heart Center) and the Wolfgang-von-Goethe-University of Frankfurt am Main, Germany approved the study (AZ 199/2016).

Laboratory assessment. Venous blood samples for routine laboratory measurements were taken prior to and directly after CABG and after 4 hours and 24 hours. Analyses for CK-MB were performed using a liquid immunoinhibition method (Cobas; Roche Diagnostics). The lower detection limit of this assay is 3 U/L and represents the lowest measurable CK-MB concentration that can be distinguished from zero. The ULN is 24 U/L.

Statistical analyses. All data for continuous variables are expressed as mean ± standard deviation or as median and interquartile range (IQR) as appropriate. Categorical variables are reported as numbers and percentages. After testing for normal distribution, values were compared by unpaired Student's *t* test or by Mann-Whitney test as appropriate. Fisher's exact test or the Chi-square test was used for categorical variables with nominal scales. Candidate variables for matching on the probability of EGF were selected by 2 experienced cardiologists (CL and AR) and grouped according to their clinical implications. As datasets were drawn from a German quality-control registry (IQTIG), the selection of variables was restricted to those that are assessed by the registry. Propensity score nearest-neighbor matching without replacement was performed using Stata's psmatch2 module by Leuven and Sianesi (Stata14; Stata Corp).[15] The detailed propensity score matching process is given in the **Supplemental Materials; Tables S1-S3**). For clinical endpoint analyses, the Kaplan-Meier method and log-rank test were applied. Univariate Cox regression analyses were performed with mortality as the outcome variable. The following univariate predictors were tested: age; sex; cardiovascular risk factors; coronary artery disease; prior MI; prior PCI; prior cardiac surgery; peripheral vascular disease; cerebrovascular disease; Society of Thoracic Surgeons and

American Society of Anesthesiologists scores; New York Heart Association and Canadian Cardiovascular Society classifications; concomitant valve surgery; left ventricular ejection fraction; CK and CK-MB at baseline; postoperative CK and CK-MB; number of grafts; graft material; duration of surgery; clamp time; bypass time; perioperative stroke; postprocedural acute kidney injury; postoperative low cardiac output; and postoperative cardiopulmonary resuscitation (CPR). Univariate predictors with *P*-values ≤.05 were entered into multivariate Cox regression analysis. Multivariate Cox regression analysis was used to calculate hazard ratios. All statistical tests were performed 2-tailed, and a significance level of *P*<.05 was considered to indicate statistical significance. For all statistical analyses, except the propensity score matching, the statistical software SPSS, version 22.0 (Statistical Package for the Social Sciences; IBM) for Windows was used.

SUPPLEMENTAL TABLE S1. Candidate variables with likelihood ratios and Wald statistics.

Variable	Likelihood Ratio	*P*-Value	Wald	*P*-Value
Patient related				
Age	3.31	.07	3.15	.08
Sex	0.9	.34	0.94	.33
Clinical related				
NYHA	1.9	.17	1.88	.17
CCS	6.87	<.01	6.21	.01
Risk factor				
Diabetes	0.98	.32	0.95	.33
Atherosclerotic burden				
CAD	8.99	<.01	5.8	.02
Prior MI	0	.98	0	.98
Prior surgery	1.11	.29	1.42	.23
PAD	5.89	.02	6.76	<.01
CVD	21.14	<.001	25.73	<.001
LVEF				
LVEF <50%	0.02	.90	0.02	.90
Surgery related				
Duration of surgery	29.13	<.001	36.23	<.001
Bypass time	12.92	<.001	14.68	<.001
Clamp time	17.39	<.001	19.47	<.001
Number of grafts	22.57	<.001	24.77	<.001
Venous graft	20.61	<.001	20.06	<.001

LIMA graft	0	>.99	0	>.99
RIMA graft	11.58	<.001	12.83	<.001
ARS graft	12.83	<.001	14.36	<.001
Fit model	**63.79**	**<.001**		

ARS = arteria radialis sinistra; ACAD = coronary artery disease; CCS = Canadian Cardiovascular Society; CVD = cardiovascular disease; LIMA = left internal mammary artery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; PAD = peripheral arterial disease; PCI = percutaneous coronary intervention; RIMA = right internal mammary artery.

Supplemental Table S1. Candidate variables with likelihood ratios and Wald statistics.

SUPPLEMENTAL TABLE S2. Probit regression for psmatch module.

