Effect of Revascularization on Coronary Chronic Total Occlusion in Patients Undergoing Coronary Artery Bypass Grafting

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Research article

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Abstract

Background: Bypass grafting for chronic total occlusions remains surgically challenging and controversial. Therefore, we evaluated the incidence and clinical outcomes of revascularization on chronic total occlusions undergoing coronary artery bypass surgery.

Methods: Among 828 patients who underwent isolated coronary artery bypass surgery from January 2010 to December 2018, 245 patients (29.5%) diagnosed with at least one chronic total occlusion were included and retrospectively reviewed. Primary endpoints were 30-day and overall mortality. Secondary endpoint was the composite outcome of major adverse cardiac and cerebrovascular events.

Results: With a mean follow-up of 56.6 ± 6.5 months in 245 patients with chronic total occlusions, 51 patients (20.9%) received incomplete revascularization for chronic total occlusions. Risk factor analysis showed that incomplete revascularization was associated with increased 30-day (odds ratio 8.62; 95% confidence interval (CI) 1.64 – 50; $p = 0.011$) and overall mortality (hazard ratio (HR) 2.13; 95% CI 1.07 – 4.21; $p = 0.03$). ICR also increased the risk of major adverse cardiac and cerebrovascular events (HR 1.98; 95% CI 1.12 – 3.54; $p = 0.01$). Freedom from overall mortality was 92.8%, 90.4%, and 86.8% in the complete revascularization group, and 86.3%, 80.0%, and 72.7% in the incomplete revascularization group, at 1, 3, and 5 years, respectively ($p = 0.004$).

Conclusions: In patients with chronic total occlusions undergoing coronary artery bypass surgery, the rate of incomplete revascularization was 20.9%, and it significantly increased the risk of mortality and major adverse cardiac and cerebrovascular events. Further studies in a large cohort are needed.

Background

Chronic total occlusions (CTOs) of coronary arteries are an exacerbation of stable coronary artery disease with advanced calcification.¹ CTOs are present in up to one third of patients undergoing coronary angiography.² Even though various degree of collateral vessels develop and contribute to the perfusion of CTO territories, revascularization on CTOs was attempted to relieve angina or heart failure with its chronic progressing nature.³

One of the options for revascularization is percutaneous coronary intervention (PCI), one advantage of which is that it is done under local anesthetics, postprocedural morbidity is minimal, and patients endure a short hospital stay.⁴ Successful PCI is associated with a significant decrease in both short- and long-term mortality.⁵ However, because of the lower initial success rate with angioplasty and a higher frequency of restenosis, reocclusion, and adverse clinical events, PCI for CTOs remains controversial. The other alternative is revascularization by coronary artery bypass grafting (CABG). Since there is generally no difference in the techniques of revascularization whether the vessel is highly stenosis or completely occluded,⁶ the presence of CTO may not affect the complexity of CABG or postoperative outcomes, including the incidence of major adverse cardiac and cerebrovascular events (MACCE).^{7,8}

Even though several studies of revascularization on CTOs with coronary arteries demonstrated favorable outcomes of CABG over PCI,^{4,8} bypass grafting remains surgically challenging. Especially, the lower rate of successful surgical revascularization has been associated with features including the presence of occlusion at a side branch, heavy calcification, and a length of CTO of more than 50 mm.^{2,9} In addition, there is lack of evidence on the survival benefit of complete revascularization for CTOs in patient undergoing CABG. Therefore, in the following study, we sought to evaluate the incidence of revascularization for CTOs and its clinical outcomes in patients undergoing CABG.

Methods

Study population

Among 828 patients who underwent isolated CABG at a single institution from January 2010 to June 2018, 245 patients (29.5%) diagnosed with at least one CTO were retrospectively reviewed from the electronic medical records. We divided the cohort into two groups, according to the degree of revascularization: the complete revascularization (CR) group, in which the patients received revascularization for all CTO lesions; and the incomplete revascularization (ICR) group, in which at least one CTO lesion remained un-bypassed. Surgical decisions for revascularization were made by the primary surgeon based on the quality of the conduit, the diameter of the native coronary artery, the degree of calcification, and the viability of the myocardium.

This study was approved by the local Institutional Review Board of our institution, Seoul St. Mary's Hospital, Seoul, Republic of Korea (approval no. KC20RASI0157). The requirement of informed consent from individual patients was waived because the study was a retrospective database review.

