

Evaluation of the Effect of a Concurrent Chronic Total Occlusion on Long-Term Mortality and Left Ventricular Function in Patients After Primary Percutaneous Coronary Intervention

Bimmer E. P. M. Claessen, MD, René J. van der Schaaf, MD, Niels J. Verouden, MD, Nienke K. Stegenga, MSc, Annemarie E. Engstrom, MD, Krischan D. Sjauw, MD, Wouter J. Kikkert, MD, Marije M. Vis, MD, Jan Baan, JR, MD, PhD, Karel T. Koch, MD, PhD, Robbert J. de Winter, MD, PhD, Jan G. P. Tijssen, PhD, Jan J. Piek, MD, PhD, José P. S. Henriques, MD, PhD

Amsterdam, the Netherlands

Objectives The aim of this study was to evaluate the effect of a concurrent chronic total occlusion (CTO) in patients with ST-segment elevation myocardial infarction (STEMI) on long-term mortality and left ventricular ejection fraction (LVEF).

Background The impact of a CTO in a non-infarct-related artery (IRA) on prognosis after STEMI is unknown.

Methods Between 1997 and 2005, we admitted 3,277 STEMI patients treated with primary percutaneous coronary intervention. Patients were categorized as single-vessel disease (SVD), multivessel disease (MVD) without CTO, and MVD with a CTO in a non-IRA. We performed a “landmark survival analysis” to 5 years follow-up with a landmark set at 30 days. Additionally, we analyzed the evolution of LVEF within 1 year.

Results Of the patients, 2,115 (65%) had SVD, 742 patients (23%) had MVD without CTO, and 420 patients (13%) had a concurrent CTO. Presence of a CTO was a strong and independent predictor for 30-day mortality (hazard ratio [HR]: 3.6, 95% confidence interval [CI]: 2.6 to 4.7, $p < 0.01$), whereas MVD without CTO was a weak predictor (HR: 1.6, 95% CI: 1.2 to 2.2, $p = 0.01$). In 30-day survivors, CTO remained a strong predictor (HR: 1.9, 95% CI: 1.4 to 2.8, $p < 0.01$), and MVD lost its independent prognostic value (HR: 1.1, 95% CI: 0.8 to 1.5, $p = 0.45$). Furthermore, CTO was associated with LVEF $\leq 40\%$ immediately after STEMI (odds ratio: 1.9, 95% CI: 1.3 to 2.8, $p < 0.01$) and a further decrease in LVEF within the first year (odds ratio: 3.5, 95% CI: 1.6 to 7.8, $p < 0.01$).

Conclusions The presence of a CTO and not MVD alone is associated with long-term mortality even when early deaths are excluded from analysis. The presence of a CTO is associated with reduced LVEF and further deterioration of LVEF. (J Am Coll Cardiol Intv 2009;2:1128–34) © 2009 by the American College of Cardiology Foundation

Primary percutaneous coronary intervention (PCI) in patients with ST-segment elevation myocardial infarction (STEMI) aims at early and sustained restoration of antegrade flow in the infarct-related artery (IRA). Successful and timely primary PCI leads to salvage of myocardium at risk and reduces mortality (1). Angiography before primary PCI has shown that multivessel coronary artery disease (MVD) is present in 40% to 65% of patients with STEMI and is associated with higher morbidity and mortality after reperfusion therapy (2–5). A concurrent chronic total occlusion (CTO) in a non-IRA is present in 12% to 13% of patients with STEMI (2,4). Recently we described in a cohort of 1,417 STEMI patients that the effect of MVD on mortality was primarily due to the presence of a CTO in a non-IRA (4). However, in the relatively short-term follow-up period of 1 year, the majority of patients died within 30 days. To provide further insight into the impact of a CTO in a non-IRA on early and late mortality after STEMI we performed a “landmark survival analysis” with a landmark at 30 days, and we increased the total follow-up period to 5 years. Furthermore, the size of our consecutive patient cohort has more than doubled. In an attempt to further investigate the effects of a CTO in a non-IRA after STEMI, we additionally analyzed the impact of a CTO in a non-IRA on residual left ventricular ejection fraction (LVEF) immediately after primary PCI and during follow-up within the first year after primary PCI.

