Increased risk of ventricular arrhythmias in survivors of out-of-hospital cardiac arrest with chronic total coronary occlusion

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BACKGROUND Chronic total occlusion (CTO) is common in out-of-hospital cardiac arrest (OHCA) survivors with coronary artery disease. It is unclear whether CTO contributes to ventricular arrhythmias in this population.

OBJECTIVE This study sought to evaluate the impact of unrevascularized CTOs on the occurrence of appropriate implantable cardioverter-defibrillator (ICD) therapy and all-cause mortality in OHCA survivors with coronary artery disease.

METHODS This was a retrospective study that included all consecutive OHCA survivors with coronary artery disease who received an ICD from 1999 until 2015. Study end points were appropriate ICD therapy and all-cause mortality.

RESULTS We identified 217 OHCA survivors (mean age 63 ± 10 years; 86% men) with coronary artery disease. Unrevascularized CTO was present in 71 of 217 patients (33%) at the time of ICD implantation. During a median follow-up of 61 months (interquartile range, 28–97 months), 57 of 217 patients (26%) experienced an appropriate ICD therapy. Patients with CTO had a higher incidence of appropriate ICD therapy in comparison to patients without CTO (log-rank, $P = .002$). Multivariate Cox regression analysis identified CTO (hazard ratio 2.07; 95% confidence interval 1.23–3.50; $P = .007$) as an independent predictor of appropriate ICD therapy. The presence of CTO was not associated with a higher mortality rate (log-rank, $P = .18$).

CONCLUSIONS In OHCA survivors with coronary artery disease receiving an ICD for secondary prevention, CTO was an independent predictor for the occurrence of ventricular arrhythmias but not for mortality.

KEYWORDS Chronic total occlusion; Ventricular tachycardia; Ventricular fibrillation; Implantable cardioverter-defibrillator; Out-of-hospital cardiac arrest

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Introduction

The exact role of chronic total occlusion (CTO) in causing life-threatening ventricular arrhythmias (VA) is not clear. In clinical practice we encounter out-of-hospital cardiac arrest (OHCA) survivors with CTO who have a relatively preserved left ventricular (LV) function and no significant rise in cardiac enzymes. One may speculate that the presence of CTO may contribute to the VA event by a complex interplay of scar and ischemia. A previous nonrandomized study showed that failed or unattempted CTO recanalization in patients with stable coronary artery disease was associated with an increased risk of sudden cardiac death in comparison to those with revascularized CTO.[1] Furthermore, several studies in patients with ischemic cardiomyopathy and severe LV dysfunction who receive an implantable cardioverter-defibrillator (ICD) for primary prevention have shown that CTO is an independent predictor of VA.[2,3] Currently, there are limited data on the prognostic implications of CTO in patients with coronary artery disease who present with OHCA due to VA. The aim of the present study was to evaluate the impact of CTO on the occurrence of VA and all-cause mortality in survivors of OHCA with coronary artery disease.

Methods

Study population

The study population was identified using the prospective ICD registry of the Department of Cardiology of the Erasmus Medical Center in Rotterdam, The Netherlands. Baseline clinical and echocardiography data, characteristics of the implant procedure, and data for all follow-up visits were prospectively recorded in a dedicated database. We identified all consecutive patients with coronary artery disease who received an ICD for secondary prevention after OHCA due to VA between December 1999 and June 2015. *Coronary artery disease* was defined as the presence of significant

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Table 1 Baseline characteristics