Probit regression — Number of obs = 3.762; LR Chi²(4) = 63.79; Prob > chi² = 0.0000; Log likelihood = -255.09575; Pseudo R2 = 0.1111

trueEGF	Coefficient	Standard Error	z	P>|z|	95% Confidence Interval	
DOS	.0034661	.0007785	4.45	0.000	.0019402	.0049919
CVD	.5836129	.1302525	4.48	0.000	.3283227	.838903
Number of grafts	.1863231	.0604776	3.08	0.002	.0677892	.3048569
CCS class	.1384826	.0613363	2.26	0.024	.0182658	.2586995
Cons	-3.990685	.295129	-13.52	0.000	-4.569127	-3.412242

Supplemental Table S2. Probit regression for psmatch module.

SUPPLEMENTAL TABLE S3. Bias reduction (bias before and after psmatch2)

Variable	Mean Treated	Mean Control	%Reduct %Bias	|Bias|	t	P>|t|	V(T) / V(C)
DOS							
Unmatched	270.42	223.2	75.1		6.01	0.000	1.38
Matched	270.42	259.85	16.8	77.6	0.83	0.407	1.07
CVD							
Unmatched	.34545	.10656	59.2		5.64	0.000	—
Matched	.34545	.34545	0.0	100.0	0.00	1.000	_
Number of grafts							
Unmatched	3.1091	2.5136	57.5		4.92	0.000	1.73*
Matched	3.1091	3.2	-8.8	84.7	-0.41	1.000	1.01
CCS class							
Unmatched	2.6727	2.3189	35.3		2.51	0.012	0.86
Matched	2.6727	2.8	-12.7	64.0	-0.69	0.491	0.99

*If variance ratio outside [0.58; 1.71] for U and [0.58; 1.71] for M.

Sample	Ps R2	LR chi²	p>chi²	Mean Bias	Med Bias	B / R	%Var
Unmatched	0.111	63.79	0.000	56.8	58.4	105.7* / 1.61	33
Matched	0.010	1.51	0.825	9.6	10.7	23.3 / 0.87	0

*If B >25%, R outside [0.5; 2].

Supplemental Table S3. Bias reduction (bias before and after psmatch2)

Results

Clinical and procedural characteristics of all patients included in the study are shown in **Table 1** and **Table 2**. The overall incidence of patients undergoing emergency CAG after CABG due to suspected EGF was 1.5% (86/5638). Patients with suspected EGF were older (*P*<.01) and more often had diabetes (*P*<.001), peripheral vascular disease (*P*<.01), and cerebral vascular disease (*P*<.001). Furthermore, these patients tended to more often have prior cardiac surgery (*P*=.05) and they more often underwent urgent CABG (*P*<.001). The duration of surgery, bypass time, and aortic clamp time were longer in patients with suspected EGF (all *P*<.001). These patients received more grafts (mean 3.1 ± 1.2 vs 2.5 ± 0.9; *P*<.001), more often had venous grafts (*P*<.001), and more often had concomitant valve surgery (*P*<.001). Postoperatively, they more often showed a low cardiac output (*P*<.001) and a need for CPR (*P*<.001) and renal replacement therapy (*P*<.001). The mortality rate was significantly higher in patients with suspected EGF compared with other CABG patients (19 [22.1%] vs 129 [2.3%]; *P*<.001). However, there was no difference in the 30-day and 1-year mortality rates between the 3 treatment groups (PCI, re-do CABG, or conservative treatment) (**Table 3**).

TABLE 1. Baseline characteristics of patients with and without early graft failure.

Variable	Suspected EGF (n = 86)	Control (n = 5638)	*P*-Value
Age (years)	70.8 ± 11.0	68.3 ± 9.4	<.01
Male	66 (76.7%)	4448 (78.9%)	.70
Body mass index (kg/m²)	28.0 ± 4.3	28.3 ± 4.9	.63
Symptoms			
NYHA	2.5 ± 0.8	2.4 ± 0.8	.13
CCS	2.6 ± 0.9	2.3 ± 1.0	.04
Clinical history			
Diabetes mellitus	24 (27.9%)	2103 (37.3%)	<.001
Multivessel CAD	84 (97.7%)	5192 (92.1%)	.06
LMCA stenosis	25 (29.1%)	1781 (31.6%)	.88
Prior MI	32 (37.2%)	2120 (37.6%)	>.99
Prior PCI	29 (33.7%)	1590 (28.2%)	.28
Prior cardiac surgery	6 (7.0%)	169 (3.0%)	.048
Peripheral vascular disease	20 (23.3%)	727 (12.9%)	<.01
Cerebral vascular disease	27 (31.4%)	592 (10.5%)	<.001
LVEF <50%	32 (37.2%)	1759 (31.2%)	.15

Data presented as mean ± standard deviation or number (%).
CAD = coronary artery disease; CCS = Canadian Cardiovascular Society; EGF = early graft failure; LMCA = left main coronary artery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; PVD = peripheral vascular disease.

