



# Comparison of long-term outcomes of medical therapy and successful recanalisation for coronary chronic total occlusions in elderly patients: a report of 1,294 patients

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**Background:** Little is known about the long-term outcomes of medical therapy (MT) versus successful percutaneous coronary intervention (PCI) in elderly patients with coronary chronic total occlusions (CTOs).

**Methods:** There were 1,294 consecutive patients with 1,520 CTOs included (2007 to 2016) and were divided into the younger group (age <65 years; n=664, 51.3%) and the older group (age ≥65 years; n=630, 48.7%). In the older group, 630 patients were divided into MT group (n=421) and successful CTO-PCI group (n=209) according to the initial treatment strategy. In the younger group, they were divided into two groups: 379 patients in the MT group and 285 patients in the successful CTO-PCI group. We performed propensity score matching to minimize any selection bias. The primary end point was cardiac mortality. The secondary end point was major adverse cardiac event (MACE).

**Results:** After 3.6 (IQR, 2.1–5.0) years follow-up, no significant difference was observed between the MT and successful CTO-PCI groups in terms of cardiac mortality (MT *vs.* successful CTO-PCI: 9.3% *vs.* 5.0%, P=0.378) and MACE (28.3% *vs.* 15.1%, P=0.070) in the older group. After propensity score matching analysis (120 pairs), the risk of cardiac mortality (6.7% *vs.* 8.3%, P=0.624) was found to be comparable between the two groups. In the younger group, the occurrence of cardiac death (MT *vs.* successful CTO-PCI: 3.7% *vs.* 1.4%, P=0.072) was similar, whereas the MACE rate (27.7% *vs.* 17.9%, P=0.003) was significantly higher in MT group. After multivariate analysis, previous myocardial infarction (MI) [hazard ratio (HR) 1.70, 95% confidence interval (CI): 1.16–2.49, P=0.006], CTO in right coronary artery (HR 1.55, 95% CI: 1.07–2.25, P=0.020), multivessel disease (HR 2.02, 95% CI: 1.10–3.72, P=0.024) and calcification (HR 1.61, 95% CI: 1.07–2.42, P=0.023) were independent predictors of MACE in elderly.

**Conclusions:** In the treatment of elderly patients with CTOs, successful CTO-PCI compared with MT alone didn't reduce the risk of cardiac death or MACE.

**Keywords:** Chronic total occlusions (CTO); elderly; medical therapy (MT); percutaneous coronary intervention (PCI)

Submitted Sep 10, 2019. Accepted for publication Oct 21, 2019.

doi: 10.21037/cdt.2019.11.01

View this article at: <http://dx.doi.org/10.21037/cdt.2019.11.01>

## Introduction

Percutaneous coronary intervention (PCI) of coronary chronic total occlusion (CTO) has remained a challenge despite the great progress in devices and skills. CTOs have been identified in up to 18% of all patients referred for diagnostic angiography and the prevalence of CTO rises with age (1,2). Most observational studies have shown that successful CTO-PCI was associated with an improvement of symptoms, left ventricular function, quality of life, and an increase in long-term survival compared with failed CTO-PCI (3-6). However, only approximately 10–20.7% of CTOs are currently undergoing attempted CTO-PCI (1,7), mainly because CTO-PCI procedures may be with lower procedural success rate, a higher expense and risk of procedural complication when compared with non-CTO elective PCI (8,9). Indeed, a substantial portion of CTO patients are treated with medical therapy (MT) instead of PCI (10,11).

In recent decades, life expectancy is increasing and the proportion of elderly people in the general population is growing. Elderly patients have a greater incidence of complex coronary arterial disease and other co-morbidities and a higher risk of postoperative complications (12). Therefore, elderly patients with CTOs were often treated by MT alone, and several studies also reported older patients have the lowest rates of revascularization (13,14). However, to date, elderly patients are regularly excluded from registries and randomized trials relevant to CTO and the clinical outcomes of successful CTO-PCI compared with MT for elderly CTO patients are limited (13). Moreover, most studies compared the outcomes of patients with successful versus unsuccessful procedures, rather than comparisons of successful CTO-PCI versus MT (15). Therefore, we investigated the long-term clinical outcomes of successful CTO-PCI versus MT in elderly patients with CTOs excluding patients with failed CTO-PCI.

## Methods

### *Study population*

This was a retrospective observational study. We consecutively enrolled 1,534 patients with at least one CTO from 2007 to 2016 at our institute. Among the patients, those who underwent failed CTO-PCI were excluded, and 1,294 patients were finally included in this analysis. Patients were grouped into the older group ( $\geq 65$  years) and the younger group ( $< 65$  years). Each study

group was divided according to the treatment strategy selected for the CTO: optimal MT versus successful CTO-PCI. Initial revascularization or MT was selected according to the presence of symptoms, viability in the CTO related territory, co-morbidity or high risk for revascularization, and the suitability of the target distal vessel for revascularization (diameter  $> 2.5$  mm); Canadian Cardiovascular Society (CCS) angina class of the patients were obtained to assess angina burden; myocardial viability and ischemia were assessed by two-dimensional echocardiography, cardiac magnetic resonance (CMR) or single-photon emission computed tomography (SPECT), which were reported in our previous published articles (16,17). Medical records and coronary angiography were reviewed to give the clinical, angiographic and procedural characteristics. We acquired the follow-up data through medical chart reviews or telephone interviews. The study outcomes will not affect the future management of the patients. The institutional review board approved the present study. The patient's personal data have been secured.