Characteristic	All patients (n = 217)	Non-CTO group (n = 146)	CTO group (n = 71)	*P*
Age (y)	63 ± 10	62 ± 11	65 ± 9	.03
Sex: male	187 (86)	123 (84)	64 (90)	.24
Medical history				
Diabetes mellitus	39 (18)	26 (18)	13 (18)	.93
Renal dysfunction (GFR <60 mL/min)	50 (23)	31 (21)	19 (27)	.36
Previous CABG	66 (30)	55 (38)	11 (16)	.001
Previous PCI	121 (56)	81 (56)	40 (56)	.91
NYHA class ≥II	144 (66)	95 (65)	49 (69)	.56
Multivessel disease	40 (18)	7 (5)	33 (47)	<.001
LVEF <35%	112 (52)	71 (49)	41 (58)	.21
QRS duration ≥130 ms	55 (25)	33 (23)	22 (31)	.18
Medication at ICD implantation				
ACE inhibitor	177 (82)	120 (82)	57 (80)	.73
β-Blocker	177 (82)	121 (83)	56 (79)	.48
Statin	171 (79)	115 (79)	56 (79)	.99
Diuretic	106 (49)	71 (49)	35 (49)	.93
Amiodarone	39 (18)	29 (20)	10 (14)	.30
Digoxin	20 (9)	14 (10)	6 (9)	.79
ICD type				.81
Single-chamber	135 (62)	93 (64)	42 (59)	
Dual-chamber	59 (27)	38 (26)	21 (30)	
CRT-D	23 (11)	15 (10)	8 (11)	

Values are presented as mean ± SD or as n (%).

ACE = angiotensin-converting-enzyme; CABG = coronary artery bypass graft; CTO = chronic total occlusion; CRT-D = cardiac resynchronization therapy with defibrillator; GFR = glomerular filtration rate; ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention.

*>50% luminal stenosis.

coronary artery stenosis (>50%) or a history of percutaneous or surgical revascularization.

For analysis of the association between CTO and VA, 2 researchers (S.C.Y. and E.Y.) analyzed every patient in our cohort for the presence of CTO at the time of ICD implantation by evaluating the coronary angiograms and catheterization reports before ICD implantation. This study was approved by the institutional review board of the Erasmus Medical Center.

Definition of study variables

CTO was defined as complete vessel occlusion with TIMI 0 flow within the occluded segment and an estimated occlusion duration of ≥3 months.[4,5] Occluded vessels that were surgically or percutaneously revascularized and secondary occluded vessels (ie, diagonal branch, posterior descending artery, and posterolateral branches) were not classified as CTO in this study. *Multivessel disease* was defined as the presence of ≥2 coronary arteries with significant nonrevascularized lesions at the time of ICD implantation.

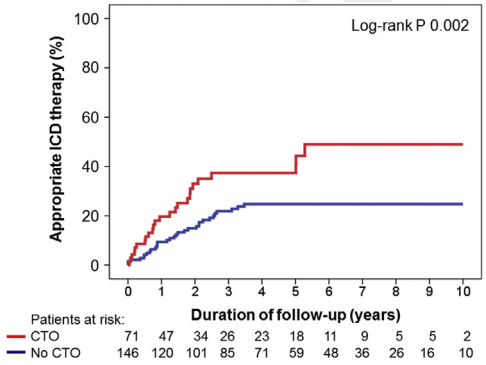

Figure 1 Cumulative event rate for appropriate ICD therapy in populations with CTO and without CTO. CTO = chronic total occlusion; ICD = implantable cardioverter-defibrillator.

Device programming

Devices were programmed with 2–3 consecutive zones (monitor zone, ventricular tachycardia zone, and ventricular fibrillation zone, usually 2 zones) with limits slightly varying per manufacturer. The cutoff rate for the VT zone was usually set at 171–182 beats/min, and the cutoff rate for the VF zone was usually set at 222–230 beats/min. In the VT zone, arrhythmias were initially treated with a series of antitachycardia pacing (ATP) bursts followed by shocks. In the VF zone, device shocks were the initial therapy or, when available, "ATP during charging." If a patient had a VA with cycle length lower than the initially programmed cutoff, another detection zone for slow VT was added. Conventional programming was used for detection duration. Detection in the VF zone was usually programmed at 18 of 24 intervals or a 2.5-second delay depending on the manufacturer. Detection in the VT zone was usually programmed at 16–20 intervals or a 5-second delay depending on the manufacturer.

Follow-up and end points

Patients were usually followed every 3–6 months. The follow-up visits included clinical assessment and device