Table 1. Baseline characteristics of patients with and without early graft failure.

TABLE 2. Procedural and postprocedural characteristics of patients with and without early graft failure.

Variable	Suspected EGF (n = 86)	Control (n = 5638)	*P*-Value
Urgency	22 (25.6%)	524 (9.3%)	<.001
Time limits (minutes)			
Surgery duration	263.5 (214.8-313.5)	216.0 (185.0-251.0)	<.001
CPB time	118.0 (87.3-150.5)	78.0 (52.0-98.0)	<.001
Aortic clamp time	76.0 (58.3-105.0)	55.5 (39.0-71.0)	<.001
Graft numbers (n)	3.1 ± 1.2	2.5 ± 0.9	<.001
Graft material			
Venous	52 (60.5%)	1798 (31.9%)	<.001
LIMA	81 (94.2%)	5266 (93.4%)	.84
RIMA	30 (34.9%)	1060 (18.8%)	<.001
ARS	27 (31.4%)	947 (16.8%)	<.001
Concomitant valve surgery	29 (33.7%)	1167 (20.7%)	<.001
Postprocedural findings			
Stroke	4 (4.7%)	293 (5.2%)	.82
Low cardiac output	19 (22.1%)	254 (4.5%)	<.001
CPR	12 (14.0%)	135 (2.4%)	<.001
Renal replacement therapy	13 (15.1%)	158 (2.8%)	<.001
Reason for CAG			
Low cardiac output	16 (18.6%)	N/A	N/A
Biomarker changes	46 (53.5%)	N/A	N/A
Echocardiographic findings	17 (19.8%)	N/A	N/A
ECG changes	5 (5.8%)	N/A	N/A
Combined reasons	19 (22.1%)	N/A	N/A
Culprit lesion			
Graft related	61 (70.9%)	N/A	N/A
Native coronary artery	14 (16.3%)	N/A	N/A
Treatment			
PCI	45 (52.3%)	N/A	N/A
Re-do CABG	31 (36.0%)	N/A	N/A

Data presented as mean ± standard deviation, median (interquartile range), or number (%).
ARS = arteria radialis sinistra; CABG = coronary artery bypass grafting; CAG = coronary angiography; CPB = cardiopulmonary bypass; CPR = cardiopulmonary resuscitation; ECG = electrocardiogram; EGF = early graft failure; IQR = interquartile range; LIMA = left internal mammary artery; PCI = percutaneous coronary intervention; RIMA = right internal mammary artery.

Table 2. Procedural and postprocedural characteristics of patients with and without early graft failure.

TABLE 3. Procedural and postprocedural characteristics of patients with and without early graft failure.

Variable	Suspected EGF (n = 86)	Control (n = 5638)	*P*-Value
30-day mortality			
Total	19 (22.1%)	129 (2.3%)	<.001
PCI	11/45 (24.4%)		.86
Re-do CABG	6/31 (19.4%)		
Conservative treatment	2/10 (20.0%)		
1-year mortality			
Total	13/48 (27.1%)	—	—
PCI	7/26 (26.9%)		.72
Re-do CABG	3/14 (21.4%)		
Conservative treatment	3/8 (37.5%)		

Data presented as number (%).
CABG = coronary artery bypass grafting; EGF = early graft failure; PCI = percutaneous coronary intervention.

Table 3. Procedural and postprocedural characteristics of patients with and without early graft failure.

Table 2 shows angiographic findings and decision-making for CAG in the patients with suspected EGF. ECG changes were a reason for emergency CAG in only a few patients. In contrast, more than half of the patients underwent CAG due to changes in biomarker levels. Over 70% of the patients who underwent CAG showed a graft-related culprit lesion, whereas 16.3% had a culprit lesion in a native coronary artery. More than one-half of the patients were treated by PCI whereas one-third underwent re-do CABG. The remaining patients were treated conservatively.

The release kinetics of CK and CK-MB at the prespecified time points is shown in **Figure 1**. In patients with EGF, plasma levels of CK (median 474.0 U/L [IQR, 321.0-927.0] vs 374.0 U/L [IQR, 262.8-513.8]; *P*=.01) and CK-MB (median 59.0 U/L [IQR, 38.5-96.0] vs 43.0 U/L [IQR, 32.8-58.3]; *P*<.01) were already significantly elevated at the first time point after CABG. The levels of CK-MB were higher at all prespecified time points after CABG in suspected EGF patients compared with controls (**Table 4**).

