

Surgical Revascularization of Chronically Occluded Coronary Arteries—What You See Is What You Get?

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Abstract

Background Revascularization strategy in coronary artery bypass grafting (CABG) surgery usually depends on coronary dimension and stenosis severity. Little is known about the relation of preoperative evaluation of scarcely or invisibly chronic occluded coronary arteries (chronic total occlusion [CTO]) and revascularization rate or anastomosis quality. We aimed to evaluate the success rates of CTO revascularization in CABG surgery and determine the influence of coronary lumen visibility and collateralization in preoperative angiograms on revascularization rates, bypass blood flow, and target vessel diameter.

Method Preoperative coronary angiograms were evaluated for 938 consecutive patients who underwent isolated CABG surgery between 2014 and 2016 and screened for occluded coronary arteries. The occluded vessels were scored for visibility using the Rentrop grading of collateral filling. Intraoperatively, dimensions of the occluded arteries were measured using conventional vessel probes, and anastomosis quality was assessed by transit time flow measurement.

Results A total of 404 (43.1%) patients were identified with at least one CTO. Revascularization rates differed from 96.2% in the left anterior descending artery, to 85.0% in left circumflex artery-dependent vessels, and 78.8% in right coronary artery territory. Coronary visibility and grade of collateralization in the preoperative angiogram had no influence on intraoperatively measured coronary diameter. Bypass blood flow in grafts revascularizing CTOs lacking collateralization were not significantly lower than those grafts leading to CTOs with higher Rentrop scores.

Conclusion Preoperative coronary assessment often differs from intraoperative findings. Our study confirms that even patients with scarcely collateralized CTOs and impaired visibility in the coronary angiogram have a high chance of complete revascularization during CABG surgery.

Keywords

- ▶ chronic total occlusion
- ▶ CTO
- ▶ complete revascularization
- ▶ CABG
- ▶ surgical revascularization

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Introduction

Chronic total occlusions (CTOs) are a common finding in patients with coronary artery disease (CAD) and occur with a prevalence of 11 to 35% in patients with CAD.^{1–4} Coronary collaterals are seen in most CTO patients in variable occurrence and extent. Cohen and Rentrop classification is used to grade these collaterals into four different categories using the visibility of the collaterals as well as the occluded vessel for scoring (►Fig. 1).⁵

Coronary collateral circulation has an important standing in CAD as it is thought to maintain myocardial viability and to prevent irreversible myocardial injury.^{4,6} Apart from that, good collateralization opens up options for retrograde percutaneous coronary intervention (PCI) strategies, whereas poor collateralization also seems to reduce chances of successful antegrade and retrograde PCIs.⁷

Werner et al evaluated the limitation of collateral circulation showing that even in well-collateralized patients without prior myocardial infarction (MI), revascularization is probably beneficial.⁸ Further studies described the benefits of revascularizing CTOs using PCI or coronary artery bypass grafting (CABG), reducing all-cause mortality, if doing so.⁹ Especially, aiming at complete revascularization (CR) is known to improve the patient's outcome.^{10–13}

CABG surgery has been described as the most successful method to fulfill CR and is therefore specified as the optimal treatment for patients with complex CAD.^{14,15}

The strategy for surgical revascularization usually depends on coronary dimensions as well as complexity and severity of CAD which is analyzed in preoperative angiograms.

Considering that, the relation of preoperatively evaluated scarcely or invisibly chronic total occluded vessels and the revascularization rate and bypass quality is not well described in the current literature.

The purpose of this study is to evaluate if coronary visibility and grade of coronary collateralization in preoperative angiograms reflect intraoperative findings and whether these should influence the decision making regarding revascularization strategies.

In the present study, we focused on analyzing the visibility and collateralization of CTO according to Cohen and Rentrop grade and evaluated successful revascularization rate, intraoperative bypass flow, and vessel size.

Patients and Methods

Patient Population

We identified 404 patients who underwent isolated on-pump CABG surgery at our center between 2014 and 2016 and were seen to have at least one CTO in the preoperative angiogram (►Table 1).

