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CLINICAL INVESTIGATION

Chronic total occlusion percutaneous coronary intervention in octogenarians and nonagenarians

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Abstract

Objective: The outcomes of chronic total occlusion (CTO) percutaneous coronary intervention (PCI) in octogenarians and nonagenarians have received limited study.

Methods: We compared in-hospital outcomes of CTO PCI between patients ≥ 80 vs. < 80 -years-old in 6233 CTO PCIs performed between 2012 and 2020 at 33 U.S. and international centers.

Results: There were 415 octogenarians and nonagenarians in our study (7% of the total population). Compared with younger patients, octo- and nonagenarians were less likely to be men (73% vs. 83.2%, $p < 0.0001$) and more likely to have atrial fibrillation (27% vs. 12%, $p < 0.0001$) and prior coronary artery

bypass graft surgery (CABG) (43% vs. 29%, $p < 0.0001$). They were more likely to have CTOs with moderate/severe calcification (71% vs. 46%, $p < 0.0001$), but had similar mean J-CTO scores (2.5 ± 1.3 vs. 2.4 ± 1.3 , $p = 0.08$). They had lower technical and procedural success (82.2% vs. 86.3%, $p = 0.0201$; 80.3% vs. 84.8%, $p = 0.016$, respectively) and higher incidence of in-hospital major adverse cardiovascular events (3.4% vs. 1.8%, $p = 0.021$). On multivariable analysis PCI in octo- and nonagenarians was not independently associated with technical and procedural success or with in-hospital MACE.

Conclusion: CTO PCI is feasible in octo- and nonagenarians, although success rates are lower, and the risk of complications is higher compared with younger patients, likely related to more comorbidities and higher coronary lesion complexity.

KEYWORDS

chronic total occlusion, octogenarians, percutaneous coronary intervention

INTRODUCTION

Old age has been associated with worse outcomes after chronic total occlusion (CTO) percutaneous coronary intervention (PCI).^{1,2} The increasing life expectancy along with increasing prevalence of CTOs with older age,³ raises questions about the risk/benefit ratio of CTO PCI in older people. We examined CTO PCI characteristics and in-hospital outcomes in octogenarians and nonagenarians in a multicenter CTO PCI registry.

METHODS

Patient population

We analyzed the frequency, characteristics and in-hospital outcomes of CTO PCI performed in octogenarians and nonagenarians vs. younger patients in a multicenter registry. Data collection was performed both prospectively and retrospectively and was recorded in a dedicated online database (PROGRESS CTO: Prospective Global Registry for the Study of Chronic Total Occlusion Intervention, clinicaltrials.gov Identifier: NCT02061436). Study data were collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at Minneapolis Heart Institute Foundation.^{4,5} The study was approved by the institutional review board of each site and a waiver of informed consent was obtained.

Key Points

- CTO PCI in octogenarians and nonagenarians is associated with lower technical and procedural success rates and higher in-hospital MACE rates compared with younger patients.
- These outcomes are likely due to higher prevalence of baseline comorbidities and CTO lesion complexity.

Why Does this Paper Matter?

Octogenarians and nonagenarians represent a significant proportion of patients that undergo CTO PCI. Success rates are lower and in-hospital MACE rates are higher in ≥ 80 -years-old patients, likely because they have more baseline comorbidities and higher lesion complexity.

Definitions

Coronary CTOs were defined as coronary lesions with thrombolysis in myocardial infarction grade 0 flow of at least 3 months duration. Estimation of the duration of occlusion was clinical, based on the first onset of angina pectoris, prior history of myocardial infarction in the target vessel territory, or comparison with a prior angiogram. *Calcification* was assessed by angiography as mild (spots), moderate (involving $\leq 50\%$ of the reference lesion

TABLE 1 Baseline characteristics of the study patients classified according to patient age