Methods

Between January 1997 and April 2006, a total of 3,562 consecutive and unselected patients were admitted to our hospital with STEMI. Acute STEMI was diagnosed when patients had symptoms of an acute myocardial infarction lasting 30 min to 6 h, accompanied by an electrocardiogram with ST-segment elevation >1 mm (0.1 mV) in ≥ 2 contiguous leads. Patients were immediately transported to the catheterization laboratory and underwent immediate angiography with a view to perform primary PCI. If the coronary anatomy was suitable for PCI, the procedure was performed with standard techniques. All procedural decisions, including device selection and adjunctive pharmacotherapy, such as glycoprotein IIb/IIIa inhibitors, were made at the discretion of the operator. All patients were treated with heparin and aspirin before PCI. If a coronary stent was implanted, ticlopidine or clopidogrel was prescribed according to the guidelines.

Baseline clinical and angiographic data were collected prospectively in a dedicated database. Upon the operator’s online assessment during emergency angiography, patients were categorized as having SVD, MVD without CTO, or MVD with concurrent CTO. For the purpose of this study, MVD was defined as ≥ 1 stenosis $>70\%$ of the coronary lumen diameter in ≥ 1 of the non-infarct-related epicardial

arteries or left main stenosis $\geq 50\%$. A CTO was defined as a 100% luminal narrowing in a non-IRA before PCI without antegrade flow or with antegrade or retrograde filling through collateral vessels. Per protocol, follow-up data including information on cardiac medication was collected by written questionnaire sent to all patients after 1 year. In addition, hospital records and outpatient reports were reviewed, and treating cardiologists were contacted. Finally, information on vital status was obtained from the Dutch national population registry (Statistics Netherlands, Voorburg, the Netherlands) per April 2007. Data for the 3,562 patients were checked for inconsistency and completeness. Duplicate patients due to recurrent STEMI ($n = 96$), patients without confirmed diagnosis of STEMI ($n = 132$), and patients lost to follow-up ($n = 57$) were excluded, resulting in a final cohort of 3,277 patients with a median follow-up of 3.1 years (interquartile range [IQR]: 1.3 to 4.6).

The LVEF was assessed by either global visual estimation on echocardiography or by nuclear scintigraphy. Baseline LVEF was assessed within 1 month after index event. Follow-up LVEF was assessed at least 1 month after but within 1 year of baseline LVEF measurement. The LVEF comparison between baseline and follow-up was only performed if serial measurements with the same technique were available.

Statistical analysis. Statistical analysis was performed with SPSS statistical software version 15.0 (SPSS, Inc., Chicago, Illinois). Differences in baseline characteristics between the 3 groups were tested for significance by the chi-square test. Statistical significance was defined as a $p < 0.05$.

Cumulative event rates for death were calculated according to the Kaplan-Meier method. Survival curves were constructed with Kaplan-Meier estimates and compared by log-rank tests. Follow-up for mortality was censored at the date of last follow-up by checking vital status in the Dutch population registry or at 5 years, whichever came first. We performed a “landmark survival analysis” with a landmark set at 30 days to provide insight into the differences in early and late death rates in patients with SVD, MVD without CTO, and MVD with concurrent CTO.

Hazard ratios (HRs) for death were calculated with Cox proportional hazard regression analyses after verification of the proportional hazards assumption. To correct for differences in baseline variables and residual LVEF, we per-