Clinical and angiographic patient characteristics were retrospectively analyzed. Data collection included the evaluation of patient electronic records regarding patient characteristics, cardiac risk factors, detailed surgery information, preoperative risk scores, scores evaluating CAD complexity, and clinical outcome.

Preoperative coronary angiograms were reviewed, screened for CTOs and collateralization was classified on the basis of Cohen and Rentrop collateral recipient filling grade. Patients who underwent prior CABG or emergency CABG due to coronary dissection during PCI were excluded

Table 1 Patient characteristics based on Cohen and Rentrop grade of collateral filling

	Rentrop 0 (n = 23)	Rentrop 1 (n = 85)	Rentrop 2 (n = 141)	Rentrop 3 (n = 155)	p-Value
Age (y) (mean ± SD)	72.26 ± 6.283	66.16 ± 9.209	65.79 ± 9.569	67.50 ± 8.853	0.011
Male (%)	22 (95.7)	78 (91.8)	114 (81.4)	140 (90.3)	0.034
Hypertension (%)	16 (69.6)	73 (85.9)	112 (80)	126 (81.3)	0.321
Hyperlipidemia (%)	14 (60.9)	54 (63.5)	93 (66.4)	102 (65.8)	0.95
Smoker (%)	6 (26.1)	32 (37.6)	59 (42.1)	52 (33.5)	0.333
Diabetes mellitus (%)	10 (43.5)	26 (30.6)	50 (35.5)	40 (25.8)	0.177
COPD (%)	2 (8.6)	6 (7.1)	19 (13.5)	18 (11.7)	0.497
Peripheral artery disease (%)	1 (4.3)	15 (17.6)	34 (24.3)	24 (15.5)	0.071
Cerebral artery disease (%)	6 (26.1)	21 (24.7)	25 (17.9)	26 (16.8)	0.372
Prior apoplex (%)	1 (4.3)	7 (8.2)	14 (9.9)	20 (12.9)	0.492
Creatinine clearance (mL/min)	65.26 ± 19.845	91.42 ± 30.35	85.77 ± 32.24	81.8 ± 32.38	0.003
LVEF (%)	42.48 ± 10.80	48.74 ± 14.00	47.94 ± 13.51	47.89 ± 13.78	0.267
Prior PCI plus stent (%)	4 (17.4)	18 (21.2)	25 (17.7)	21 (13.5)	0.49

Abbreviations: COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; SD, standard deviation.

from this study. Further exclusion criteria were off-pump procedures and any other additional surgical procedure other than CABG.

Apart from that, patients were included in which the left internal mammary artery (LIMA) was used as a graft to revascularize the left anterior descending artery (LAD) and venous grafts, primarily the great saphenous vein, were used as single vessels to revascularize the left circumflex artery (LCX) and right coronary artery (RCA) territories.

Definitions and Procedures

CTO of a coronary artery was defined as total luminal diameter stenosis, Thrombolysis in Myocardial Infarction (TIMI) Study Group Flow Grading of zero, and known or assumed existence of the occlusion for more than 3 months.

Coronary collateral vessels were classified by visual assessment following the grading system published by Cohen and Rentrop (►Fig. 1).⁵

The complexity of CAD was assessed preoperatively using the anatomical SYNTAX Score¹⁶ and SYNTAX II Score—a tool combining clinical and anatomical factors.¹⁷

As a measurement for surgical risk of mortality and morbidity, EuroSCORE I and Society of Thoracic Surgery (STS) Adult Cardiac Surgery risk score were calculated.

LAD territory CTO comprises an occlusion in the LAD and major diagonal branches, whereas an occlusion in the LCX domain and major marginal or intermedial branches was classified as LCX territory CTO. RCA territory CTO involves occlusions in the RCA and its distal branches—the right posterior descending artery and right posterior lateral artery.

Left ventricular (LV) function was classified using preoperative echocardiography data and defined as normal LV function if ejection fraction (EF) was $\geq 50\%$. An EF 30 to 49% was defined as mildly reduced LV function and $<30\%$ as severely reduced LV function.