	≥80-years-old N = 415	<80-years-old N = 5635	p-value
Men, n (%)	303 (73)	4665 (83.2)	<0.001
BMI (kg/m ²) ^a	27.4 [24.3–30]	30 [26.7–34.2]	<0.001
Ad hoc CTO PCI, n (%)	41 (11)	527 (10)	0.69
CAD presentation			0.36
Acute coronary syndrome, n (%)	108 (28.3)	1303 (24.7)	
Stable angina pectoris, n (%)	245 (64.3)	3502 (66.4)	
Other, n (%)	28 (7.4)	467 (8.9)	
Indication of CTO-PCI			0.0004
Symptom relief, n (%)	240 (69.4)	3282 (68.8)	
Acute coronary syndrome, n (%)	36 (10.4)	262 (5.5)	
Ischemia reduction, n (%)	29 (8.4)	604 (12.7)	
Reduced ejection fraction, n (%)	13 (3.8)	238 (5)	
Staged for complete revascularization stable angina, n (%)	13 (3.8)	250 (5.2)	
Other, n (%)	15 (4.3)	137 (2.9)	
Smoking			<0.001
Current/recent, n (within 1 year) (%)	20 (5)	1463 (26.9)	
Past, n (%)	207 (52)	2057 (37.9)	
Never, n (%)	171 (43)	1914 (35)	
Atrial fibrillation, n (%)	65 (27)	388 (11.8)	<0.001
Diabetes mellitus, n (%)	152 (37.4)	2341 (42.6)	0.04
Dyslipidemia, n (%)	382 (93.4)	4862 (87.8)	<0.001
Prior valve surgery/procedure, n (%)	24 (6.1)	108 (2)	<0.001
Hypertension, n (%)	383 (94)	4968 (89.8)	<0.001
Prior MI, n (%)	168 (43.1)	2455 (46.3)	0.22
Prior heart failure, n (%)	131 (33)	1577 (29.3)	0.11
Prior CABG, n (%)	174 (43.3)	1586 (28.9)	<0.001
Prior PCI, n (%)	254 (63.8)	3327 (61.1)	0.27
Ejection fraction, n (%) ^b	50 ± 13	50 ± 13	0.9
Cerebrovascular disease, n (%)	54 (13.3)	543 (10)	0.033
Stress test done within 90 days, n (%)	130 (35.7)	1956 (39.1)	0.19
Positive stress test results, n (%)	122 (93.9)	1751 (92.2)	0.78
Myocardial viability testing performed, n (%)	81 (24)	1413 (31.1)	0.0062
Viable myocardium at CTO perfused area, n (%)	66 (93%)	1219 (95%)	0.72
Peripheral arterial disease, n (%)	70 (17.3)	761 (14)	0.07
Chronic lung disease, n (%)	67 (16.6)	774 (14.3)	0.2
Anemia, n (%)	104 (39.9)	793 (21.2)	<0.0001
eGFR (1.73 ml/min/m ²) ^b	59 ± 19	73 ± 24	<0.0001

Abbreviations: BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CTO, chronic total occlusion; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention.

^aMedian [IQR].

^bMean ± SD.

diameter), and severe (involving >50% of the reference lesion diameter). Moderate *proximal vessel tortuosity* was defined as the presence of at least two bends >70° or one bend >90° and severe tortuosity as two bends >90° or one bend >120° in the CTO vessel. A procedure was defined as retrograde if an attempt was made to cross the lesion through a collateral vessel or bypass graft supplying the target vessel distal to the lesion; if not, the procedure was classified as antegrade-only. Antegrade dissection/reentry was defined as antegrade PCI during which a guidewire was intentionally introduced into the sub-intimal space proximal to the lesion, or reentry into the distal true lumen was attempted after intentional or inadvertent subintimal guidewire crossing.