### *Treatment strategy*

MT comprised the use of  $\beta$ -blockers, angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB), nitrate and statins in addition to antiplatelets. Coronary interventions were performed using contemporary techniques. All patients without contraindications were given a loading dose of 300 mg of aspirin, 600 mg of clopidogrel before PCI. For patients with more than one CTO, only one CTO vessel was targeted and no further attempt was made during the study period. The choice of opening for CTO artery was based on localization of the occlusion and ischemia/viability in the CTO related territory by operators. After intervention, patients received and maintained dual-antiplatelet therapy for at least 12 months. All patients underwent two-dimensional echocardiography.

### *Definitions and study outcomes*

A "CTO lesion" was defined as 100% stenosis with antegrade thrombolysis in myocardial infarction (MI) 0 flow for  $> 3$  months (3). Duration was estimated based on the onset of symptoms, history of MI consistent with the location of the occlusion or angiography or coronary CT. The "primary efficacy endpoint" was cardiac mortality.

The “secondary outcome” was the incidence of major adverse cardiac event (MACE), including cardiac death, MI, and target vessel revascularization (TVR). Definitions of PCI success, cardiac death, MI, TVR and chronic kidney disease (CKD) had been described in our previous published article (16).

### Statistical analysis

Continuous variables were presented as the mean  $\pm$  standard deviation or median and quartile (25–75%) and compared with the Student's *t*-test or Mann-Whitney U test. Categorical data were presented as percentages and were compared using the chi-square test or Fisher's exact test. The Kruskal-Wallis test was used to compare non-parametric data. Propensity matching was performed to minimize any selection bias and maintain a balance in covariates between the two groups. The propensity scores were calculated by the using of a multivariable logistic regression model. Event-free survival during follow-up was evaluated according to the Kaplan-Meier method and survival among groups was compared using the log-rank test. Cox proportional hazards methods were used to estimate the independent effect of multiple independent variables on the risk of MACE. All univariate variables with P values <0.05 were included in the multivariate model. Stata Version 15.1 (StataCorp LLC, TX, USA) was used for all statistical analyses. For all tests, a P value of <0.05 was considered statistically significant.

## Results

### Characteristics of the study patients

Of the 1,294 patients with 1,520 CTOs, the younger group (age <65 years) included 664 (51.3%) patients, and the older group (age  $\geq$ 65 years) included 630 (48.7%) patients. In the older group, they were divided into two groups: 421 in the MT group and 209 patients in the successful CTO-PCI group. In the younger group, they were divided into two groups: 379 patients in the MT group and 285 patients in the successful CTO-PCI group. There were five CTO-dedicated operators during this period.

The baseline characteristics of the study population are described in *Tables 1* and *2*. Compared to patients <65 years, patients in the older group included more women and fewer smokers, and had more hypertension, CKD, multivessel disease and calcification; and were less likely to

have familial history of coronary artery disease (CAD), with high SYNTAX score. As for medication, elderly patients were less often had taking  $\beta$ -blocker (*Table 1*).

In the younger group, male patients, smokers, previous MI, heart failure, CTO of left circumflex coronary artery (LCX), multivessel disease, blunt stump, calcification, high Japanese-chronic total occlusion (J-CTO) score and SYNTAX score were more prevalent in the MT group than in the successful CTO-PCI group, whereas high left ventricular ejection fraction (LVEF) and taking clopidogrel were more common in the successful CTO-PCI (*Table 1*).

In the older group, patients in the MT group were older and more often had CKD and heart failure compared to the successful CTO-PCI group. As for lesion characteristics, CTO of LCX, multivessel disease, blunt stump, calcification, high J-CTO score and SYNTAX score were more frequently in the MT group than in the successful CTO-PCI group. CTO of the left anterior descending coronary artery were presented more frequently in patients in the successful CTO-PCI group compared with patients in the MT group (*Table 2*).

There were 120 matched pairs of patients after undertaking propensity score matching. No statistically significant differences were observed in clinical and lesion characteristics in the propensity score matched population between the MT and successful CTO-PCI groups (*Table 2*).

As for procedural complications and in-hospital outcomes, there were no significant differences in the prevalence of coronary dissection, coronary perforation, major bleeding, in-hospital death, MI, stroke and ventricular fibrillation (*Table 3*).