Kidney disease was classified using creatinine clearance. A preoperative creatinine clearance < 60 mL/min was defined as chronic kidney disease.

To evaluate bypass quality, mean graft flow was measured by transit time flow measurement (TTFM) in all bypass grafts. Flow values were measured intraoperatively after weaning from cardiopulmonary bypass and hemodynamic stabilization using the Medistim QuickFit probes for TTFM.

Coronary diameter was assessed intraoperatively using 0.5, 1, 1.5, and 2 mm vessel probes.

Statistical Analysis

Statistical analysis was performed using SPSS Statistics (version 24, IBM, Armonk, New York, United States).

►Figs. 1 and 2 are designed using Adobe Illustrator CC 2019 (Adobe Systems Software Ireland Limited, Dublin, Republic of Ireland). ►Figs. 3 and 4 are designed using GraphPad-Prism version 7.0 (La Jolla, California, United States).

Continuous variables are expressed as the mean \pm standard deviation and were compared using Student's *t*-test for normally distributed continuous parameter and Mann-Whitney's *U*-test for not normally distributed variables. Categorical variables were presented as percentages and analyzed using the chi-square test or Fisher's exact test. Kolmogorov-Smirnov's test was performed to analyze

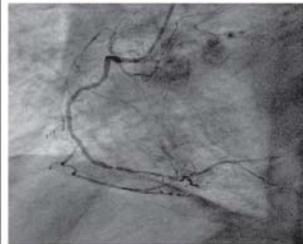
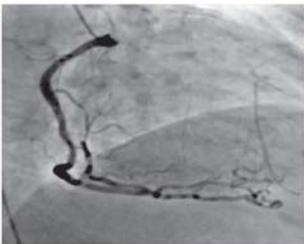
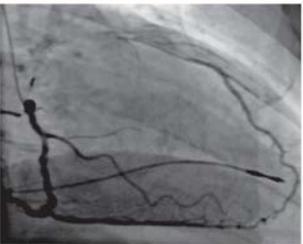
Rentrop 0	Rentrop 1	Rentrop 2	Rentrop 3
			
			
No visible filling of any collateral channels	Collateral filling of branches of the vessel to be dilated without any dye reaching the epicardial segment of that vessel (ie, RCA injection showing retrograde filling of septal branches to their origin from the LAD, without visualization of the latter occluded artery)	Partial collateral filling of the epicardial segment of the vessel being dilated	Complete collateral filling of the vessel being dilated

Fig. 1 Schematic and coronary angiogram examples for grading according to Cohen and Rentrop grade of collateral filling.

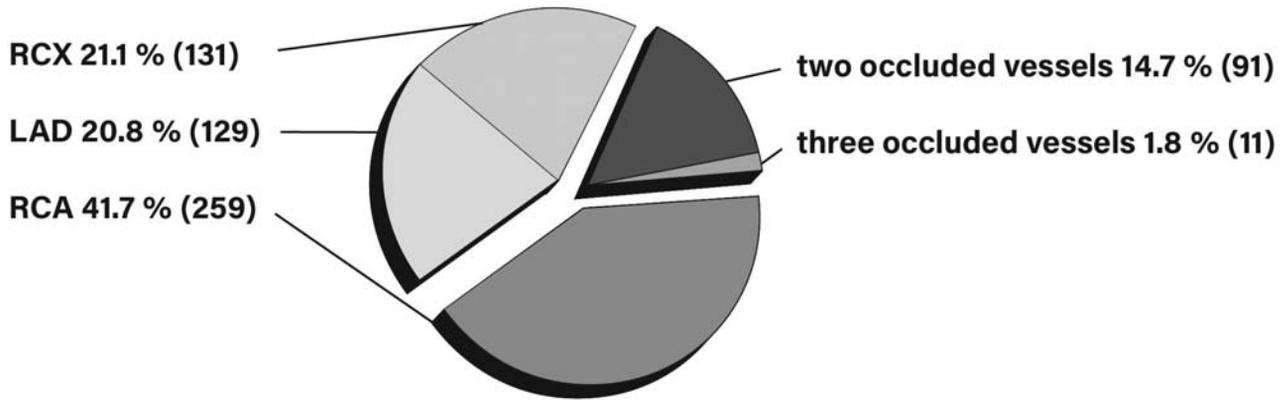


Fig. 2 Distribution of different CTO locations. Patients predominantly had one occluded vessel. Most frequently affecting the RCA (41.7%). CTO, chronic total occlusion; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