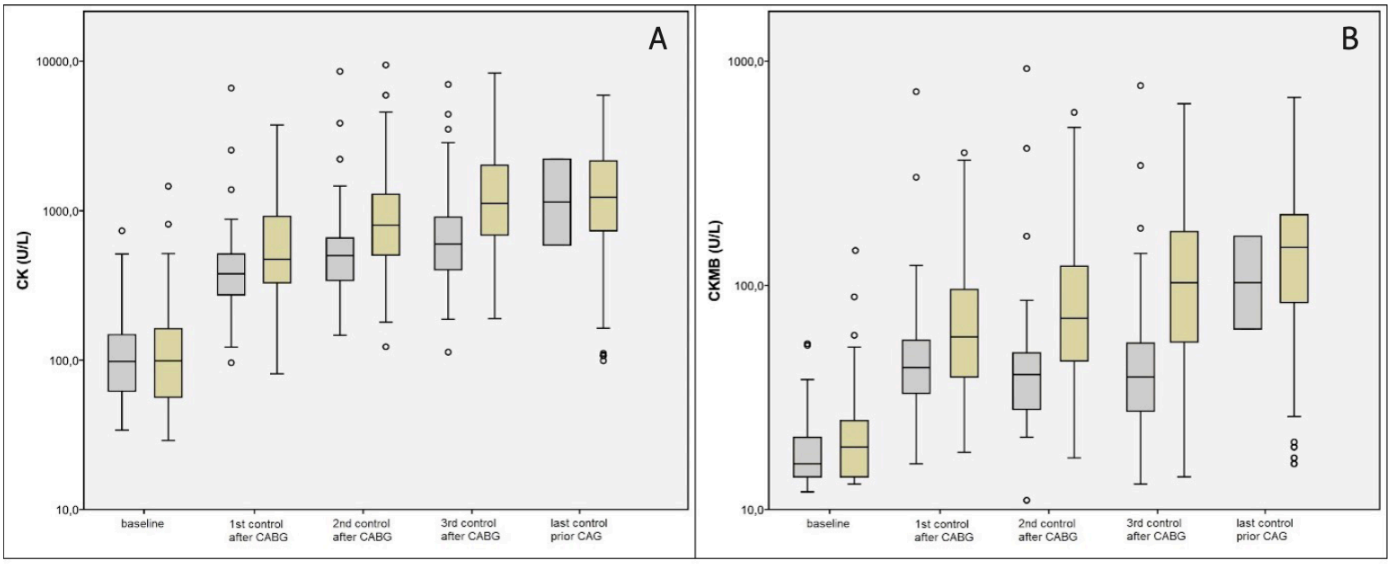

Figure 1. Time course of (A) CK and (B) CK-MB plasma levels (median [IQR]) during perioperative phase in patients undergoing coronary artery bypass grafting (CABG). Blood was drawn at baseline, directly after CABG, 4 hours and 24 hours after CABG, and before coronary angiography (CAG). Beige bars indicate patients with early graft failure and gray bars indicate matched controls. Individual outliers are shown as separate data points.

TABLE 4. Perioperative CK and CK-MB levels in patients with early graft failure and matched controls.			
Variables	EGF (n = 54)	Matched Control (n = 50)	*P*-Value
CK at baseline (U/L)	94.0 (56.0-163.5)	98.0 (62.0-149.0)	.82
CK-MB at baseline (U/L)	16.5 (14.0-26.0)	16.0 (14.0-22.0)	.15
CK at 1st control (U/L)	474.0 (321.0-927.0)	374.0 (262.8-513.8)	.01
CK-MB at 1st control (U/L)	59.0 (38.5-96.0)	43.0 (32.8-58.3)	<.01
CK/CK-MB ratio (U/L)	10.8 (9.0-14.5)	10.8 (8.5-14.6)	.51
CK at 2nd control (U/L)	802.0 (504.0-1295.0)	502.0 (336.5-665.0)	<.001
CK-MB at 2nd control (U/L)	71.5 (45.8-123.8)	40.0 (29.0-51.0)	<.001
CK/CK-MB ratio (U/L)	9.2 (7.8-11.1)	7.9 (6.3-10.6)	.12
CK at 3rd control (U/L)	1120.0 (686.0-2129.0)	598.5 (401.8-910.5)	<.001
CK-MB at 3rd control (U/L)	103.0 (56.0-175.0)	39.0 (27.8-59.3)	<.001
CK/CK-MB ratio (U/L)	9.2 (7.4-11.2)	6.1 (4.4-9.3)	<.001

Data presented as median (interquartile range). CK = creatine kinase.

Table 4. Perioperative CK and CK-MB levels in patients with early graft failure and matched controls.

According to the recommendation of the Society for Cardiovascular Angiography and Interventions (SCAI), a CK-MB increase of ≥10 fold would identify only a minority of patients with EGF as having postoperative MI (only 5 out of 61 patients [8.1%] at the third control [48 hours] after CABG). Applying a post-CABG CK-MB increase of ≥5 fold would identify 26 patients (43%) with EGF-related postoperative MI at the third time point. The CK/CK-MB ratio ≥10% would identify 64%, 36%, and 43% of patients for having EGF-related postoperative MI with regard to the 3 different time points.