### Clinical outcomes

The median overall follow-up duration was 3.6 (IQR, 2.1–5.0) years. The cardiac death rate was higher in the older patients than in the younger patients (older *vs.* younger: 8.6% *vs.* 2.7%,  $P < 0.001$ ), but the MACE rate (older *vs.* younger: 26.0% *vs.* 23.5%,  $P = 0.290$ ) was comparable between the two groups. In the younger group, the occurrence of cardiac death (successful CTO-PCI *vs.* MT: 1.4% *vs.* 3.7%,  $P = 0.072$ ) was similar between the two groups, whereas the MACE rate (successful CTO-PCI *vs.* MT: 17.9% *vs.* 27.7%,  $P = 0.003$ ) was significantly higher in MT group (*Table 4*) (*Figure 1*).

In the older group, no significant differences were observed between the successful CTO-PCI and MT groups in terms of cardiac death (successful CTO-PCI *vs.* MT:

**Table 1** Baseline clinical, angiographic and procedural characteristics of all patients aged <65 years and aged ≥65 years, and patients aged <65 years in the medical therapy and successful PCI groups

Variables	Total population			Age <65 years		
	Age <65 years (n=664)	Age ≥65 years (n=630)	P value	MT (n=379)	Successful PCI (n=285)	P value
Age, years	56.0±6.9	72.7±5.2	<0.001	55.7±7.1	56.6±6.7	0.361
Male, n (%)	555 (83.6)	435 (69.0)	<0.001	328 (86.5)	227 (79.6)	0.018
Smoking, n (%)	350 (52.7)	177 (28.1)	<0.001	214 (56.5)	136 (47.7)	0.025
Hypertension, n (%)	418 (63.0)	462 (73.3)	<0.001	235 (62.0)	183 (64.2)	0.560
Diabetes mellitus, n (%)	226 (34.0)	238 (37.8)	0.161	130 (34.3)	96 (33.7)	0.868
Dyslipidemia, n (%)	488 (73.5)	440 (69.8)	0.120	276 (72.8)	212 (74.4)	0.716
Familial history of CAD, n (%)	101 (15.2)	48 (7.6)	<0.001	60 (15.8)	41 (14.4)	0.608
Previous MI, n (%)	308 (46.4)	293 (46.5)	0.965	201 (53.0)	107 (37.5)	<0.001
CKD, n (%)	26 (4.0)	83 (13.2)	<0.001	18 (4.7)	8 (2.8)	0.189
Heart failure, n (%)	106 (16.0)	126 (20.0)	0.060	75 (19.8)	31 (10.9)	0.002
LVEF	52.6±9.5	52.9±8.6	0.013	50.8±10.2	55.1±7.8	<0.001
Baseline medication, n (%)						
Aspirin	651 (98.0)	618 (98.1)	0.945	369 (97.4)	282 (98.9)	0.144
Clopidogrel	617 (92.9)	583 (92.5)	0.791	343 (90.5)	274 (96.1)	0.005
Statin	637 (95.9)	595 (94.4)	0.210	363 (95.8)	274 (96.1)	0.815
β blocker	524 (78.9)	468 (74.3)	0.049	303 (79.9)	221 (77.5)	0.452
ACEI or ARB	411 (61.9)	419 (66.5)	0.084	238 (62.8)	173 (60.7)	0.582
One CTO lesion, n (%)	571 (86.0)	537 (85.2)	0.698	324 (85.5)	247 (86.7)	0.665
Two CTO lesions, n (%)	86 (13.0)	87 (13.8)	0.650	51 (13.5)	35 (12.3)	0.655
LAD, n (%)	238 (35.8)	221 (35.1)	0.774	127 (33.5)	111 (38.9)	0.148
LCX, n (%)	184 (27.7)	180 (28.6)	0.731	119 (31.4)	65 (22.8)	0.014
RCA, n (%)	319 (48.0)	306 (48.6)	0.849	186 (49.1)	133 (46.7)	0.538
Multivessel disease, n (%)	520 (78.3)	534 (84.8)	0.003	330 (87.1)	190 (66.7)	<0.001
Proximal or mid, CTO location, n (%)	505 (76.1)	475 (75.4)	0.783	284 (74.9)	221 (77.5)	0.435
Blunt stump, n (%)	290 (43.7)	309 (49.0)	0.053	195 (51.5)	95 (33.3)	<0.001
Calcification, n (%)	99 (14.9)	158 (25.1)	<0.001	71 (18.7)	28 (9.8)	0.001
Bending >45°, n (%)	309 (46.5)	277 (44.0)	0.354	180 (47.5)	129 (45.3)	0.568
Length ≥20 mm, n (%)	419 (63.1)	385 (61.1)	0.460	237 (64.5)	182 (63.9)	0.726
J-CTO score	1.65±1.14	1.76±1.24	0.139	1.78±1.12	1.48±1.06	<0.001
SYNTAX score	20.7±8.4	23.0±8.4	0.025	22.3±8.9	18.3±7.2	0.044
Contrast volume, mL	182±91	175±82	0.838	145±71	229±91	<0.001

Values are presented as the mean ± standard deviation or n (%). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; CAD, coronary artery disease; CKD, chronic kidney disease; CTO, chronic total occlusion; J-CTO, Japanese-chronic total occlusion; LAD, left ascending coronary artery; LCX, left circumflex coronary artery; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery.