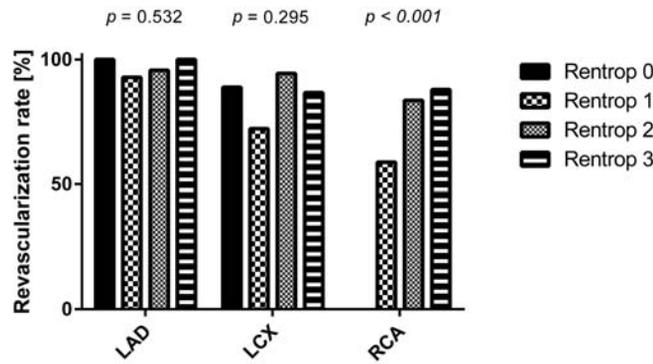


Fig. 3 Percentage of the revascularized occluded vessels depending on Rentrop grading. In occluded LAD- and LCX-dependent vessels, the grade of collateralization and therefore the visibility of the vessel had no influence on revascularization. In the RCA vessels, a higher Rentrop grade was seen to have a better chance of revascularization. LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

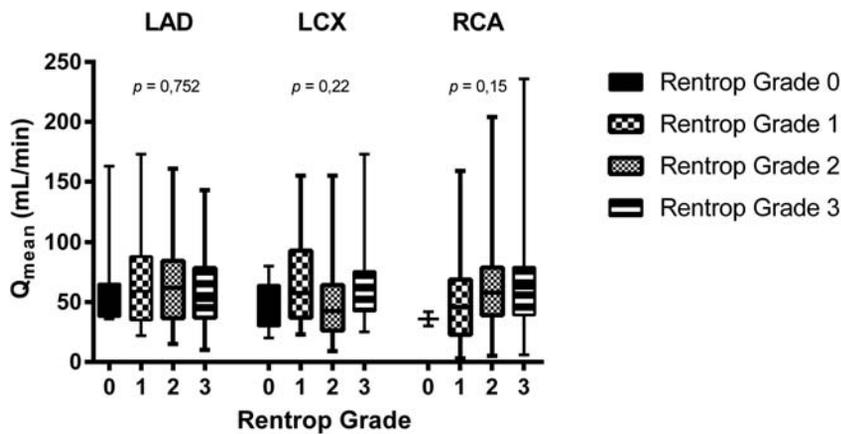


Fig. 4 Bypass blood flow in mL/min measured in the graft leading to occluded vessels using transit time flow measurement. In none of the three major vessels, collateralization and preoperative visibility had a significant influence on bypass blood flow. LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

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normal distribution. The association between Rentrop grade of collateralization and mean graft flow was analyzed by one-way analysis of variance (ANOVA) or Kruskal–Wallis' test. Post hoc analysis was performed within the groups by using the Scheffé's test and Bonferroni's test. Spearman's rank correlation analysis was used to evaluate the correlation of intraoperatively measured coronary diameter and Rentrop grade.

A multiple linear regression model was performed and analyzed using an ANOVA. The *p*-values of <0.05 are considered as statistically significant.

Results

Patient Characteristics

Of all 938 patients who underwent isolated CABG surgery between 2014 and 2016, 404 patients were identified with an occlusion of at least one coronary artery, resulting in a CTO prevalence of 43.1%.

In these 404 patients, 621 CTOs were identified, most commonly located in the RCA territory. CTO was observed in more than one vessel in 102 patients (25.2%). One hundred twenty-nine (20.8%) patients had an occluded LAD, 131 (21.1%) the LCX, and 259 (41.7%) the RCA, or one of their major branches was affected by total occlusion (►Fig. 2).