Technical success was defined as successful CTO revascularization with achievement of <30% residual diameter stenosis within the treated segment and restoration of TIMI grade 3 antegrade flow. *Procedural success* was defined as the achievement of technical success without any in-hospital complications. *In-hospital major adverse cardiac events (MACE)* included any of the following adverse events prior to hospital discharge: death, myocardial infarction, recurrent symptoms requiring urgent repeat target vessel revascularization with PCI or coronary artery bypass graft surgery (CABG), tamponade requiring

either pericardiocentesis or surgery, and stroke. *Myocardial infarction (MI)* was defined using the Third Universal Definition of Myocardial Infarction (type 4a MI).⁶ The Japanese CTO (*J-CTO*) score was calculated as described by Morino et al,⁷ the *PROGRESS-CTO score* as described by Christopoulos et al,⁸ the *PROGRESS-CTO complications score* as described by Danek et al⁹ and the *EuroCTO (CASTLE) score* as described by Szijgyarto et al.¹⁰

Statistical analysis

Categorical variables were expressed as percentages and were compared using Pearson's chi-square test or Fisher's exact test. Continuous variables were presented as mean ± SD or median (interquartile range [IQR]) unless otherwise specified and were compared using the Student's *t*-test and one-way analysis of variance (ANOVA) for normally distributed variables and the Wilcoxon rank-sum test, or the Kruskal–Wallis test for nonparametric continuous variables, as appropriate. No additional analyses were performed to address missing data. All statistical analyses were performed with JMP 13.0 (SAS Institute, Cary, North Carolina). A *p*-value of 0.05 was considered statistically significant.

TABLE 2 Baseline angiographic characteristics of the study lesions classified according to patient age

	≥80-years-old N = 422	<80-years-old N = 5811	<i>p</i> -value
Target vessel			<0.001
RCA, <i>n</i> (%)	177 (43.5)	2997 (53.4)	
LAD, <i>n</i> (%)	147 (36.1)	1406 (25.1)	
LCX, <i>n</i> (%)	72 (17.7)	1104 (19.7)	
Other, <i>n</i> (%)	11 (2.7)	104 (1.9)	
Lesion length ^a	25 [15, 40]	25 [15, 40]	0.18
Vessel diameter ^a	3 [2.5–3]	3 [2.5–3]	0.57
Proximal cap ambiguity, <i>n</i> (%)	114 (31.2)	1849 (36.1)	0.06
Interventional collaterals, <i>n</i> (%)	190 (51.9)	2870 (57.4)	0.041
Moderate/severe calcification, <i>n</i> (%)	267 (70.5)	2421 (46)	<0.001
Moderate/severe proximal tortuosity, <i>n</i> (%)	117 (31)	1619 (30.9)	0.98
In-stent restenosis, <i>n</i> (%)	52 (12.9)	887 (16.1)	0.1
J-CTO score ^b	2.5 ± 1.3	2.4 ± 1.3	0.09
CASTLE score ^b	2.9 ± 1.3	1.9 ± 1.3	<0.0001
PROGRESS-CTO score ^b	1.3 ± 1	1.3 ± 1	0.27
PROGRESS-CTO complications score ^b	4.4 ± 1.2	2.7 ± 1.9	<0.001

^aMedian [IQR].

^bMean ± SD.

Abbreviations: CTO, chronic total occlusion; IQR, interquartile range; LAD, left anterior descending; LCX, circumflex; RCA, right coronary artery; SD, standard deviation.

Multivariable logistic regression was used to examine the association between age ≥ 80 years old and technical success, procedural success and in-hospital MACE after adjusting for confounding variables selected on univariable association ($p < 0.10$). Three separate multivariable analysis models were built based on the aforementioned endpoints.

RESULTS

Patient characteristics

Of the 6824 CTO PCIs included in the PROGRESS-CTO registry, patient age was missing in 581 cases (8.5%) who were excluded from the analysis. Between 2012 and 2019 6233 CTO PCIs were performed in 6050 patients at 33 U.S. and international centers, of whom 404 were

octogenarians and 11 were nonagenarians (415 patients: 7% of total population). The baseline characteristics of the study patients are summarized in Table 1. Compared with younger patients, octogenarians/nonagenarians were less likely to be men (73% vs. 83%, $p < 0.0001$), had lower median body mass index (BMI) (27 vs. 30, $p < 0.0001$), and were more likely to have atrial fibrillation (27% vs. 12%, $p < 0.001$) and prior coronary artery bypass graft surgery (CABG) (43% vs. 29%, $p < 0.001$).