**Table 2** Baseline clinical, angiographic and procedural characteristics of patients aged  $\geq 65$  years in the medical therapy and successful PCI groups

Variables	Total patients aged $\geq 65$ years			Propensity-matched patients aged $\geq 65$ years		
	Medical therapy (n=421)	Successful PCI (n=209)	P value	Medical therapy (n=120)	Successful PCI (n=120)	P value
Age, years	73.0 $\pm$ 5.3	71.9 $\pm$ 5.0	0.009	72.7 $\pm$ 4.7	71.9 $\pm$ 5.0	0.306
Male, n (%)	295 (70.1)	140 (67.0)	0.430	82 (68.3)	82 (68.3)	1.000
Smoking, n (%)	112 (26.6)	65 (31.1)	0.237	41 (34.2)	41 (34.2)	1.000
Hypertension, n (%)	313 (74.3)	149 (71.3)	0.414	90 (75.0)	85 (70.8)	0.468
Diabetes mellitus, n (%)	160 (38.0)	78 (37.3)	0.868	47 (39.2)	39 (32.5)	0.282
Dyslipidemia, n (%)	301 (71.5)	139 (66.5)	0.241	83 (69.2)	83 (69.2)	1.000
Familial history of CAD, n (%)	33 (7.8)	15 (7.2)	0.768	6 (5.0)	9 (7.5)	0.424
Previous MI, n (%)	205 (48.7)	88 (42.1)	0.119	52 (43.3)	52 (43.3)	1.000
CKD, n (%)	65 (15.4)	18 (8.7)	0.016	12 (10.0)	11 (9.2)	0.826
Heart failure, n (%)	95 (22.6)	31 (14.8)	0.022	24 (20.0)	14 (11.7)	0.077
LVEF	52.5 $\pm$ 8.9	53.5 $\pm$ 8.0	0.696	53.1 $\pm$ 8.8	53.9 $\pm$ 7.5	0.888
Baseline medication, n (%)						
Aspirin	414 (98.3)	204 (97.6)	0.528	118 (98.3)	118 (98.3)	1.000
Clopidogrel	387 (91.9)	196 (93.8)	0.404	112 (93.3)	117 (97.5)	0.123
Statin	395 (93.8)	200 (95.7)	0.335	110 (91.7)	115 (95.8)	0.182
$\beta$ blocker	309 (73.4)	159 (76.1)	0.469	95 (79.2)	98 (81.7)	0.626
ACEI or ARB	285 (67.7)	134 (64.1)	0.370	80 (66.7)	87 (72.5)	0.891
One CTO lesion, n (%)	361 (85.7)	176 (84.2)	0.608	102 (85.0)	101 (84.2)	0.858
Two CTO lesions, n (%)	55 (13.1)	32 (15.3)	0.441	18 (15.0)	18 (15.0)	1.000
LAD, n (%)	136 (32.3)	85 (40.7)	0.038	40 (33.3)	50 (41.7)	0.182
LCX, n (%)	137 (32.5)	43 (20.6)	0.002	38 (31.7)	29 (24.2)	0.195
RCA, n (%)	204 (48.5)	102 (48.8)	0.934	55 (45.8)	55 (45.8)	1.000
Multivessel disease, n (%)	377 (89.5)	157 (75.1)	<0.001	100 (83.3)	96 (80.0)	0.505
Proximal or mid, CTO location, n (%)	324 (77.0)	151 (72.2)	0.196	84 (70.0)	82 (68.3)	0.780
Blunt stump, n (%)	233 (55.3)	76 (36.4)	<0.001	46 (38.3)	48 (40.0)	0.791
Calcification, n (%)	119 (28.3)	39 (18.7)	0.009	29 (24.2)	23 (19.2)	0.347
Bending $>45^\circ$ , n (%)	188 (44.7)	89 (42.6)	0.622	46 (38.3)	43 (35.8)	0.688
length $\geq 20$ mm, n (%)	272 (64.6)	113 (54.1)	0.011	64 (53.3)	59 (49.2)	0.518
J-CTO score	1.90 $\pm$ 1.27	1.48 $\pm$ 1.11	0.002	1.48 $\pm$ 1.21	1.41 $\pm$ 1.10	1.000
SYNTAX score	24.1 $\pm$ 8.8	20.9 $\pm$ 7.0	0.019	22.7 $\pm$ 8.2	22.1 $\pm$ 7.6	0.568
Number of stents	0	1.33 $\pm$ 0.77	–	0	1.33 $\pm$ 0.76	–
Total stent length, mm	0	38.9 $\pm$ 22.7	–	0	39.0 $\pm$ 23.2	–

Values are presented as the mean  $\pm$  standard deviation or n (%). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; CAD, coronary artery disease; CKD, chronic kidney disease; CTO, chronic total occlusion; J-CTO, Japanese-chronic total occlusion; LAD, left ascending coronary artery; LCX, left circumflex coronary artery; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery.