After matching the 2 cohorts, there were no significant differences in the baseline and procedural characteristics (**Supplemental Table S4** and **Supplemental Table S5**) except for sex (matched EGF male 70.4% vs matched control male 88.0%; *P*=.03) and urgent CABG (matched EGF 29.6% vs matched control 50.0%; *P*<.001). Venous grafts were used more often in patients with EGF (*P*<.01), they more often had postoperative low cardiac output (*P*=.03) and acute kidney injury with renal replacement therapy (*P*=.04), and they tended to have longer hospitalization. The 30-day mortality rate of the EGF patients was significantly higher than that of the matched controls (*P*=.02) (**Figure 2**). In the multivariate analysis, only clinically apparent EGF, postoperative low cardiac output, CK level at baseline, and postoperative CK and CK-MB levels remained independent variables (**Table 5**).

SUPPLEMENTAL TABLE S4. Baseline characteristics of matched patients with and without early graft failure.			
Variable	Matched EGF (n = 54)	Matched Control (n = 50)	*P*-Value
Age (years)	70.4 ± 12.4	68.5 ± 9.0	.10
Male	38 (70.4%)	44 (88.0%)	.03
Body mass index (kg/m²)	28.4 ± 4.1	28.6 ± 5.9	.66
Risk scores			
ASA	3.43 ± 0.54	3.30 ± 0.47	.27
STS score	2.67 ± 3.93	1.70 ± 3.86	.02
Cardiovascular risk factors			
Hypertension	52 (96.3%)	45 (90.0%)	.43
Hyperlipidemia	37 (68.5%)	46 (92.0%)	<.01

Hyperlipidemia			
Smoking	23 (42.6%)	20 (40.0%)	.99
Diabetes mellitus	18 (33.3%)	20 (40.0%)	.54
Symptoms			
NYHA class	2.6 ± 0.8	2.3 ± 0.8	.84
CCS class	2.6 ± 1.0	2.3 ± 1.1	.51
Clinical history			
Multivessel CAD	52 (96.3%)	47 (94.0%)	.45
LMCA stenosis	15 (27.8%)	17 (34.0%)	.83
Prior MI	20 (37.0%)	20 (40.0%)	.99
Prior PCI	14 (25.9%)	12 (24.0%)	.14
Prior cardiac surgery	3 (5.6%)	1 (2.0%)	.62
Peripheral occlusive disease	12 (22.2%)	8 (16.0%)	.47
Prior stroke	5 (9.3%)	0 (0.0%)	—
Cerebral occlusive disease	15 (27.8%)	18 (36.0%)	.41
LVEF (%)	53.3 ± 11.7	49.5 ± 8.8	<.01
LVEF <50%	26 (36.6%)	17 (34.0%)	.92
Renal function			
Creatinine (mg/dL)	0.91 (0.81-1.17)	1.0 (0.8-1.1)	.54

Data presented as mean ± standard deviation, number (%), or median (interquartile range).
ASA = American Society of Anesthesiologists; CAD = coronary artery disease; CCS = Canadian Cardiovascular Society; EGF = early graft failure; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; STS = Society of Thoracic Surgeons.

Supplemental Table S4. Baseline characteristics of matched patients with and without early graft failure.

SUPPLEMENTAL TABLE S5. Procedural and postprocedural characteristics of matched patients with and without early graft failure.

Variable	Matched EGF (n = 54)	Matched Control (n = 50)	*P*-Value
Urgent	16 (29.6%)	25 (50.0%)	<.001
Procedural step			
Surgery duration (minutes)	267.2 (213.0-305.0)	251.0 (215.0-322.0)	.49
CPB time (minutes)	117.0 (71.0-149.0)	97.5 (16.5-130.0)	.33
Aortic clamp time (minutes)	63.5 (47.8-86.5)	75.0 (49.0-94.0)	.27
ICU time (days)	5.0 (3.0-10.3)	1.0 (1.0-4.0)	<.001
Hospitalization time (days)	14.0 (10.0-20.0)	12.0 (9.0-16.0)	.06
Ventilation time (minutes)	1352.5 (833.8-7182.3)	719.0 (612.5-983.0)	<.001
Graft numbers (n)	3.1 ± 1.2	2.8 ± 0.9	.30
Graft material			
Venous	33 (61.1%)	17 (34.0%)	<.01
LIMA	50 (92.6%)	48 (96.0%)	.68
RIMA	21 (38.9%)	12 (24.0%)	.14
ARS	17 (31.5%)	16 (32.0%)	.99
Concomitant valve surgery	26 (36.7%)	20 (40.0%)	.37
Postprocedural findings			
Stroke	2 (3.7%)	3 (6.0%)	.55
Low cardiac output	13 (24.1%)	3 (6.0%)	.03
Cardiopulmonary resuscitation	7 (13.0%)	4 (8.0%)	.13
Acute kidney injury	31 (57.4%)	25 (50.0%)	.39
Renal replacement therapy	12 (22.2%)	2 (4.0%)	.04
Outcome			
30-day mortality	11 (20.4%)	2 (4.0%)	.02