►Table 1 shows the baseline characteristics of the patients with identified CTOs divided by Rentrop classification. It shows that patients who had no collaterals were significantly older and had a significantly reduced creatinine

clearance compared with patients with collaterals. Apart from that, the groups were comparable.

The clinical presentation, the day the patients were admitted to our unit, is shown in ►Table 2. We saw that patients with poor collateralization had a significantly higher incidence of ST elevation MI (STEMI) or a non-ST elevation MI. Probably due to that, the number of patients with a mildly reduced EF was significantly higher in the patients without collateralization but not the number of patients with a highly reduced EF. Patients without collateralization were graded as higher risk patients when looking at the EuroSCORE I and the STS score. However, the patients with no collateralization showed no significant differences in the SYNTAX Score or the SYNTAX II Score even if these patients seem to have higher score rating in tendency.

Not only did the collateralization have no significant effect on the SYNTAX Score, but patients were also seen to have no differences in revascularization rates when looking at the LCA-dependent territories. Only RCA-dependent vessels with no collateralization had significantly lower chance of being revascularized as seen in ►Fig. 3.

The procedural success rate for CR was 82.9% among all CTO patients.

Patients with invisible occluded coronary arteries (Rentrop 0) had a revascularization rate of 82.6%. It was conspicuous that poor collateralization (Rentrop 1) displayed the lowest rate of successful CR (68.2%).

In patients with LAD occlusion, the revascularization rate was as high as 96.2%, lower rates were observed when

Table 2 Clinical presentation and preoperative risk evaluation

	Rentrop 0 (n = 23)	Rentrop 1 (n = 85)	Rentrop 2 (n = 141)	Rentrop 3 (n = 155)	<i>p</i> -Value
NYHA (mean ± SD)	2.87 ± 0.968	2.71 ± 0.721	2.63 ± 0.814	2.63 ± 0.79	0.523
CCS (mean ± SD)	2.78 ± 0.951	2.11 ± 1.024	1.99 ± 1.119	2.12 ± 1.19	0.019
NSTEMI (%)	17 (73.91)	50 (58.82)	68 (48.23)	69 (44.52)	0.021
STEMI (%)	7 (30.44)	12 (14.12)	10 (7.09)	12 (7.74)	0.003
LVEF >50% (%)	6 (26.09)	48 (56.47)	77 (54.61)	88 (56.77)	0.048
LVEF 30–50% (%)	15 (65.22)	30 (35.29)	53 (37.59)	52 (33.55)	0.033
LVEF <30% (%)	2 (8.7)	7 (8.24)	11 (7.8)	15 (9.68)	0.95
LVEF % (mean ± SD)	42.48 ± 10.8	48.74 ± 14	47.94 ± 13.51	47.89 ± 13.79	0.267
Left main stenosis (%)	11 (47.82)	25 (29.41)	39 (27.66)	49 (34.77)	0.271
EuroSCORE I	7.74 ± 4.59	4.85 ± 0.96	3.56 ± 0.38	3.29 ± 0.26	0.002
SYNTAX score	32.24 ± 7.89	28.24 ± 8.03	28.54 ± 8.26	27.92 ± 7.78	0.119
SYNTAX II PCI score	42.65 ± 11.95	36.45 ± 11.33	38.46 ± 12.64	37.33 ± 11.65	0.138
SYNTAX II CABG score	37.84 ± 8.54	32.72 ± 11.29	32.68 ± 13.59	33.35 ± 12.01	0.278
STS score mortality risk	5.51 ± 11.07	1.9 ± 3.12	2.29 ± 3.79	1.98 ± 2.73	0.001
STS score mortality or morbidity risk	23.08 ± 20.99	14.5 ± 11.26	15.82 ± 12.77	14.91 ± 11.32	0.03

Abbreviations: CABG, coronary artery bypass grafting; CCS, Canadian Cardiovascular Society; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; NSTEMI, non-ST elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST elevation myocardial infarction; STS, Society of Thoracic Surgery.