**Table 3** Procedural complications and in-hospital outcomes, according to patients' age

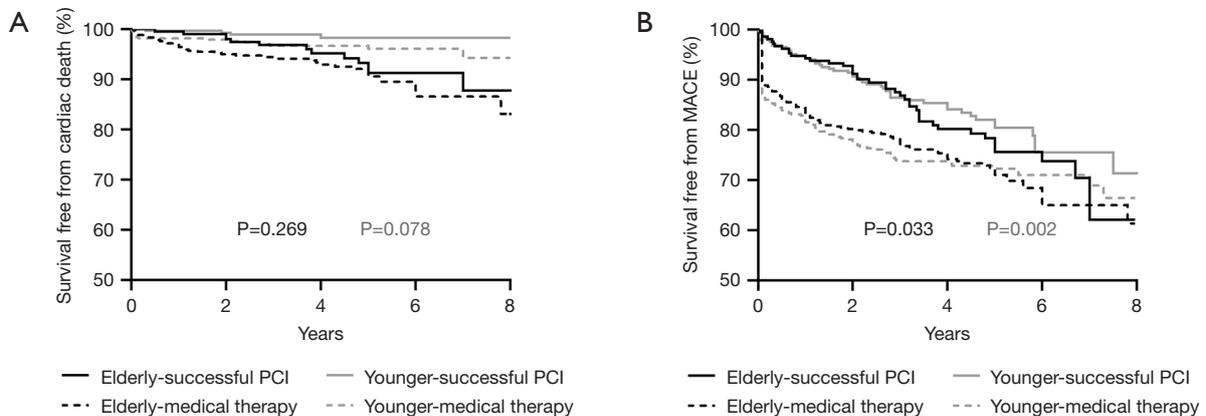
Events	Age <65 years (n=664)	Age ≥65 years (n=630)	P value
Coronary dissection, n (%)	13 (2.0)	6 (1.0)	0.133
Coronary perforation, n (%)	5 (0.8)	3 (0.5)	0.726
In-hospital death, n (%)	6 (0.9)	2 (0.3)	0.289
Major bleeding, n (%)	2 (0.3)	0 (0.0)	0.500
Myocardial infarction, n (%)	3 (0.5)	1 (0.2)	0.625
Stroke, n (%)	1 (0.2)	0 (0.0)	1.000
Ventricular fibrillation, n (%)	5 (0.8)	1 (0.2)	0.219

Values are presented as n (%).

**Table 4** Clinical outcomes in younger and elderly patients, and patients aged <65 years in medical therapy and successful PCI groups

Variables	Total patients			Patients aged <65 years		
	Age <65 years (n=664)	Age ≥65 years (n=630)	P value	Medical therapy (n=379)	Successful PCI (n=285)	P value
Cardiac death, %	18 (2.7)	54 (8.6)	<0.001	14 (3.7)	4 (1.4)	0.072
MI, %	46 (6.9)	49 (7.8)	0.558	27 (7.1)	19 (6.7)	0.818
TVR, %	113 (17.0)	88 (13.3)	0.130	75 (11.3)	38 (5.7)	0.028
MACE, %	156 (23.5)	164 (26.0)	0.290	105 (27.7)	51 (17.9)	0.003

Values are presented as n (%). MACE, major adverse cardiovascular events; MI, myocardial infarction; PCI, percutaneous coronary intervention; TVR, target-vessel revascularization.

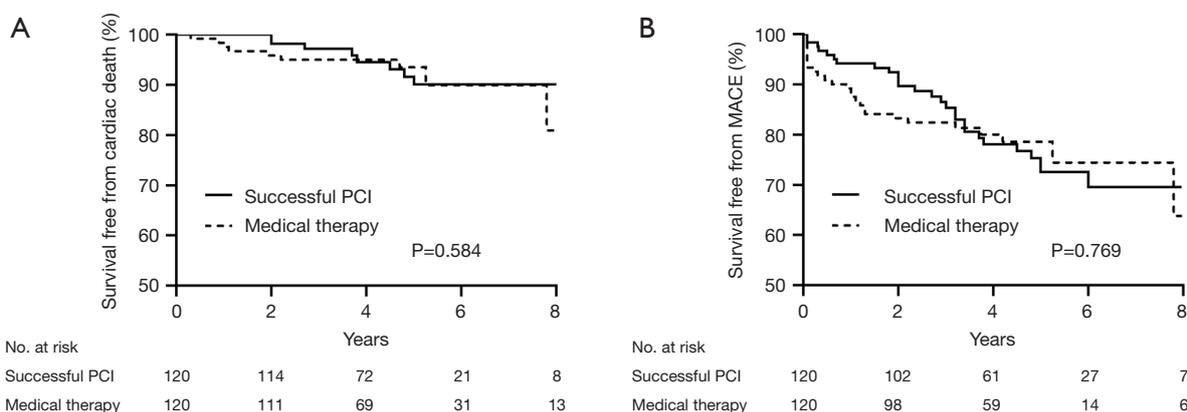


**Figure 1** Kaplan-Meier curves for cardiac death (A) and MACE (B) during follow-up for successful CTO-PCI versus medical therapy in younger and elderly patients. CTO, chronic total occlusion; MACE, major adverse cardiovascular events; PCI, percutaneous coronary intervention.