Data presented as mean ± standard deviation, number (%), or median (interquartile range).
ARS = arteria radialis sinistra; CPB = cardiopulmonary bypass; ICU = intensive care unit; LIMA = left internal mammary artery; RIMA = right internal mammary artery.

Supplemental Table S5. Procedural and postprocedural characteristics of matched patients with and without early graft failure.

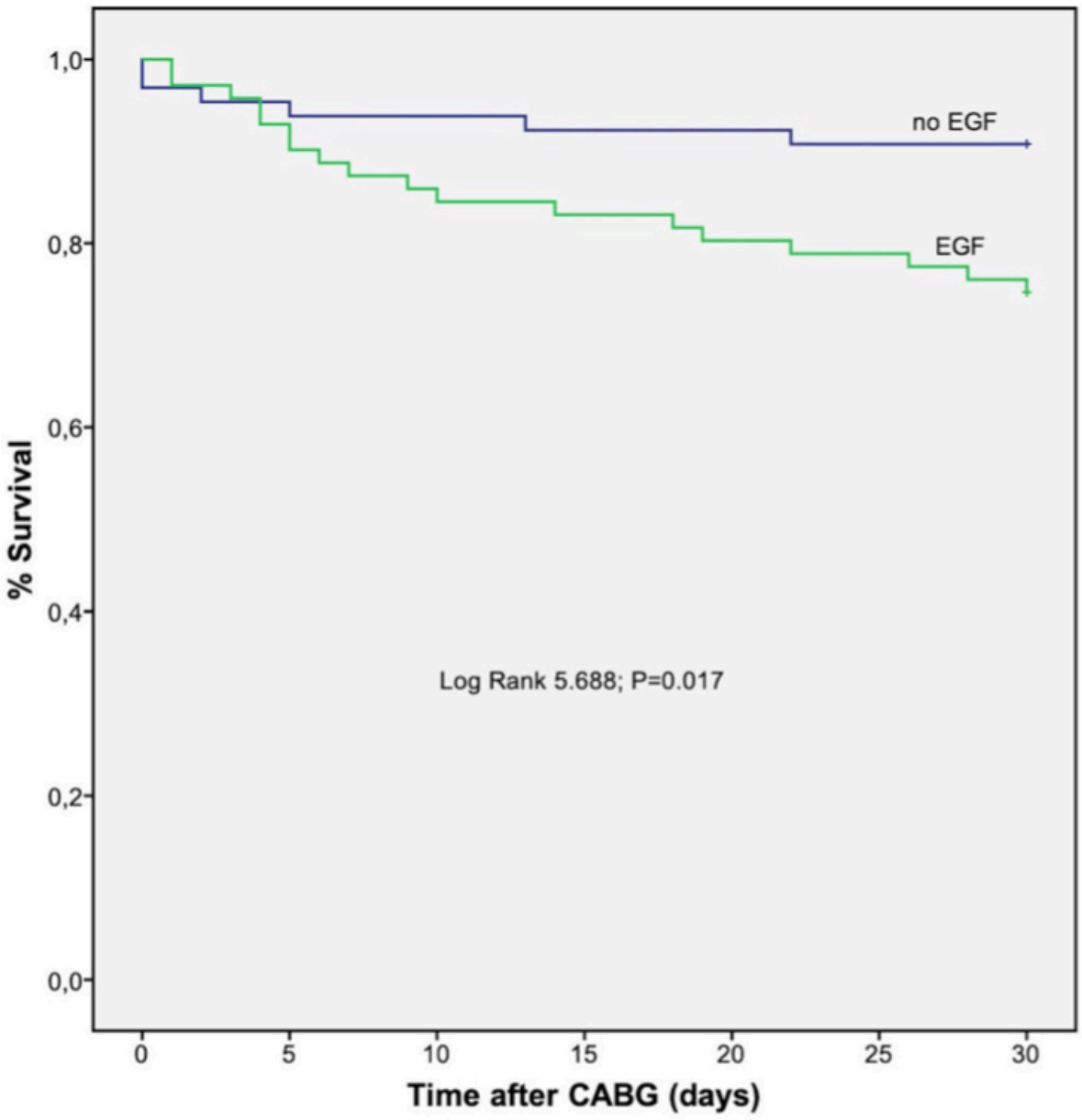

Figure 2. Kaplan-Meier survival curves of patients with and without early graft failure (EGF) during the 30-day follow up period. CABG = coronary artery bypass grafting.