Table 3 Revascularization rate

	Rentrop 0 (n = 23)	Rentrop 1 (n = 85)	Rentrop 2 (n = 141)	Rentrop 3 (n = 155)	Revascularization rate (%) (n = 404)
Single LAD occlusion (%) (n = 72)	7 (100)	13 (92.9)	22 (95.7)	28 (100)	70 (97.22)
Single RCX occlusion (%) (n = 60)	8 (88.9)	13 (72.2)	17 (94.4)	13 (86.7)	51 (85)
Single RCA occlusion (%) (n = 170)	0 (0)	20 (58.8)	56 (83.6)	58 (87.9)	134 (78.82)
Two occluded vessels (%) (n = 91)	4 (100)	11 (68.75)	22 (78.6)	37 (86)	74 (81.32)
Three occluded vessels (%) (n = 11)	0 (0)	1 (33.3)	3 (75)	2 (66.7)	6 (54.55)
Total (%) (n = 404)	19 (82.6)	58 (68.2)	120 (85.1)	138 (89)	335 (82.92)

Abbreviations: LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

revascularizing LCX-dependent vessels (85.0%) and the RCA-dependent territory (78.8%) (►Table 3).

After being revascularized, the patency of the bypass graft was verified using TTFM. We saw that blood flow velocity in grafts leading to poorly collateralized vessels was not significantly different from grafts revascularizing collateralized CTOs. Even if blood flow to vessels graded as Rentrop 0 seemed to be somewhat lower in tendency (►Table 4 and ►Fig. 4).

Using the blood flow velocity as a parameter for bypass quality, we computed a multiple linear regression model. We aimed at identifying parameters that would predict good flow characteristics in the different coronary artery territories and in the differently graded CTOs. We found no good predictors for all coronary artery territories. If anything, one could say that the tallness of a patient has a positive influence on blood flow velocity in the LIMA graft if anastomosed to an occluded LAD, if graded as Rentrop 1 or 2 (►Table 5).

We also compared the intraoperative measurement of coronary vessel size. This was routinely done using 1 to 2 mm vessel probes. Correlation analysis demonstrated no significant correlation between intraoperative measured coronary diameter in CTOs and Rentrop grade of collateral recipient filling in LAD ($r_s = 0.114$, $p = 0.219$) and RCA ($r_s = 0.105$, $p = 0.137$) territories. However, evaluation showed a weak positive correlation between the grade of collateralization and coronary vessel diameter in LCX territory ($r_s = 0.295$, $p = 0.002$).

Discussion

Preoperative coronary assessment is crucial for optimal planning of the surgical strategy. It is seen as one of the

most important factors for the patient's future well-being.¹⁸ Many studies have shown that complete coronary revascularization leads to a reduction in long-term mortality making this the aim of every CABG operation or PCI intervention.^{13,19,20} CTOs increase the complexity of the PCI approach and CR is almost impossible to achieve if collaterals are scarce or even absent. In CABG surgery, CTOs pose smaller threat but always leave an uncertainty when planning the operation as one cannot be sure what size vessels one might find and whether the vessel is worth the graft.²¹

Due to the unknown status of the target vessel and the uncertainty when planning CABG surgery, one might assume that preoperative not or barely visible occluded coronary arteries come along with a higher risk of not being revascularizable due to small vessel size or severe calcification. Unexpectedly, our data showed that patients undergoing isolated CABG surgery revealed the contrary: Preoperatively assessed invisible or scarcely visible occluded coronary arteries were seen to have equivalent intraoperatively measured vessel sizes compared with well visible CTOs. In contrast to LAD- and RCA-dependent vessels, our analysis only showed a weak correlation between the grade of collateralization and the vessel size in LCX-dependent arteries. Our study therefore confirms the observation which revealed no significant target vessel diameter differences between Rentrop gradings.²² This means that the actual vessel size cannot be predicted by preoperatively evaluated grade of collateralization and occluded coronary arteries probably will appear as vessels worth revascularizing even if invisible in the preoperative angiogram.