Abbreviations and Acronyms

CI = confidence interval

CTO = chronic total occlusion

HR = hazard ratio

IQR = interquartile range

IRA = infarct-related artery

LVEF = left ventricular ejection fraction

MVD = multivessel disease

OR = odds ratio

PCI = percutaneous coronary intervention

STEMI = ST-segment elevation myocardial infarction

SVD = single-vessel disease

Table 1. Baseline Clinical and Angiographic Characteristics

	Total STEMI Cohort (n = 3,277)				Patients With LVEF Available (n = 1,745)				Patients With Serial LVEF (n = 356)			
	SVD (n = 2,115) (65%)	MVD (n = 742) (23%)	CTO (n = 420) (13%)	p Value	SVD (n = 1,159) (66%)	MVD (n = 386) (22%)	CTO (n = 200) (11%)	p Value	SVD (n = 247) (69%)	MVD (n = 75) (21%)	CTO (n = 34) (10%)	p Value
Baseline characteristics												
Age ≥60 yrs	928 (44)	464 (63)	276 (66)	<0.01	503 (43)	226 (59)	132 (66)	<0.01	95 (39)	42 (56)	20 (59)	<0.01
Male	1,498 (71)	554 (75)	315 (75)	0.04	839 (72)	293 (76)	153 (77)	0.25	185 (75)	60 (80)	28 (83)	0.47
Hypertension	598 (28)	266 (36)	136 (32)	<0.01	335 (29)	143 (37)	74 (37)	<0.01	72 (29)	31 (41)	15 (44)	0.05
Smoker	1,045 (49)	283 (38)	159 (38)	<0.01	592 (51)	150 (39)	79 (40)	<0.01	123 (50)	36 (48)	17 (50)	0.96
Diabetes	183 (8.7)	118 (16)	82 (20)	<0.01	98 (8.5)	62 (16)	41 (21)	<0.01	17 (6.9)	16 (21)	8 (23)	<0.01
Hypercholesterolemia	443 (21)	175 (24)	120 (29)	<0.01	237 (20)	94 (24)	60 (30)	<0.01	52 (21)	18 (24)	15 (44)	0.01
Family history of CVD	873 (41)	306 (41)	151 (36)	0.12	494 (43)	169 (44)	79 (40)	0.61	111 (45)	37 (49)	15 (45)	0.78
Previous MI	190 (9.0)	141 (19)	163 (39)	<0.01	91 (7.9)	61 (16)	71 (36)	<0.01	18 (7.3)	15 (20)	9 (27)	<0.01
Shock	145 (6.9)	87 (12)	91 (22)	<0.01	82 (7.1)	40 (10)	34 (17)	<0.01	22 (8.9)	9 (12)	6 (18)	0.26
Angiographic characteristics												
LAD-related MI	1,045 (49)	295 (40)	210 (50)	<0.01	606 (52)	157 (41)	89 (45)	<0.01	152 (62)	36 (48)	19 (56)	0.11
RCX-related MI	268 (13)	102 (14)	82 (20)	<0.01	143 (12)	52 (14)	38 (19)	0.04	56 (11)	10 (13)	3 (8.8)	0.73
RCA-related MI	799 (38)	344 (46)	127 (30)	<0.01	409 (35)	176 (46)	73 (37)	<0.01	69 (28)	29 (39)	12 (35)	0.18
Procedural success	2,003 (97)	686 (95)	360 (91)	<0.01	1,101 (98)	366 (97)	180 (94)	0.12	235 (97)	70 (93)	32 (94)	0.08
Pre-PCI TIMI flow grade 0	1,394 (66)	481 (65)	271 (65)	0.34	756 (65)	245 (64)	129 (65)	0.24	167 (68)	49 (65)	21 (62)	0.85
Post-PCI TIMI flow grade 3	1,866 (88)	620 (84)	337 (80)	<0.01	1,027 (89)	333 (87)	166 (83)	0.06	220 (89)	63 (84)	30 (88)	0.50
Categorical variables are described as absolute numbers (%) and compared by means of the chi-square test. CTO = chronic total occlusion; CVD = cardiovascular disease; LAD = left anterior descending coronary artery; LM = left main coronary artery; MI = myocardial infarction; MVD = multivessel disease; PCI = percutaneous coronary intervention; RCA = right coronary artery; RCX = circumflex coronary artery; SVD = single-vessel disease; TIMI = Thrombolysis In Myocardial Infarction.												

formed forward stepwise Cox regression multivariate analysis, including all clinical and angiographic variables with a significantly different distribution in the model. Covariates included in multivariate analysis include MVD without concurrent CTO, age >60 years, male sex, hypertension, smoking, diabetes mellitus, hypercholesterolemia, previous MI, shock, left anterior descending coronary artery-related MI, procedural success, and post-PCI TIMI flow grade 3. A covariate was allowed in the model if it influenced the model with a likelihood ratio significance level of $p < 0.05$ and removed if its significance level exceeded $p = 0.1$.