Angiographic characteristics

The baseline angiographic characteristics of the study CTOs are listed in Table 2. The most common target vessel was the right coronary artery (RCA) (43.5% in the ≥ 80 group vs. 53.4% in the < 80 group, followed by the left anterior descending artery (LAD) (36.1% in the ≥ 80

TABLE 3 Technical aspects of the study procedures classified according to patient age

	≥ 80 -years-old <i>N</i> = 422	< 80 -years-old <i>N</i> = 5811	<i>p</i> -value
Dual injection, <i>n</i> (%)	246 (68.6)	3428 (68.8)	0.92
Radial access, <i>n</i> (%)	154 (37)	2878 (51)	< 0.0001
Femoral access, <i>n</i> (%)	353 (85.1)	4246 (75.4)	< 0.0001
Crossing strategies used			
AWE, <i>n</i> (%)	355 (84.1)	4938 (84.5)	0.64
ADR, <i>n</i> (%)	101 (23.9)	1418 (24.4)	0.83
Retrograde, <i>n</i> (%)	152 (36)	1855 (31.9)	0.08
First crossing strategy			
AWE, <i>n</i> (%)	333 (81)	4669 (81.3)	
ADR, <i>n</i> (%)	20 (4.9)	309 (5.4)	
Retrograde, <i>n</i> (%)	55 (13.4)	718 (12.5)	
Successful crossing strategy			
AWE, <i>n</i> (%)	214 (51.9)	2981 (52)	0.95
ADR, <i>n</i> (%)	59 (14.3)	845 (14.7)	
Retrograde, <i>n</i> (%)	78 (18.9)	1113 (19.4)	
IVUS use, <i>n</i> (%)	134 (41.4)	1864 (40)	0.64
OCT use, <i>n</i> (%)	9 (3)	84 (2)	0.21
Non-CTO PCI at the same time, <i>n</i> (%)	125 (32)	1326 (25.1)	0.002
Balloon uncrossable lesions, <i>n</i> (%)	53 (16.6)	457 (10.4)	< 0.001
Balloon undilatable lesions, <i>n</i> (%)	35 (15)	324 (9.4)	0.006
LVAD use, <i>n</i> (%)			
Prophylactic, <i>n</i> (%)	21 (5.8)	209 (4.3)	0.17
Urgent, <i>n</i> (%)	13 (61.9)	150 (71.7)	0.34
	9 (42.9)	41 (19.6)	0.0138
Technical success, <i>n</i> (%)	347 (82.2)	5013 (86.3)	0.021

Abbreviations: ADR, antegrade dissection re-entry; AWE, antegrade wire escalation; LVAD, left ventricular assist device.

group vs. 25.1% in the <80 group). CTOs in the ≥ 80 group were more likely to have moderate or severe calcification (71% vs 46%, $p < 0.001$).

Technical characteristics and procedural outcomes

The technical aspects of the procedures are summarized in Table 3. There was no difference in crossing strategies between the ≥ 80 year-old-group and < 80-year-old patients. Non-CTOs were treated at the same time in 32% of patients in the ≥ 80 group compared with 25% in the <80 group ($p = 0.018$). Octogenarians and nonagenarians were more likely to have balloon uncrossable (17% vs. 10%, $p < 0.001$) and balloon undilatable (15% vs. 9%, $p = 0.006$) lesions.

Procedural outcomes are summarized in Table 4. Compared with younger patients octogenarians and nonagenarians had lower technical success (82% vs. 86%, $p = 0.021$) and procedural success (80.3% vs. 84.8%, $p = 0.016$) and higher in-hospital MACE (3.4% vs. 1.8%, $p = 0.021$). Most in-hospital MACE events were cardiac tamponade requiring pericardiocentesis (Figure 1A). Compared with patients aged <80 years old, the ≥ 80 year-old-group had higher rates of perforation (8.2% vs. 4.5%, $p < 0.001$). The ratio of perforations requiring pericardiocentesis according to age group is shown in Figure 1B.