Data Collection

CTO was defined as 100% luminal diameter stenosis without a discernable lumen, the absence of antegrade flow, known or assumed to be ≥ 3 months' duration, based on the prior angiography, and the presence of bridging collaterals or concordant acute coronary syndrome. The angiographic data were reviewed and interpreted by cardiologists in the coronary angiographic laboratory. All CTOs in the left anterior descending coronary artery (LAD) and the major diagonal branches were grouped as CTOs in the LAD distribution. Similarly, CTOs in the left circumflex (LCX) and the major obtuse marginal branches were classified as the LCX distribution CTOs. CTOs in the right coronary artery (RCA) and its major branches were classified as CTOs in the RCA territory. Good collateral was defined as good coronary collateralization based on the Rentrop classification, grade of 2 or 3. According to the Rentrop classification, the degree of recipient artery contrast filling is used to classify collateral vessels: Grade 0, no collateral; Grade 1, recipient side branch filling only; Grade 2, partial filling of main recipient vessel; and Grade 3, complete filling of main epicardial recipient vessel.

Primary endpoints were 30-day and overall mortality. The secondary endpoint was the composite outcome of MACCE. MACCE was defined as all-cause mortality, stroke or transient ischemic attack, and

acute coronary syndrome requiring repeated revascularization.

Follow-up information about outcomes was obtained from out-patient visits, telephone interviews, and medical records of the national health insurance.

Statistical Analysis

Data are expressed as mean $\pm$ standard deviation for continuous variables and as number and percentages for categorical variables. Continuous parameters were compared with Student's *t*-test, and discrete variables were compared using the χ^2 test or the Fisher's exact test, as appropriate. Regarding the risk factor analysis for 30-day mortality, only univariate analysis using logistic regression was performed due to the small event number ($n = 9$). We did univariate and multivariate analyses for the entire patient cohort using the Cox proportional hazards model for overall mortality and MACCE. We included the most clinically relevant variables in the multivariate analysis if their univariate significance was $p \leq 0.1$, and used the backward elimination method for variable selections. Cumulative event rates and survival curves were generated using the Kaplan-Meier method with the log-rank test. The critical value of $p \leq 0.05$ was used for statistical significance. We did all analyses with IBM SPSS Statistics for Windows, Version 24.0 (IBM Corp., Armonk, NY).

Results

Baseline Characteristics

With a mean follow-up duration of 56.6 ± 6.5 months in 245 patients with CTOs who underwent isolated CABG, 51 patients (20.9%) received ICR for CTO lesions. Baseline characteristics and comparison of the two groups are summarized in Table 1. In the ICR group, patients were older ($p = 0.04$), had more comorbidities, like diabetes ($p = 0.006$) and end-stage renal disease ($p = 0.011$).

Table 1
Baseline Characteristics

Variable	Total (n = 245)	ICR (n = 51)	CR (n = 194)	P Value
Age, years	66.5 ± 9.97	69.1 ± 9.0	65.7 ± 10.1	0.04
Sex (male)	181 (73.9)	42 (82.4)	139 (71.6)	0.12
Comorbidities	98 (40.0)	29 (56.9)	69 (35.6)	0.006
DM	154 (62.9)	33 (64.7)	121 (62.4)	0.75
Hypertension	30 (12.2)	9 (17.6)	21 (10.8)	0.18
CVA	12 (4.9)	6 (11.8)	6 (3.1)	0.011
ESRD				
LVEF, %	51.5 ± 12.7	49.8 ± 12.1	51.8 ± 12.9	0.34
No. of bypass	2.38 ± 0.95	1.78 ± 0.73	2.54 ± 0.92	< 0.001
Emergency	30 (12.2)	8 (15.7)	22 (11.3)	0.39
IABP	15 (6.1)	5 (9.8)	10 (5.2)	0.21
Good collateral [†]	120 (50.2)	22 (44.0)	98 (51.9)	0.32
No. of CTO	164 (66.9)	35 (68.6)	129 (66.5)	0.51
1	76 (31.0)	16 (31.4)	60 (30.9)	
2	5 (2.0)	0 (0)	5 (2.6)	
3				
Territory of CTO	100 (40.8)	2 (3.9)	98 (51.3)	< 0.001
LAD	82 (33.4)	17 (33.3)	65 (34.2)	0.91
LCX	143 (58.8)	38 (74.5)	105 (54.7)	0.01
RCA				
CPB time, mins	61.4 ± 38.9	51.8 ± 44.2	63.9 ± 37.1	0.05
ACC time, mins	39.0 ± 28.4	28.1 ± 26.5	41.8 ± 28.2	0.002

[†]Collateral flow, Rentrop grade ≥ 2

ACC, aortic cross clamp; CPB, cardiopulmonary bypass; CR, complete revascularization; CTO, chronic total occlusion; CVA, cerebrovascular accident; DM, diabetes mellitus; ESRD, end-stage renal disease; IABP, intra-aortic balloon pump; ICR, incomplete revascularization; LAD, left anterior descending artery; LCX, left circumflex artery; LVEF, left ventricular ejection fraction; MACCE, major adverse cardiac and cerebrovascular event; No., number; RCA, right coronary artery.