The LVEF was dichotomized as either >40% or ≤40%. This cutoff point for left ventricular function was preselected, because of its well-recognized clinical significance (6). To study the effect of a concurrent CTO on recovery of left ventricular function, LVEF was stratified into 4 incremental categories: >50%, 41% to 50%, 30% to 40%, and <30%. Recovery of LVEF was defined as an increase in LVEF by at least 1 category, unchanged LVEF was defined as no change in category, and decreased LVEF was defined as a decrease by at least 1 category.

To study the independent value of a concurrent CTO on residual LVEF after primary PCI for STEMI and on decreased LVEF at follow-up, stepwise logistic regression was used, including the aforementioned variables in the analyses. Patients who were already in the lowest category for LVEF (n = 15) were excluded from this last analysis.

Results

Follow-up was complete for all patients with a follow-up duration of at least 1 year. Median follow-up duration was 3.1 years (IQR 1.3 to 4.6). Among the 3,277 patients with STEMI, 2,115 patients (65%) had SVD, 742 patients (23%) had MVD without CTO, and 420 patients (13%) had MVD with a concurrent CTO. Table 1 shows the baseline clinical and angiographic characteristics for the 3 patient groups. Patients with MVD (with or without concurrent CTO) were older and more often had hypertension, hypercholesterolemia, and diabetes compared with SVD patients. Furthermore, CTO patients more often had a previous MI and cardiogenic shock at presentation compared with patients with SVD and MVD without CTO.

Mortality. Figure 1 shows the cumulative mortality for patients with SVD, MVD without CTO, and MVD with a concurrent CTO during the first 30 days after STEMI and the 5 years thereafter. Kaplan-Meier estimates for death at 30 days were 4.9% in the SVD group, 9.7% in the MVD without CTO group, and 24% in the MVD with concurrent CTO group. Kaplan-Meier estimates for death at 5 years, excluding patients who died within the first 30 days after STEMI were 10% in the SVD group, 12% in the MVD without CTO group, and 19% in the MVD with concurrent CTO group. Finally, Kaplan-Meier estimates for total mortality at 5 years were 14% in the SVD group, 20% in the

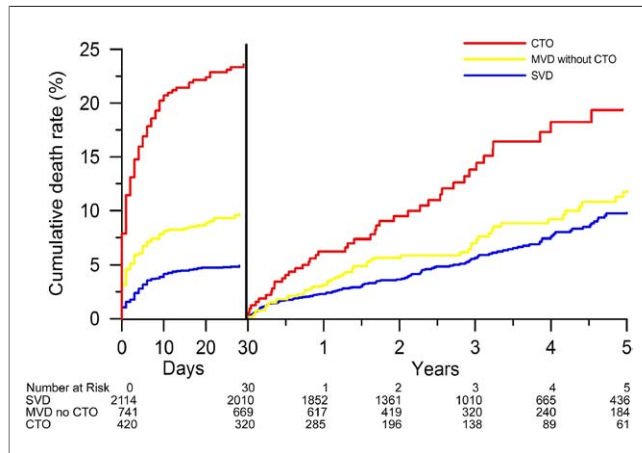


Figure 1. Landmark Survival Analysis

Cumulative risk of death during the first 30 days after primary percutaneous coronary intervention (PCI) and thereafter for patients with single-vessel disease (SVD), multivessel disease (MVD), and a chronic total occlusion (CTO).

MVD without CTO group, and 38% in the MVD with concurrent CTO group.