On multivariable analysis, age ≥ 80 -years-old was not associated with procedural success (adjusted odds ratio of 1.15; CI 95%, 0.86–1.54; $p = 0.34$) (Figure S1A), technical success (adjusted odds ratio of 1.18; CI 95%, 0.86–1.64; $p = 0.30$) (Figure S1B) or in-hospital MACE (adjusted odds ratio of 1.4 CI 95%, 0.49–4; $p = 0.5$) (Figure S1C).

DISCUSSION

The main findings of our study are that octo- and nonagenarians represented 7% of consecutive patients in whom CTO PCI was performed in a multicenter CTO PCI registry and had lower technical and procedural success rates and higher MACE rates compared with younger patients. On multivariable analysis, however, age ≥ 80 years, was not associated with lower procedural or technical success and higher rate of in-hospital MACE.

The lower CTO PCI success rate in octo- and nonagenarians is likely due to more complex anatomy, such as greater degree of calcification, a feature that hinders CTO crossing and increases the risk of complications, such as perforation. Moreover, operators are likely to stop crossing attempts earlier in very old patients due to fear of complications.¹¹ Indeed the risk of MACE was nearly twice higher in the ≥ 80 -year-old group, with higher risk of perforation, which is consistent with the higher

TABLE 4 Procedural outcomes classified according to patient age

	≥ 80 -years-old N = 415	<80-years-old N = 5635	p-value
Procedural success, n (%)	331 (80.3)	4741 (84.8)	0.016
In-hospital MACE, n (%)	14 (3.4)	100 (1.8)	0.021
Death, n (%)	2 (0.5)	19 (0.3)	0.65
Procedure time (min) ^a	133 [84, 196]	116 [75, 171]	<0.001
Contrast volume (ml) ^a	220 [157, 300]	225 [160, 305]	0.08
Patient AK dose (Gy) ^a	2.3 [1.2–3.8]	2.4 [1.3–4]	0.18
Fluoroscopy time (min) ^a	51 [29–77]	43 [26–69]	<0.001
Perforation, n (%)	34 (8.2)	252 (4.5)	<0.001
Perforation type			0.89
Ellis Class 1, n (%)	6 (25)	37 (18.8)	
Ellis Class 2, n (%)	9 (37.5)	80 (40.6)	
Ellis Class 3, n (%)	6 (25)	49 (24.9)	
Ellis Class 4, n (%)	3 (12.5)	31 (15.7)	
Vascular access site complication, n (%)	5 (1.2)	79 (1.4)	0.74
Bleeding, n (%)	4 (1)	42 (0.8)	0.62

Abbreviations: AK, Air Kerma; MACE, major adverse cardiovascular events.

^aMedian [IQR].