Variable	Total (n = 245)	ICR (n = 51)	CR (n = 194)	P Value
30-day mortality	9 (3.7)	6 (11.8)	3 (1.5)	0.001
Overall mortality	44 (18.0)	17 (33.3)	27 (13.9)	0.001
MACCE	63 (25.7)	22 (43.1)	41 (21.1)	0.001
†Collateral flow, Rentrop grade ≥ 2				
ACC, aortic cross clamp; CPB, cardiopulmonary bypass; CR, complete revascularization; CTO, chronic total occlusion; CVA, cerebrovascular accident; DM, diabetes mellitus; ESRD, end-stage renal disease; IABP, intra-aortic balloon pump; ICR, incomplete revascularization; LAD, left anterior descending artery; LCX, left circumflex artery; LVEF, left ventricular ejection fraction; MACCE, major adverse cardiac and cerebrovascular event; No., number; RCA, right coronary artery.				

Regarding CTO territories, the RCA territory were involved predominantly in both groups (ICR vs CR, 74.5% vs 54.7%, respectively). The rate of CR was higher in the LAD territory (3.9% vs 51.3%, $p < 0.001$), but lower in the RCA territory (74.5% vs 54.7%, $p = 0.01$). The ICR group showed higher mortality at 30 days (11.8% vs 1.5%, $p = 0.001$) and overall (33.3% vs 13.9%, $p = 0.001$), and higher incidence of MACCE (43.1% vs 21.1%, $p = 0.001$).

Risk Factor Analyses for Outcomes

In the analysis of risk factors for 30-day mortality, longer cardiopulmonary bypass time (odds ratio (OR) 1.04; 95% confidence interval (CI) 1.02–1.07; $p < 0.001$) and low left ventricular ejection fraction (LVEF) (OR 1.09; 95% CI 1.03–1.15; $p = 0.005$) were identified as significant risk factors. Also, ICR for CTO lesions was associated with increased risk for 30-day mortality (OR 8.62; 95% CI 1.64–50; $p = 0.011$) (Table 2).

Table 2
Univariate Analysis for 30-day Mortality

Univariate Analysis			
Variables	OR	95% CI	<i>P</i> Value
Age	1.06	0.98–1.15	0.13
Sex (male)	1.43	0.34–5.91	0.62
Comorbidities	0.41	0.08–2.04	0.28
DM	1.18	0.29–4.87	0.81
Hypertension	0.25	0.06–1.09	0.06
CVA	2.55	0.29–22.28	0.39
ESRD			
LVEF	0.92	0.87–0.97	0.005
IABP	4.90	0.92–25.98	0.06
No. of CTO	reference	0.21–3.05	0.74
1	0.80	0.45–44.24	0.20
2	4.47		
3			
CPB time	1.04	1.02–1.07	< 0.001
ACC time	1.00	0.98–1.03	0.81
Revascularization of CTO	reference	1.64–50.0	0.011
CR	8.62		
ICR			
ACC, aortic cross clamp; CI, confidence interval; CPB, cardiopulmonary bypass; CR, complete revascularization; CTO, chronic total occlusion; CVA, cerebrovascular accident; DM, diabetes mellitus; ESRD, end-stage renal disease; IABP, intra-aortic balloon pump; ICR, incomplete revascularization; LVEF, left ventricular ejection fraction; MACCE, major adverse cardiac and cerebrovascular event; No., number; OR, odds ratio.			

In the analysis of risk factors for overall mortality, the multivariate analysis showed that the ICR was significantly associated with increased overall mortality (hazard ratio (HR) 2.13; 95% CI 1.07–4.21; $p = 0.03$) as well as old age (HR 1.03; 95% CI 1.00–1.07; $p = 0.03$) (Table 3).