During the first 30 days after STEMI, the mortality rate was significantly higher in patients with a concurrent CTO in a non-IRA, compared with patients with SVD (unadjusted HR: 5.3, 95% confidence interval [CI]: 4.0 to 7.0, $p < 0.01$). Compared with patients with SVD, mortality was also higher in patients with MVD without a concurrent CTO (unadjusted HR: 2.0, 95% CI: 1.5 to 2.7, $p < 0.01$). Table 2 shows the adjusted Cox proportional HRs for death during the first 30 days, and during 30 days to 5 years after primary PCI. After adjusting for the aforementioned variables, the presence of a CTO in a non-IRA was still found to be a strong and independent predictor for both 30-day mortality, with an HR of 3.6 (95% CI: 2.6 to 4.7, $p < 0.01$)

and 5-year mortality, excluding deaths within the first 30 days (HR: 1.9, 95% CI: 0.8 to 1.6, $p < 0.01$). The presence of MVD without a concurrent CTO was also found to be a statistically significant independent predictor for 30-day mortality (HR: 1.6, 95% CI: 1.2 to 2.2, $p = 0.01$) but not for 5-year mortality excluding deaths within the first 30 days (HR: 1.1, 95% CI: 0.8 to 1.6, $p = 0.51$).

Impact of a CTO on LVEF. In our study population of 3,277 patients, residual LVEF measurements were available in 1,745 patients (53%). A total of 1,674 patients underwent echocardiography, and 71 patients underwent scintigraphy within 30 days after the index event. Median time to LVEF measurement was 3 days (IQR 2 to 5 days); time to LVEF measurement was not statistically different among SVD, MVD, and CTO patient groups. Among the 1,745 patients for whom LVEF data were retrieved, 1,159 patients (66%) had SVD, 386 patients (22%) had MVD, and 200 patients (11%) had a concurrent CTO. The baseline clinical and angiographic characteristics of patients with LVEF are shown in Table 1 and compare well to characteristics of the total cohort. This indicates that this subset seems a representative sample of the total STEMI cohort.

Of the 1,745 patients, a total of 307 patients (18%) had an LVEF $\leq 40\%$. Figure 2 shows the proportions of patients with an LVEF $\leq 40\%$ in each patient group. The proportions of patients with an LVEF $\leq 40\%$ were 16% in the SVD group, 18% in the MVD without CTO group, and 28% in the MVD with concurrent CTO group ($p < 0.01$). The presence of a CTO in a non-IRA was a significant predictor for a residual LVEF $\leq 40\%$ (odds ratio [OR]: 2.0, 95% CI: 1.4 to 2.8). After correction for the presence of MVD without CTO and differences in the aforementioned variables, the presence of a CTO in a non-IRA remained an independent predictor for a residual LVEF $\leq 40\%$ with an OR of 1.8 (95% CI: 1.2 to 2.7, $p < 0.01$). Other indepen-

Table 2. Independent Predictors for Death During the First 30 Days and During 30 Days to 5 Years After Primary PCI

	Predictors for Death During the First 30 Days After Primary PCI			Predictors for Death From 30 Days to 5 Yrs After Primary PCI		
	HR	95% CI	p Value	HR	95% CI	p Value
Shock	7.4	5.8-9.6	<0.01	1.6	1.0-2.4	0.04
CTO	3.6	2.6-4.7	<0.01	1.9	1.4-2.8	<0.01
MVD without CTO	1.6	1.2-2.2	0.01	1.1	0.8-1.6	0.51
LAD-related MI	1.4	1.1-1.7	0.01	1.7	1.3-2.2	<0.01
Hypertension	0.7	0.5-0.9	<0.01	1.1	0.8-1/5	0.52
Hypercholesterolemia	0.6	0.5-0.9	<0.01	0.8	0.6-1.1	0.12
Smoking	0.5	0.4-0.7	<0.01	0.8	0.6-1.0	0.07
Post-PCI TIMI flow grade 3	0.4	0.3-0.5	<0.01	0.6	0.5-0.9	<0.01
Age >60 yrs	1.3	0.9-1.7	0.13	3.3	2.4-4.5	<0.01

Covariates were allowed in the forward stepwise Cox regression model if they influenced the model with a likelihood ratio significance level of $p < 0.05$ and removed if its significance level exceeded $p = 0.1$. Covariates that were included in the analysis but were removed: male sex, diabetes mellitus, and previous MI. The variable "Age >60 yrs" was forced into the model for the first 30 days. The variables "MVD without CTO," "Hypertension," "Hypercholesterolemia," and "Smoking" were forced into the model for the 5 yrs thereafter.

CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 1.

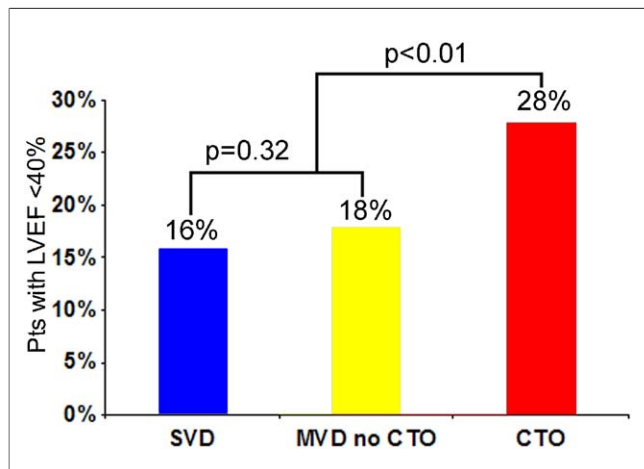


Figure 2. Proportion of Patients With LVEF <40% After ST-Segment Elevation Myocardial Infarction

LVEF = left ventricular ejection fraction; Pts = patients; other abbreviations as in Figure 1.

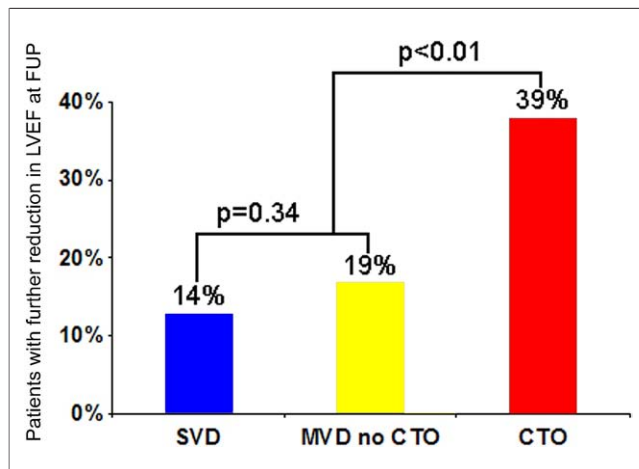


Figure 3. Proportion of Patients With a Decrease in LVEF of at Least 1 Category Between Baseline and 1-Year Follow-Up

FUP = follow-up; other abbreviations as in Figures 1 and 2.

dent predictors for a residual LVEF $\leq 40\%$ are shown in Table 3.

Left ventricular function during follow-up. Of the 1,745 patients with baseline LVEF available, serial LVEF measurements were performed in 356 patients (20%). A total of 242 patients (68%) were classified as having SVD, 74 (21%) as having MVD without CTO, and 36 (10%) as having MVD with a concurrent CTO. Baseline clinical and procedural characteristics are shown in Table 1.

Echocardiography was the only imaging modality used in this subgroup of patients with serial LVEF measurements. Median time between baseline and follow-up echo was 177 days (IQR 89 to 285) with no significant differences in time between echoes among the 3 groups. Patients with SVD more often showed an increase in LVEF at follow-up compared with patients with MVD with and without concurrent CTO ($p = 0.02$). The proportion of patients

who had an increase in LVEF was 37%, 24%, and 21% for patients with SVD, MVD without CTO, and MVD with concurrent CTO, respectively. Figure 3 shows the proportions of patients who had a decrease in LVEF at follow-up in each patient group. Patients with a concurrent CTO significantly more often had a decrease in LVEF compared with patients with SVD and MVD without CTO ($p < 0.01$). The proportion of patients who had a decrease in LVEF was 14%, 19%, and 39% for patients with SVD, MVD without CTO, and MVD with concurrent CTO, respectively.