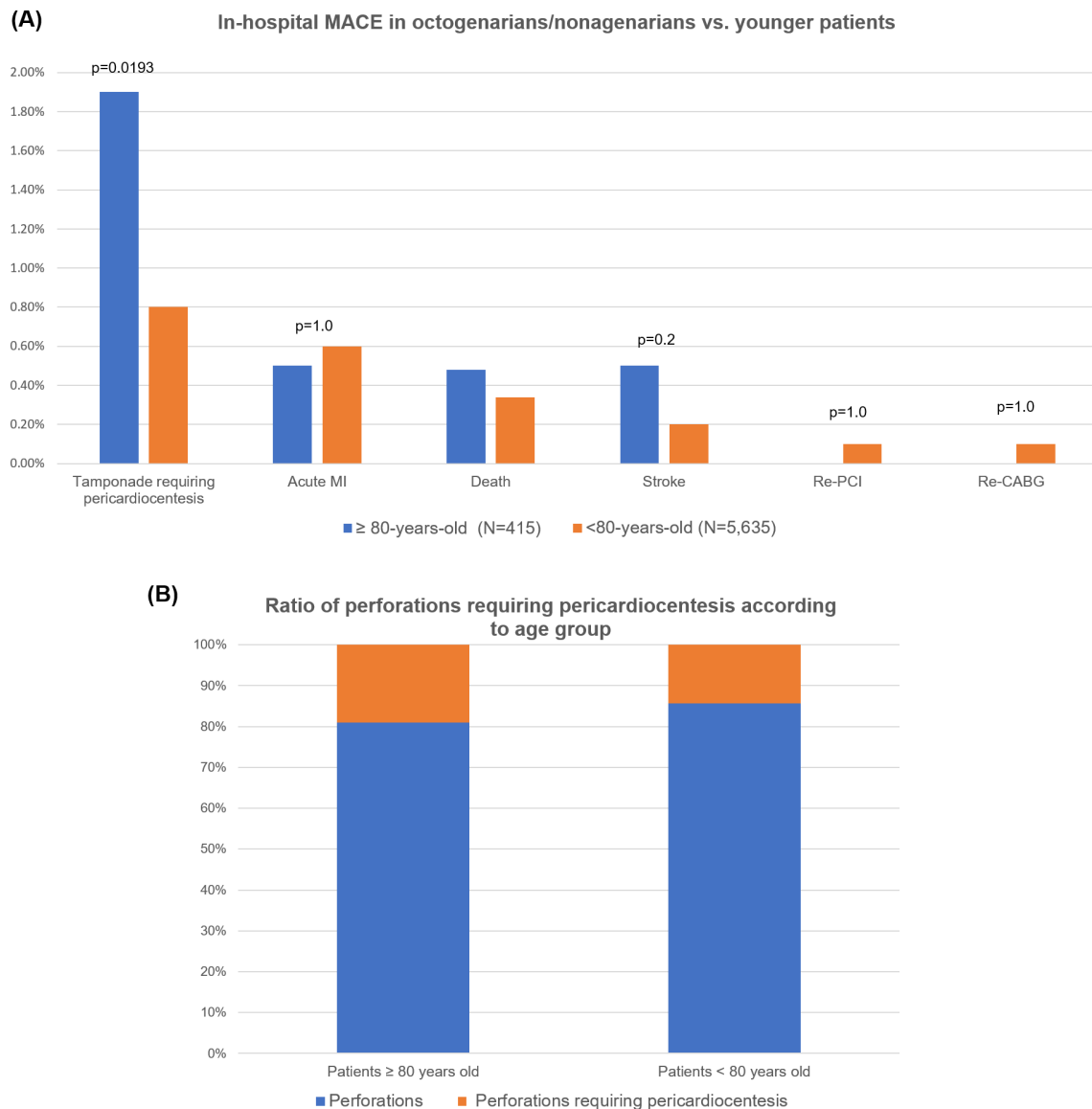


FIGURE 1 (A) In-hospital major adverse cardiovascular events (MACE) after chronic total occlusion (CTO) percutaneous coronary intervention (PCI) according to age. (B) Perforations and perforations requiring pericardiocentesis after chronic total occlusion (CTO) percutaneous coronary intervention (PCI) in octo- and nonagenarians

Progress-CTO complications score in this group (4.4 vs. 2.7, $p < 0.001$). However, most perforations (in both age groups) were Ellis classes 1 and 2 and did not result in MACE, a finding similar to the study by Hirai et al.¹² Older patients should ideally be treated at high volume, experienced CTO PCI centers to maximize the likelihood of success and minimize the risk of complications.¹³⁻¹⁵ Experienced operators are also more likely to successfully treat complications should they arise.^{16,17}

Previous studies

Elective PCI performed in octogenarians has been associated with worse outcomes.¹⁸ In a previous analysis of the PROGRESS-CTO registry, Karatasakis et al reported that

higher age (>65) was independently associated with technical failure and in-hospital MACE after CTO PCI.¹ Toma et al found no difference in in-hospital MACE after CTO PCI when comparing older versus younger patients and successful CTO PCI was independently associated with better long-term survival in older patients.¹⁹ Andre et al found a similar success rate for CTO-PCI in older patients (defined as ≥ 75 -years-old) as compared with younger patients.²⁰ Zhang et al reported that CTO PCI did not significantly improve long-term clinical outcomes in older patients (defined as ≥ 75 -years-old).²¹ Hoebbers et al reported similar success rates for CTO PCI in patients ≥ 75 -years-old and younger patients and found that successful revascularization was associated with lower MACE (composite of mortality, myocardial infarction, or coronary artery bypass graft surgery [CABG]) at