Table 3
Univariate and Multivariate Analyses for Overall Mortality

Univariate Analysis				Multivariate Analysis		
Variables	HR	95% CI	<i>P</i> Value	HR	95% CI	<i>P</i> Value
Age	1.04	1.01–1.08	0.01	1.03	1.00–1.07	0.03
Sex (male)	0.96	0.48–1.91	0.92			
Comorbidities	0.93	0.47–1.82	0.83			
DM	1.31	0.66–2.66	0.42			
Hypertension	0.55	0.23–1.34	0.19			
CVA	3.55	1.07–11.77	0.04			
ESRD						
LVEF	0.95	0.93–0.98	< 0.001	0.96	0.94–0.98	0.002
IABP	2.44	0.79–7.56	0.12			
No. of CTO	reference	0.35–1.54	0.41			
1	0.74	1.67–13.51	0.03			
2	4.75					
3						
Territory of CTO	0.81	0.41–1.60	0.55			
LAD	1.50	0.76–2.96	0.23			
LCX	1.22	0.62–2.41	0.56			
RCA						
CPB time	1.01	1.00–1.02	0.008	1.01	1.00–1.02	0.03
ACC time	1.00	0.99–1.01	0.44			
Revascularization of CTO	reference	1.28–4.35	0.006	2.13	1.07–4.21	0.03
CR	2.38					
ICR						
ACC, aortic cross clamp; CI, confidence interval; CPB, cardiopulmonary bypass; CR, complete revascularization; CTO, chronic total occlusion; CVA, cerebrovascular accident; DM, diabetes mellitus; ESRD, end-stage renal disease; HR, hazard ratio; IABP, intra-aortic balloon pump; ICR, incomplete revascularization; LAD, left anterior descending artery; LCX, left circumflex artery; LVEF, left ventricular ejection fraction; MACCE, major adverse cardiac and cerebrovascular event; No., number; RCA, right coronary artery.						

In the analysis of risk factors for MACCE, low LVEF (HR 1.04; 95% CI 1.01–1.06; $p = 0.01$) and ICR for CTOs (HR 1.98; 95% CI 1.12–3.54; $p = 0.01$) were associated with increased risk for MACCE (Table 4).

Table 4
Univariate and Multivariate Analyses for MACCE

Variables	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	<i>P</i> Value	HR	95% CI	<i>P</i> Value
Age	1.01	0.99–1.01	0.20			
Sex (male)	1.31	0.71–2.41	0.38			
Comorbidities	1.21	0.74–2.00	0.44			
DM	1.13	0.67–1.92	0.62			
Hypertension	1.64	0.85–3.15	0.13			
CVA	2.37	1.01–5.53	0.05			
ESRD						
LVEF	0.97	0.95–0.98	0.002	0.96	0.94–0.99	0.01
IABP	1.74	0.74–4.05	0.19			
No. of CTO	reference	0.57–1.68	0.95			
1	0.98	0.95–7.61	0.06			
2	2.69					
3						
Territory of CTO	1.12	0.67–1.86	0.64			
LAD	1.04	0.62–1.75	0.86			
LCX	1.12	0.67–1.87	0.64			
RCA						
CPB time	1.00	0.99–1.00	0.73			
ACC time	0.99	0.98–1.00	0.14			
Revascularization of CTO	reference	1.30–3.70	0.003	1.98	1.12–3.54	0.01
CR	2.17					
ICR						
ACC, aortic cross clamp; CI, confidence interval; CPB, cardiopulmonary bypass; CR, complete revascularization; CTO, chronic total occlusion; CVA, cerebrovascular accident; DM, diabetes mellitus; ESRD, end-stage renal disease; HR, hazard ratio; IABP, intra-aortic balloon pump; ICR, incomplete revascularization; LAD, left anterior descending artery; LCX, left circumflex artery; LVEF, left ventricular ejection fraction; MACCE, major adverse cardiac and cerebrovascular event; No., number; RCA, right coronary artery.						

Freedom from Overall Mortality and MACCE Between Groups

Freedom from overall mortality and MACCE was significantly higher in the CR group. Freedom from overall mortality was 92.8%, 90.4%, and 86.8% in the CR group, and 86.3%, 80.0%, and 72.7% in the ICR group, at 1, 3, and 5 years, respectively ($p = 0.005$) (Fig. 1). Freedom from MACCE was 91.3%, 83.4%, and 77.6% in the CR group, and 79.8%, 72.7%, and 53.6% in the ICR group at 1, 3, and 5 years, respectively ($p = 0.003$) (Fig. 2).