TABLE 5. Hazard ratios and 95% confidence intervals on a logarithmic scale.			
Variables	Hazard Ratio	95.0% Confidence Interval	*P*-Value
Age	1.086	0.995-1.184	.06
New York Heart Association class	1.438	0.639-3.235	.38
Canadian Cardiovascular Society class	0.558	0.29-1.075	.08
Prior myocardial infarction	0.274	0.064-1.169	.08
ASA score	2.324	0.587-9.198	.23
Postoperative cardiopulmonary resuscitation	1.030	0.197-5.386	.97
Low cardiac output	37.294	7.625-182.415	<.001
Renal replacement therapy	0.691	0.202-2.365	.56
Hospitalization time	0.827	0.734-0.932	<.01
ARS graft	2.412	0.346-16.815	.37
CK at baseline	1.003	1.001-1.005	.02
Postoperative CK	0.997	0.994-1	.03
Postoperative CK-MB	1.036	1.010-1.063	<.01
Early graft failure	38.382	5.174-237.201	<.01

ARS = arteria radialis sinistra; ASA = American Society of Anesthesiologists; CCS = Canadian Cardiovascular Society; CK = creatine kinase; CK-MB = creatine kinase MB fragment.

Table 5. Hazard ratios and 95% confidence intervals on a logarithmic scale.

Discussion

Patients with EGF and subsequent postoperative MI after CABG have a worse outcome than patients without this complication.[1,4,5,14,16] In the present study, we examined the incidence and outcome of clinically apparent EGF in consecutive patients undergoing CABG. The most important findings are that: (1) clinically apparent EGF is rare; (2) patients with EGF have higher postoperative CK-MB levels than controls; (3) cerebrovascular disease, number of grafts, and duration of surgery are independent predictors of clinically apparent EGF; and (4) clinically apparent EGF is an independent predictor of mortality within 30 days after CABG.

The identification of EGF after CABG is challenging. The presence of clinical signs of EGF-related postoperative MI is not easy to detect in patients undergoing CABG, all of whom experience chest pain due to the trauma of surgery. Postoperative ECGs might be a helpful diagnostic tool, but often show rather unspecific changes, eg, new bundle-branch blocks or repolarization abnormalities. In this study, only a minority of patients underwent emergency CAGs due to ECG changes, which were primarily a result of malign rhythm disorders with the need for defibrillation. These findings underline the results of Jakobsen et al, who demonstrate that ECG changes were observed in only 1 out of 5 cases with EGF.[17]

Echocardiography is another important means of identifying EGF. The visual detection of new loss of viable myocardium or new regional wall-motion abnormality is consistent with an ischemic etiology due to EGF. In this context, the practicability and utility of transthoracic echocardiography depends on various conditions, including patient-related factors such as obesity and chronic lung diseases as well as observer variability. In the present study, echocardiography played a role in decision making in only 15% of patients undergoing emergency CAG. Transesophageal echocardiography may serve as an alternative to overcome the above-mentioned shortcomings of transthoracic echocardiography during the acute postoperative phase; however, De Mey et al did not find any association between new regional wall-motion abnormalities detected by transesophageal echocardiography and EGF.[19]

In the absence of clear symptoms, electrocardiographic changes, and unclear echocardiographic findings, biomarkers can play a central role in distinguishing between patients with and without postoperative MI. In our study, more than half of the patients were indicated for CAG as a result of changes in biomarker status. In routine clinical practice, it is difficult to assess the precise time point of the onset of myocardial ischemia in patients with EGF. Therefore, pinpointing the time of the release of biomarkers in the early postoperative phase is mandatory. Our study showed that CK-MB release occurred directly after the operation at the first postoperative time point (directly after CABG), with a significant difference between patients with and without clinically apparent EGF. Nevertheless, it is difficult to clearly

discriminate between postoperative MI (due to EGF or an acute coronary event involving the native coronary arteries) and myocardial injury secondary to the operation based solely on biomarker elevation. Non-graft-related ischemia can be related to inappropriate myocardial protection, excessive surgical manipulations, and air or plaque embolization,[20] whereas graft-related postoperative MI is associated with early graft thrombosis, anastomotic stenosis, bypass kinks, overstretching or tension, significant spasm, or incomplete revascularization.[21,22] Although both pathologies influence the outcome, it is important to differentiate between these entities given that graft-related PMI can be treated via re-revascularization. Immediate re-revascularization is even more important because it stops ongoing myocardial cell damage and might prevent the loss of viable myocardium. The revascularization strategy depends on different factors, most importantly coronary anatomy, culprit lesion location, and hemodynamic status.