5-year follow-up.²² Tanaka et al found no difference in technical success (77% vs. 79%, $p = 0.66$) and in-hospital complications between patients ≥ 75 -years-old and younger patients.²³ Patients with successful PCI had significantly higher 3-year cardiac survival (97.6% vs 76.9%, $p = 0.005$) compared with patients with failed CTO PCI attempt. Strengths of our study compared with prior studies include large sample size, especially in the older individuals group and the definition of old as ≥ 80 -years old.

Limitations

Our study has limitations. First, it is an observational, retrospective study with all inherent limitations. Second, selection bias is possible. Third, frailty was not assessed. Fourth, our study only reported in-hospital outcomes without long-term follow-up. Fifth, potential improvement of quality of life after CTO PCI was not assessed. In older patients, quality of life measures such as angina pectoris relief may be more relevant than longevity. Fifth, there was no clinical event adjudication by a clinical events committee. Finally, all procedures were performed at high-volume, experienced PCI centers, limiting the generalizability of our findings to less experienced centers.

Conclusions

CTO PCI in octogenarians and nonagenarians is associated with lower technical and procedural success rates and higher in-hospital MACE rates compared with younger patients, likely due to higher prevalence of baseline comorbidities and higher CTO lesion complexity.

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Study data were collected and managed using Research Electronic Data Capture (REDCap) electronic data capture tools hosted at the Minneapolis Heart Institute Foundation (MHIF), Minneapolis, Minnesota. REDCap is a secure, web-based application designed to support data capture for research studies, providing: (1) an intuitive interface for validated data entry; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for importing data from external sources.

FINANCIAL DISCLOSURE

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CONFLICT OF INTEREST

Khaldoon Alaswad: received consulting fees from Terumo, Boston Scientific, has been an unpaid consultant for Abbott laboratories, has been a consultant for LivaNova and Teleflex and received speaker honoraria from CSI.

Ethisam Mahmoud: consultant for Abiomed, Medtronic, Boston Scientific, and chairs multiple Data, Safety and Monitoring Boards.

Farrouc A. Jaffer: sponsored research from Canon and Siemens; consultant for Boston Scientific, Abbott Vascular, Siemens, Philips, and Biotronik; equity interest, Intravascular imaging incorporated. Massachusetts General Hospital has a patent licensing arrangement with Canon, and FAJ has the right to receive royalties.

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All other authors: nothing to disclose.

AUTHOR CONTRIBUTIONS

Evangelia Vemmo: conception and design, acquisition of the data, analysis and interpretation of the data, drafting the manuscript, critical revision of the manuscript for important intellectual content, final approval of the manuscript.

Khaldoon Alaswad: conception and design, critical revision of the manuscript for important intellectual content and final approval of the version submitted.

Mitul Patel: conception and design, critical revision of the manuscript for important intellectual content and final approval of the version submitted.

Ethisam Mahmud: conception and design, critical revision of the manuscript for important intellectual content and final approval of the version submitted.

James W. Choi: conception and design, critical revision of the manuscript for important intellectual content and final approval of the version submitted.

Farouc A. Jaffer: conception and design, critical revision of the manuscript for important intellectual content and final approval of the version submitted.

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Phil Dattilo: conception and design, critical revision of the manuscript for important intellectual content and final approval of the version submitted.

Dimitri Karpaliotis: conception and design, critical revision of the manuscript for important intellectual content and final approval of the version submitted.

Oleg Krestyaninov: conception and design, critical revision of the manuscript for important intellectual content and final approval of the version submitted.

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The sponsors had no role in the design and performance of the study.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

Data S1 Multivariable logistic regression for technical, procedural success and in-hospital major adverse cardiovascular events (MACE).

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