Discussion

The main findings of this study can be summarized as follows. First, CTO is found in about 29% of patients undergoing CABG. Among them, 80% of patients received complete bypass grafting for all CTOs. Second, ICR for CTO lesions was associated with increased 30-day and overall mortality. Also, ICR was related to increased MACCE after bypass grafting for CTOs. The rates of CR for CTOs were 86% in Fefer et al., nearly 85% in Banerjee et al., and 80% in our study, which was similar to those previous studies.^{9,10}

In our study, ICR for CTOs was one of the independent risk factors for 30-day and overall mortality. Unlike our study, Fefer et al. showed that ICR for CTOs was not associated with increased long-term mortality.¹⁰ The following theories were supported by the conclusion of their study; the territory supplied by CTO can be non-viable, all non-revascularized territories were in the RCA and LCX territories, and the collateral flow often exists to CTO territory. However, their study lacked assessment of viability and had limited long-term follow-up data. In contrast, Kleisli et al. demonstrated that patients who underwent CABG with ICR had worse outcomes than did patients with CR.¹¹ Data from SYNTAX also showed that patients with ICR had more adverse events than did patients with CR.¹² Therefore, ICR for CTOs was associated with short- and long-term outcomes, as a negative factor.⁴ As a result, the overall survival in the ICR group for CTOs was significantly lower than that in the CR group.

Farooq et al. concluded that ICR for CTO lesions was associated with significantly higher frequencies of all-cause revascularization and MACCE than was CR.¹³ These findings are similar to the results shown in our study. Target vessel revascularization in the ICR group was significantly higher, as shown in Fig. 3. This event seemed to occur mostly within about 4 years after CABG.

In patients with CTO lesions, the possibility of CR was affected by many other factors, such as the revascularization for CTOs driven by the patient's general condition and the angiographic findings. In this study, patients in the ICR group were older and had more comorbidities, such as diabetes and renal replacement, than did the CR group. According to other literature, patients with ICR were also significantly older and had higher prevalence of comorbidities, including diabetes, hypertension, and heart failure.^{9,10} Also, an anatomical coronary complexity with multiple long and diseased or small segments could have influenced the result of revascularization. Revascularization in patient with this sort of anatomical

complexity and poor general condition may be a challenge, and longer surgical procedures are associated with higher postoperative morbidities, longer periods of hospitalization, and slower return to normal activities.⁴

There are several limitations in this study. First, it is a retrospective study in a single institution with a small cohort. Given its observational nature and small sample size, potential confounders might have remained. However, incidence of CTOs was uncommon, so the number of patients with CTOs in our study was similar to that in previous studies for CTOs in CABG. Next, we did not evaluate the viability of the myocardium on CTO lesions routinely unless the myocardial thickness was maintained. Because assessment of viability in all patients undergoing CABG is not cost effective and has limited and uncertain accuracy, with uncertain false-positive and false-negative rates, uncertain prevalence of hibernating myocardium, and thus uncertain predictive values.¹² Finally, we collected just hard endpoint follow-up data, like readmission due to heart failure and cardiac function on transthoracic echocardiography, so there is limited information on the relief of angina, history of repeated PCI, and MACCE during the follow-up period.

Conclusions

In patients with CTO lesions undergoing CABG, the rate of ICR was 20.9%, and incomplete revascularization for CTOs was significantly associated with increased risk of MACCE, and 30-day and overall mortality. Further studies with a larger cohort may be necessary to validate this issue.

List Of Abbreviations

CABG, coronary artery bypass grafting

CR, complete revascularization

CTO, chronic total occlusion

ICR, incomplete revascularization

LAD, left anterior descending

LCX, left circumflex

LVEF, left ventricular ejection fraction

MACCE, major adverse cardiac and cerebrovascular events

PCI, percutaneous coronary intervention

RCA, right coronary artery

Declarations

Ethics approval and consent to participate

This study was approved by the local Institutional Review Board of our institution, Seoul St. Mary's Hospital, Seoul, Republic of Korea (approval no. KC20RASI0157).

Consent to publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

There was no funding source used for the study.

Authors' contributions

JL, HWK, JK and HS have made substantial contributions to the acquisition, analysis, interpretation of data. JL was a major contributor in writing the manuscript. YSK and JYL have designed the study and analyzed and interpreted the data. All authors have approved the submitted version.

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Figures

Patients at risk

CR	179	130	86	47
ICR	43	35	26	13

Figure 1

Freedom from overall mortality between the two groups, complete (CR, blue line) and incomplete revascularization (ICR, red line).

Patients at risk

CR	156	94	56	31
ICR	36	25	15	8

Figure 2

Freedom from major adverse cardiac and cerebrovascular event (MACCE) between the two groups, complete (CR, blue line) and incomplete revascularization (ICR, red line).

Patients at risk

CR	154	95	55	30
ICR	35	24	15	8

Figure 3

Freedom from repeat revascularization on target vessel after coronary artery bypass grafting (CABG) between the two groups, complete (CR, blue line) and incomplete revascularization (ICR, red line).