Post-CABG myocardial ischemia can be suspected based on poor hemodynamic status, including low cardiac output with the need for inotrope support and/or complex rhythm disorders like ventricular tachycardia. We observed low cardiac output as the major driver for emergency CAG in more than 20% of the patients. Emergency invasive diagnostics are necessary in such cases to clarify whether EGF is the underlying cause or not. More than 60% of patients with postoperative MI after CABG have EGF, whereas up to one-third have a negative angiographic finding.[17] These numbers are consistent with our observation that 70.9% of the patients undergoing emergency CAG after CABG were found to have EGF.

Another major finding of the present study is the higher mortality rate of EGF patients. Even after matching for patient- and procedure-related factors, the outcomes of EGF patients were still worse compared with those of the matched controls. We were able to demonstrate that the duration of surgery, the presence of cerebrovascular disease, the number of grafts, and the Canadian Cardiovascular Society classification are independent predictors of EGF, which should be considered when the decision-making process for emergency CAG is prolonged.

These results have important clinical implications. The ability to interpret the combination of biomarker increase in combination with patient symptoms, ECG, and imaging results is important for early diagnosis, individual risk stratification, and individualized therapy. The acceleration of the process of emergency CAG in patients with suspected EGF is of tremendous importance to provide early revascularization, preserve left ventricular function, and improve outcome in these high-risk patients. The impact of CAG timing after CABG should be addressed in further studies to clarify the prognostic implications.

Study limitations. Some limitations to this study must be considered. Although the data were collected prospectively, this is a retrospective analysis. Investigation on periprocedural MI is limited by the CK-MB measurement and small event count, thus limiting the sample size. Unfortunately, 1-year follow-up data were only available for 55% of the patients with suspected early graft failure. Our analysis, however, reflects “real-world” patients enrolled in an all-comers fashion rather than a highly selected trial population, which—together with the large number of patients—strengthens the external validity.

Conclusion

Emergency CAG after CABG is rare and is primarily carried out in patients with EGF. The 30-day mortality of patients with EGF is high. Rapid perioperative CAG with subsequent treatment decision is mandatory in these patients.

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Supplemental Materials

Detailed propensity score matching process. Propensity score nearest-neighbor matching without replacement was performed using Stata's psmatch2 module by Leuven and Sianesi (Stata 14; Stata Corp).[15] Candidate variables for matching based on the probability of early graft failure (EGF) were selected by 2 experienced cardiologists (CL and AR) and grouped according to their clinical implications. As datasets were drawn from a German quality control registry (IQTIG), selection of variables was restricted to those listed within the registry.

The following variables were selected:

• Patient related: age and sex.

• Symptoms and signs: New York Heart Association and Canadian Cardiovascular Society (CCS) classifications.

• Atherosclerotic risk factors: diabetes (others are not part of IQTIG).

• Atherosclerotic burden: coronary artery disease, number of vessels, prior myocardial infarction, prior surgery, peripheral atherosclerotic disease, cerebrovascular disease.

• Functional: left ventricular ejection fraction.

• Surgery related: duration of surgery, clamp time, bypass time.

• Graft related: number of grafts, graft material (venous, left internal mammary artery, right internal mammary artery, arteria radialis sinistra).

In a first step, the predictive power of the candidate variables on EGF were investigated by using univariate logistic regression analysis for each candidate variable. Likelihood ratios (LRs) and Wald statistics were recorded for each variable (**Supplemental Table S1**). To avoid inflation of collinearity in each group, only the variable with highest LR in each group was considered for propensity score matching.

In a second step, the remaining candidate variables were included in a multivariate logistic regression model by forward selection. Patient-related variables and left ventricular ejection fractions were all non-significant. CCS classification was the only clinical indicator with a significant effect on EGF. Duration of surgery, presence of cardiovascular disease, and number of grafts were the candidate variables with the highest LRs in the other groups and were therefore included in the multivariate logistic regression, which proved all included candidate variables to be independently predictive of EGF. The fit model had a LR of 63.79 ($P<.001$) (**Supplemental Table S2**).

Propensity score matching for EGF was therefore performed based on the variables duration of surgery, cardiovascular disease, number of grafts, and CCS classification. To validate the effectiveness of the matching procedure, standardized differences were computed with Stata's pstest module before and after matching, which showed significant reduction of bias for all aforementioned matching variables (**Supplemental Table S3**).