**Table 5** Clinical outcomes in total and propensity-matched patients aged  $\geq 65$  years in medical therapy and successful PCI groups

Variables	Total patients aged $\geq 65$ years			Propensity-matched patients aged $\geq 65$ years		
	Medical therapy (n=421)	Successful PCI (n=209)	P value	Medical therapy (n=120)	Successful PCI (n=120)	P value
Cardiac death, %	39 (9.3)	15 (5.0)	0.378	10 (8.3)	8 (6.7)	0.624
MI, %	38 (9.0)	11 (3.7)	0.097	9 (7.5)	8 (6.7)	0.801
TVR, %	61 (14.5)	27 (9.0)	0.592	17 (14.2)	17 (14.2)	1.000
MACE, %	119 (28.3)	45 (15.1)	0.070	29 (24.2)	28 (23.3)	0.879

Values are presented as n (%). MACE, major adverse cardiovascular events; MI, myocardial infarction; PCI, percutaneous coronary intervention; TVR, target-vessel revascularization.



**Figure 2** Kaplan-Meier curves for cardiac death (A) and MACE (B) during follow-up for successful CTO-PCI versus medical therapy in propensity-matched elderly patients. MACE, major adverse cardiovascular events; CTO, chronic total occlusion; PCI, percutaneous coronary intervention.

5.0% vs. 9.3%,  $P=0.378$ ) and MACE (15.1% vs. 28.3%,  $P=0.070$ ). In propensity-matched patients, no significant differences were observed between the two groups in terms of cardiac death (successful CTO-PCI vs. MT: 6.7% vs. 8.3%,  $P=0.624$ ) and MACE (23.3% vs. 24.2%,  $P=0.879$ ) (Table 5) (Figures 1 and 2).

No significant interaction existed between age and treatment strategy with regarding to cardiac mortality ( $P=0.292$ ). The cardiovascular survival benefit after successful CTO-PCI was similar in younger and older patients (Figure 3).

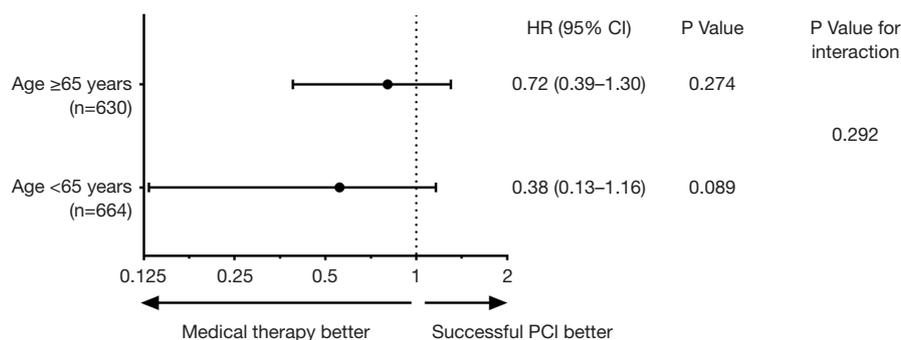
Table 6 shows independent predictors of MACE in elderly and younger patients. After multivariate analysis, previous MI [hazard ratio (HR) 1.70, 95% confidence interval (CI): 1.16–2.46,  $P=0.006$ ], right coronary artery (HR 1.55, 95% CI: 1.07–2.25,  $P=0.020$ ), multivessel disease (HR 2.02, 95% CI: 1.10–3.72,  $P=0.024$ ) and calcification

(HR 1.61, 95% CI: 1.07–2.42,  $P=0.023$ ) were independent predictors of MACE in the elderly.

## Discussion

We evaluated the long-term cardiovascular survival of MT versus successful CTO-PCI in elderly patients with CTOs. Several major findings emerge from this study: (I) elderly patients more often had CKD, calcification of CTO lesions and complex lesions; (II) successful CTO-PCI did not reduce cardiovascular mortality or MACE compared with MT alone in elderly patients with CTOs; (III) successful CTO-PCI was associated with a reduction in MACE in younger patients.

To the best of our knowledge, this is one of the largest observational studies reporting the effect of MT in unselected CTO patients aged  $\geq 65$  years. CTO is more



**Figure 3** Age subgroup analysis for cardiovascular mortality. CI, confidence interval(s); HR, hazard ratio; PCI, percutaneous coronary intervention.