Logistic regression analysis was used to identify independent predictors of deterioration of LVEF. After correction for the aforementioned variables, the presence of a concurrent CTO was associated with a decrease in LVEF with an OR of 3.5 (95% CI: 1.6 to 7.8, $p < 0.01$). Patients older than 60 years were found to have an OR of 1.9 (95% CI: 1.0 to 3.4, $p = 0.03$) for a decrease in LVEF (Table 4). The presence of MVD without CTO was not independently associated with a decrease in LVEF (OR: 1.3, 95% CI: 0.6 to 2.6, $p = 0.26$).

Table 3. Independent Predictors for LVEF $\leq 40\%$ After STEMI

	OR	95% CI	p Value
LAD-related MI	5.3	3.9-7.2	<0.01
Shock	2.6	1.7-3.8	<0.01
Diabetes mellitus	1.7	1.1-2.5	<0.01
CTO	1.9	1.3-2.8	<0.01
Age >60 yrs	1.5	1.1-2.3	<0.01
Previous MI	1.6	1.1-2.3	0.02
Hypertension	0.6	0.5-0.9	<0.01
MVD without CTO	1.2	0.9-1.7	0.27

Covariates were allowed in the logistic regression model if they influenced the model with a likelihood ratio significance level of $p < 0.05$ and removed if its significance level exceeded $p = 0.1$. Covariates that were included in the analysis but were removed: male sex, smoking, hypercholesterolemia, and procedural success. MVD without CTO was forced into the model.

LVEF = left ventricular ejection fraction; OR = odds ratio; STEMI = ST-segment elevation myocardial infarction; other abbreviations as in Tables 1 and 2.

Table 4. Independent Predictors for a Decrease in LVEF During Follow-Up

	OR	95% CI	p Value
Age >60 yrs	1.9	1.0-3.4	0.03
CTO	3.5	1.6-7.8	<0.01
MVD without CTO	1.3	0.6-2.6	0.64

Covariates were allowed in the logistic regression model if they influenced the model with a likelihood ratio significance level of $p < 0.05$ and removed if its significance level exceeded $p = 0.1$. Covariates that were included in the analysis but were removed: male sex, shock, diabetes, LAD-related infarction, hypertension, hypercholesterolemia, smoking, previous MI, and procedural success. MVD without CTO was forced into the model.

Abbreviations as in Tables 1 and 3.

Discussion

Our study in a cohort of 3,277 patients confirmed and extended the previous observation that the impact of MVD on mortality in STEMI patients is almost entirely due to the presence of a CTO and not due to the presence of MVD alone (2). The presence of a CTO in a non-IRA was found to be a strong and independent predictor for both early mortality (within 30 days after STEMI) and late mortality (from 30 days to 5 years after STEMI). In contrast, MVD without a concurrent CTO was found to be only a relatively weak predictor for early mortality. Moreover, MVD without CTO lost its independent predictive value for mortality after excluding patients who died within 30 days after STEMI. Furthermore, we found that a CTO and not MVD alone is associated with both a reduced residual LVEF after the index event and a further deterioration in LVEF during follow-up.

The high mortality rate of STEMI patients with a concurrent CTO can in part be explained by the higher risk profile of CTO patients. The CTO patients had more risk factors associated with worse clinical outcome when compared with SVD patients. Additionally, they more often had a previous MI and presented more often in shock on admission when compared with SVD patients and MVD patients without CTO. However, after adjustment for these differences in baseline characteristics, the presence of a CTO in a non-IRA remained a strong and independent predictor for early mortality with an HR of 3.6 and for late mortality with an HR of 1.9. The presence of MVD without a CTO was also a statistically significant predictor for early mortality although substantially less powerful with an HR of only 1.6. Only cardiogenic shock was a more potent predictor for early mortality, with an HR of 7.4. Age >60 years was the only more potent predictor for late mortality, with an HR of 3.3.