Furthermore, in the regression analysis, we could not find a good predictor for the quality of the bypass leading to an

Table 4 Mean graft flow measurements according to Rentrop grade

	Rentrop 0	Rentrop 1	Rentrop 2	Rentrop 3	p-Value
Blood flow LIMA to LAD (mL/min)	61.72 ± 45.8	69.37 ± 44	65.52 ± 35.3	59.51 ± 32	0.752
Blood flow venous graft to LCX-dependent vessels (mL/min)	47.56 ± 19.9	66.67 ± 33.5	52.69 ± 36.2	64.84 ± 34.8	0.219
Blood flow venous graft to RCA-dependent vessels (mL/min)	36 ± 6	50.44 ± 35.1	61.59 ± 36.1	65.03 ± 36.3	0.15

Abbreviations: LAD, left anterior descending artery; LCX, left circumflex artery; LIMA, left internal mammary artery; RCA, right coronary artery.

occluded vessel. If any, taller patients seem to have better blood flows on their LIMA grafts if these lead to occluded vessels graded as Rentrop 1 or 2. We think this is probably caused by the fact that more patients have more LIMA grafts and therefore might have higher blood flow on the graft. In general, we do not think this should have an impact on decision making.

The overall CTO prevalence in patients with CAD is estimated to be less than 20%.² In our study, 43.1% of the referred patients had an occluded artery, so CTO has to be regarded as a major reason for referral to surgery. We could also show that CABG surgery seems to be the superior therapy for achievement of CR in CTO patients. In our nonselected patient cohort, we completely revascularized 82.6% of the patients and even achieved revascularization rates of 96.2% if the LAD was occluded. In comparison, published revascularization rates in selected PCI cohorts usually do not exceed 80% except for single-experienced centers where at the most 50% of all-comers were treated achieving a 90% success rate.^{23,24}

The focus in CTO revascularization—as in all therapies—needs to be on patient benefit. Unfortunately, this study was not designed to answer this question in total. Especially, revascularizing vessels seemingly lacking collaterals in the angiography might appear senseless as these could only perfuse scar tissue and not improve the patients' outcome. Nevertheless, our findings show that even vessels graded as Rentrop 0 usually have a revascularizable size and lumen. This makes it hard to believe that these vessels have no blood flow and leave no viable cardiomyocytes. This feeling is supported by a nuclear imaging study in which collateral blood flow graded by Rentrop could not predict myocardial viability or functional improvement.²⁵ Another study showed that revascularizing not infarct-related CTO vessels increases LV function in the CTO territory after STEMI.²⁶

We tried to support our hypothesis by looking at bypass blood flow as a parameter for bypass quality. One might think that chronically occluded target vessels lacking collateralization are more severely diseased downstream of the occlusion than vessels with retrograde blood flow. This would have an influence on bypass blood flow and graft patency.²¹ We therefore quantified bypass blood flow using TTFM. We were able to show that occluded vessels lacking collateralization had no significant reduction in blood flow. We therefore confirm Oshima et al's statement that collateralization—if graded according to Rentrop—seems to have no influence on bypass blood flow.²¹ As low flow in the intraoperative TTFM has been shown to predict early graft failure, it is our opinion that long-term graft patency due to low flow need not be a concern in CTOs even if no collateralization is seen in the preoperative angiogram.²¹

Overall, our data show that we should not utterly rely on the preoperative angiogram when evaluating occluded coronary arteries. Especially in patients with poor collateralization, we should expect to get more than we see. These vessels were seen to be revascularizable with a good chance of long-term graft patency. Knowing that, we need to focus on

answering the question of patient benefit and long-term outcome in the future.

Conflict of Interest

None declared.

Authors' Contributions

F.M. came up with the idea and supervised the project, D.L., our PhD student, and C.G. put a lot of effort into building up this database. While D.L. worked hard on generating the scores and reviewed all the coronary angiograms, C.G. put effort in collecting patient data and did most of the statistical analyses as well as the writing of the article.

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