**Table 6** Multivariable predictors of major adverse cardiovascular events in patients aged <65 years and aged ≥65 years

Variables	HR (95% CI)	P value
Patients aged ≥65 years		
Previous MI	1.70 (1.16-2.49)	0.006
RCA	1.55 (1.07-2.25)	0.020
Multivessel disease	2.02 (1.10-3.72)	0.024
Calcification	1.61 (1.07-2.42)	0.023
Age (per-year increment)	1.03 (0.99-1.07)	0.118
Heart failure	1.45 (0.93-2.27)	0.099
Patients aged <65 years		
Heart failure	1.98 (1.25-3.12)	0.003
Multivessel disease	1.70 (1.01-2.85)	0.046
Calcification	1.73 (1.08-2.79)	0.023
Diabetes mellitus	1.39 (0.95-2.03)	0.086
Two CTO lesions	1.53 (0.92-2.55)	0.103

CI, confidence interval(s); CTO, chronic total occlusion; HR, hazard ratio; MI, myocardial infarction; RCA, right coronary artery.

commonly seen in the older population, and these patients often have multiple comorbidities, including CKD, peripheral artery disease and stroke, which increase the risks associated with PCI (1,12,18). In addition, elderly patients are known to have more extensive CAD, tortuosity and severe calcification of vessels (19,20). This increases the complexity of PCI and the risk of periprocedural complications (21). Interventional cardiologists are often reluctant to perform complex CTO-PCI in elderly patients

because of the perception of poor clinical outcomes in this high-risk population even though the development of equipment and techniques has greatly improved the success rate of CTO-PCI. In our study, elderly patients indeed more often had CKD, calcification of CTO lesions and complex lesions compared with younger group, and these differences may result in a decreased CTO-PCI in elderly CTO patients.

In the Trial of Invasive versus Medical therapy in Elderly patients (TIME) trial conducted in patients with chronic stable angina, long-term survival, relief of angina and quality of life were similar for elderly patients assigned to invasive and medical treatment (22). Moreover, according to the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial, relief of angina and quality of life were also similar for elderly patients with chronic stable angina who were treated by MT and those who underwent PCI (23). Similarly, our study also suggested that PCI was not superior to MT in elderly patients with CTOs.

Most previous literature focused on the association of successful CTO revascularization with clinical outcome compared with failed CTO-PCI in patients who underwent PCI, and have shown a better efficacy in term of successful CTO-PCI (24,25). However, these studies did not include patients managed medically without a CTO-PCI attempt (15). Therefore, compared to previous studies, the strengths of our study may better reflect the clinical significance of PCI compared with MT alone in elderly patients with CTOs.

Until now, there is no widely accepted guideline or consensus on treating elderly CTO patients, and clinical outcome of CTO-PCI in this population is unknown.

In the present study, we performed the propensity score matching to maintain a balance in covariates and reduce potential confounding factors and we found that successful CTO-PCI did not reduce the prevalence of cardiac death or MACE, as compared with MT alone among elderly patients with CTOs, consistent with the finding of Lee and his colleagues (26). Our previous studies also suggested that successful CTO-PCI was not associated with reduced MACE or cardiac death compared with MT (27,28). Hence, aggressive CTO-PCI in elderly patients with coronary CTOs should be determined carefully considering multiple comorbidities, lesional complexities and operative complications.

### Study limitations

This study is limited by its observational nature, even though we have performed the propensity score matching to maintain a balance in covariates

### Conclusions

In the treatment of elderly patients with CTOs, successful CTO-PCI is not associated with reduced the risk of cardiac death or MACE compared with MT alone. Aggressive CTO-PCI should be considered carefully among this population. Well-designed, large randomized clinical trials are needed to support this finding.

### Acknowledgments

*Funding:* This work was supported by the China Cardiovascular Disease Alliance VG Youth Fund Project (No. 2017-CCA-VG-046), Beijing United Heart Foundation (No. BJUHFCOARF201801-02) and Beijing Lisheng Cardiovascular Health Foundation (No. LHJJ20158521).

### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The institutional review board approved the present study.

### References

1. Fefer P, Knudtson ML, Cheema AN, et al. Current perspectives on coronary chronic total occlusions: the Canadian Multicenter Chronic Total Occlusions registry. *J Am Coll Cardiol* 2012;59:991-7.
2. Grantham JA, Marso SP, Spertus J, et al. Chronic total occlusion angioplasty in the United States. *JACC Cardiovasc Interv* 2009;2:479-86.
3. Sianos G, Werner GS, Galassi AR, et al. Recanalisation of chronic total coronary occlusions: 2012 consensus document from the EuroCTO club. *EuroIntervention* 2012;8:139-45.
4. Sirnes PA, Myreng Y, Mølstaad P, et al. Improvement in left ventricular ejection fraction and wall motion after successful recanalization of chronic coronary occlusions. *Eur Heart J* 1998;19:273-81.
5. George S, Cockburn J, Clayton TC, et al. Long-term follow-up of elective chronic total coronary occlusion angioplasty: analysis from the U.K. Central Cardiac Audit Database. *J Am Coll Cardiol* 2014;64:235-43.
6. Kirk Christensen M, Freeman PF, Rasmussen JG, et al. Chronic total coronary occlusion: treatment results. *Scand Cardiovasc J* 2017;51:197-201.
7. Ladwiniec A, Allgar V, Thackray S, et al. Medical therapy, percutaneous coronary intervention and prognosis in patients with chronic total occlusions. *Heart* 2015;101:1907-14.
8. Rathore S, Matsuo H, Terashima M, et al. Procedural and in-hospital outcomes after percutaneous coronary intervention for chronic total occlusions of coronary arteries 2002 to 2008: impact of novel guidewire techniques. *JACC Cardiovasc Interv* 2009;2:489-97.
9. Gada H, Whitlow PL, Marwick TH. Establishing the cost-effectiveness of percutaneous coronary intervention for chronic total occlusion in stable angina: a decision-analytic model. *Heart* 2012;98:1790-7.
10. Azzalini L, Jolicœur EM, Pighi M, et al. Epidemiology, management strategies, and outcomes of patients with chronic total coronary occlusion. *Am J Cardiol* 2016;118:1128-35.
11. Tomasello SD, Boukhris M, Giubilato S, et al. Management strategies in patients affected by chronic total occlusions: results from the Italian Registry of Chronic Total Occlusions. *Eur Heart J* 2015;36:3189-98.
12. Formiga F, Ferrer A, Sanz H, et al. Patterns of comorbidity and multimorbidity in the oldest old: the Octabaix study. *Eur J Intern Med* 2013;24:40e44.