In an attempt to further explore the underlying mechanism for the increased mortality in STEMI patients with a concurrent CTO, we analyzed residual LVEF in 1,745 patients. The baseline characteristics of these 1,745 patients compare well to those of the entire STEMI cohort, indicating that they were a representative sample. As expected, the proportion of patients with a residual LVEF $\leq 40\%$ was significantly higher in CTO patients (28%) compared with SVD patients (16%) and MVD patients without CTO (18%). The difference between the 2 latter groups was nonsignificant. Even after correction for differences in baseline characteristics in a multivariate logistic regression model, the presence of a CTO remained a strong predictor for a residual LVEF $\leq 40\%$. The presence of MVD alone was not associated with an LVEF $\leq 40\%$.

By analyzing serial echocardiograms, we found that patients with a CTO in a non-IRA more often had a further decrease of LVEF in the first year after the index STEMI.

In a multivariate model, the presence of a CTO was associated with a decrease in LVEF with an OR of 3.5, whereas the presence of MVD alone was not associated with a decrease in LVEF. These findings suggest that STEMI patients with a CTO in a non-IRA undergo a more pronounced negative left ventricular remodeling process. This can also, at least partly, explain the higher mortality among patients with a CTO in a non-IRA.

Clinical implications. Currently, multivessel PCI during primary PCI in the absence of cardiogenic shock or multiple culprit arteries is discouraged, because a beneficial effect on clinical end points has not been demonstrated (7). The only 2 small-sized randomized trials investigating multivessel PCI during the index event failed to show a clinical benefit from multivessel PCI (8,9). Although, in these 2 trials, multivessel PCI was not associated with an increased rate of in-hospital complications, it is likely that multivessel PCI is associated with an increased risk of contrast nephropathy. Additionally, multivessel PCI in the prothrombotic milieu of the hyperacute phase of infarction might result in more adverse thrombotic events (10–12). A number of observational studies are hampered by selection bias and have reported inconclusive results (13–17).

The current study might at least partly explain why a benefit for multivessel PCI has not been clearly demonstrated. In our cohort, we found that the presence of a CTO in a non-IRA drives mortality in MVD patients. Only 30% of MVD patients have a concurrent CTO; moreover, CTO patients have been excluded from previous studies because of the high complexity of these lesions. The current study identified a CTO in a non-IRA as a potentially modifiable risk factor for both short- and long-term mortality after STEMI. An adequately powered randomized controlled trial is warranted to investigate a possible benefit of opening a CTO early after STEMI. Therefore we have recently initiated the randomized controlled international multicenter EXPLORE (Evaluating XIENCE V and LVF in PCI on Occlusions after STEMI) trial (18). This trial will investigate the effects of opening a concurrent CTO on LV function and remodeling after PCI for STEMI.

Study limitations. There are several limitations to this study, the main limitation being its observational nature. Non-culprit lesion stenosis severity was assessed at the infarct angiography in the acute setting and by the performing cardiologist. Therefore, some overestimation of non-culprit lesions might have occurred (19). This might, for a small part, account for the good prognosis of MVD patients without CTO in this study. Detailed information on peri- and post-procedural medication was not available; therefore we were not able to assess differences in adherence to guideline-based post-STEMI therapies. Unfortunately, LVEF assessment was not routinely performed in all patients. Additionally, LVEF was measured with incremental categories and not as a continuous variable. Although

LVEF assessment was not available in all patients, the baseline characteristics compare well between the LVEF subsets of patients and the total STEMI cohort, indicating that these subsets are a representative sample of the total STEMI cohort. Furthermore, the unfavorable effects of a CTO in a non-IRA were found consistently in every analysis.

Conclusions

The poor prognosis of STEMI patients with MVD is driven by the presence of a CTO in a non-IRA. The presence of a CTO and not MVD alone is associated with long-term mortality, even when early deaths are excluded from analysis. Furthermore, the presence of a CTO and not MVD alone is associated with reduced residual LVEF after the index event and with a further deterioration of LVEF during follow-up. These findings warrant further investigation on additional revascularization of CTOs in STEMI patients with MVD.

Reprint requests and correspondence: Dr. José P. S. Henriques, Department of Cardiology, Academic Medical Centre, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands. E-mail: j.p.henriques@amc.uva.nl.

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Key Words: chronic total occlusion ■ left ventricular function ■ mortality ■ myocardial infarction ■ prognosis.