13. Zhang HP, Ai H, Zhao Y, et al. Effect of Chronic Total Occlusion Percutaneous Coronary Intervention on Clinical Outcomes in Elderly Patients. *Am J Med Sci* 2018;355:174-82.
14. Rosengren A, Wallentin L, Simoons M, et al. Age, clinical presentation, and outcome of acute coronary syndromes in the Euroheart acute coronary syndrome survey. *Eur Heart J* 2006;27:789-95.
15. Godino C, Bassanelli G, Economou FI, et al. Predictors of cardiac death in patients with coronary chronic total occlusion not revascularized by PCI. *Int J Cardiol* 2013;168:1402-9.
16. Guo L, Wu J, Zhong L, et al. Two-year clinical outcomes of medical therapy vs. revascularization for patients with coronary chronic total occlusion. *Hellenic J Cardiol* 2019. [Epub ahead of print].
17. Guo L, Lv HC, Zhong L, et al. Gender differences in long-term outcomes of medical therapy and successful percutaneous coronary intervention for coronary chronic total occlusions. *J Interv Cardiol* 2019. [Epub ahead of print].
18. Saltzman AJ, Stone GW, Claessen BE, et al. Long-term impact of chronic kidney disease in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention: The HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial. *JACC Cardiovasc Interv* 2011;4:1011-9.
19. Behan M, Dixon G, Haworth P, et al. PCI in octogenarians: Our centre 'real world' experience. *Age Ageing* 2009;38:469-73.
20. Hsu JT, Kyo E, Chu CM, et al. Impact of calcification length ratio on the intervention for chronic total occlusions. *Int J Cardiol* 2011;150:135-41.
21. André R, Dumonteil N, Lhermusier T, et al. In-hospital and long-term outcomes after percutaneous coronary intervention for chronic total occlusion in elderly patients: A consecutive, prospective, single-centre study. *Arch Cardiovasc Dis* 2016;109:13-21.
22. Pfisterer M. Long-term outcome in elderly patients with chronic angina managed invasively versus by optimized medical therapy: Four-year follow-up of the randomized Trial of Invasive versus Medical therapy in Elderly patients (TIME). *Circulation* 2004;110:1213-8.
23. Boden WE, O'Rourke RA, Teo KK, et al. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med* 2007;356:1503-16.
24. Tanaka Y, Takeshita S, Takahashi S, et al. Comparison of short- and long-term outcomes of percutaneous coronary intervention for chronic total occlusions between patients aged  $\geq 75$  years and those aged  $< 75$  years. *Am J Cardiol* 2013;112:761-6.
25. Hoebbers LP, Claessen BE, Dangas GD, et al. Long-term clinical outcomes after percutaneous coronary intervention for chronic total occlusions in elderly patients ( $\geq 75$  years): five-year outcomes from a 1,791 patient multi-national registry. *Catheter Cardiovasc Interv* 2013;82:85-92.
26. Lee SH, Yang JH, Choi SH, et al. Long-term clinical outcomes of medical therapy for coronary chronic total occlusions in elderly patients ( $\geq 75$  years). *Circ J* 2015;79:1780-6.
27. Guo L, Zhang SF, Wu J, et al. Successful recanalisation of coronary chronic total occlusions is not associated with improved cardiovascular survival compared with initial medical therapy. *Scand Cardiovasc J* 2019;53:305-11.
28. Guo L, Zhong L, Chen K, et al. Long-term clinical outcomes of optimal medical therapy vs. successful percutaneous coronary intervention for patients with coronary chronic total occlusions. *Hellenic J Cardiol* 2018;59:281-7.

**Cite this article as:** Guo L, Lv H, Zhong L, Wu J, Ding H, Xu J, Huang R. Comparison of long-term outcomes of medical therapy and successful recanalisation for coronary chronic total occlusions in elderly patients: a report of 1,294 patients. *Cardiovasc Diagn Ther* 2019;9(6):586-595. doi: 10.21037/cdt.2019.11.01