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ORIGINAL RESEARCH

Complex Percutaneous Coronary Intervention Outcomes in Older Adults

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BACKGROUND: Complex percutaneous coronary intervention (PCI) is increasingly performed in older adults (age ≥75 years) with stable ischemic heart disease. However, little is known about clinical outcomes.

METHODS AND RESULTS: We derived a cohort of older adults undergoing elective PCI for stable ischemic heart disease across a large health system. We compared 12-month event-free survival (freedom from all-cause death, nonfatal myocardial infarction, stroke, and major bleeding), all-cause death, target lesion revascularization, and bleeding events for patients receiving complex versus noncomplex PCI and derived risk estimates with Cox regression models. We included 513 patients (mean age, 81±5 years). Patients receiving complex PCI versus noncomplex PCI did not significantly differ across a host of clinical characteristics including cardiovascular disease features, noncardiac comorbidities, guideline-directed medical therapy use, and frailty. Patients receiving complex PCI versus noncomplex PCI experienced worse event-free survival (80.4% versus 86.8%), which was not significant in adjusted analyses (hazard ratio [HR], 1.38 [95% CI, 0.88–2.16]). All-cause death at 1 year for patients undergoing complex PCI was nearly double that seen for patients receiving noncomplex PCI (10.2% versus 5.9%), and the risk was significant in models adjusted for clinical characteristics (HR, 1.97 [95% CI, 1.02–3.79]). Target lesion revascularization risk was lower for patients receiving complex PCI (2.2% versus 3.5%, adjusted HR), but bleeding events were not statistically different between groups (25.3% versus 20.5%; *P*=0.19).

CONCLUSIONS: Complex PCI in older adults with stable ischemic heart disease was associated with lower risk of target lesion revascularization but higher all-cause death compared with noncomplex PCI.

Key Words: complex percutaneous coronary intervention ■ coronary artery disease ■ older adults ■ revascularization

See Editorial by Davies et al.

National surveys project exponential growth of the older adult population during the 21st century.[1] Cardiovascular disease is the leading cause of death in older adults (age ≥75 years)[2] and coronary artery disease (CAD) is a substantial contributor to morbidity and death for this age group.[2,3] Distinct from younger patients with CAD, older adults with CAD have additional unique medical considerations, such as frailty, multimorbidity, and increased periprocedural risks, which make CAD management more challenging.[4] Therefore, further investigation into the optimal management of CAD in older adults represents a pressing need.

While coronary artery revascularization for older patients with acute coronary syndrome is often indicated to improve clinical outcomes, revascularization for stable ischemic heart disease (SIHD) is primarily indicated for patients with persistent symptoms despite optimal medical therapy or in select cases where anatomy and clinical characteristics suggest survival benefit (ie, left main disease).[5–7] Older adults frequently have more complex

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CLINICAL PERSPECTIVE

What Is New?

- In this detailed retrospective review of older adults receiving complex percutaneous coronary intervention for stable ischemic heart disease, we observed higher all-cause death in the complex percutaneous coronary intervention group compared with the noncomplex PCI group after adjusting for clinical characteristics and percutaneous coronary intervention features.

What Are the Clinical Implications?

- Further investigation of the safety of elective complex percutaneous coronary intervention in older adults is needed as these procedures become more common in the older adult population.

Nonstandard Abbreviations and Acronyms

EFS	event-free survival
SIHD	stable ischemic heart disease
STICH	Surgical Treatment in Ischemic Heart Failure
TLR	target lesion revascularization

coronary anatomy compared with younger patients with CAD; in addition, they are often deemed prohibitively high risk for surgical coronary artery bypass grafting (CABG) and have a higher risk aversion to CABG.[3,8–10] Complex percutaneous coronary intervention (PCI) for SIHD is thus becoming increasingly common in older adults.[8,11] Unfortunately, available data are limited to inform complex PCI in older adults, and a consistent definition of complex PCI is lacking.[12] A number of studies have evaluated the association between advanced chronologic age and increasing risk, reporting worse outcomes and higher rates of complications with PCI among older adults compared with younger populations[8,13–17]; however, no studies have specifically looked at how the risk of complex PCI compares with that of noncomplex PCI within the older adult population to more precisely determine the specific risk conferred by the increasing complexity of the intervention. Given the paucity of complex PCI data in this population, coupled with the increasing prevalence in clinical practice, focused investigations of complex interventions in older adults are needed to elucidate whether the benefits in this at-risk population outweigh the risks of intervention.[18]

In this study of complex PCI in older adults, we examine death, major cardiovascular events, target lesion revascularization (TLR), and bleeding at 1 year in older adults undergoing complex versus noncomplex PCI for SIHD. We propose a definition of complex PCI based on procedures with inherent technical risk, such as bifurcation lesions and atherectomy, though we secondarily examine complex PCI based on stent and lesion length numeric cutoffs as has been done previously by other groups.[18–20] Finally, we compare bleeding events between patients who underwent complex and noncomplex PCI and derive risk estimates for each outcome in analyses adjusted for patient demographics and clinical characteristics.

METHODS

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Data Source

We collected data on all older adults (defined as aged ≥75 years) undergoing PCI from June 25, 2018, to March 30, 2021, at a large academic health system composed of 5 network hospitals. All variables were manually extracted from the electronic medical record by the study authors (J.H. and S.W.) with discrepancies resolved by the senior author (M.N.). Data were obtained from surrounding area hospitals that use the same electronic medical record system (Epic; Epic Systems, Verona, WI) to maximize capture of all outcomes via Care Everywhere. Outside records were specifically examined for cardiology outpatient notes and hospital admissions.

Study Population

Older adults (aged ≥75 years) undergoing elective PCI for SIHD during the study period were included. The following patients were excluded: (1) patients undergoing emergent or urgent PCI; and (2) patients lost to follow-up (defined as complete loss of contact with the medical system before the end of the study period) within 1 year of the index revascularization (which includes the initial PCI and any subsequent staged PCI, if applicable; ie, the clock starts at the staged procedure, if performed). Patients undergoing elective PCI following myocardial infarction (MI), for example, as a staged procedure to emergent or urgent revascularization, were included.

Complex PCI Definition

We defined complex PCI as any PCI including a procedure or lesion that may carry inherently elevated risk of complications or PCI failure. As is typically done in the literature, we make a distinction between complex PCI (which is procedure-focused) and high-risk PCI (which is patient-focused) and do not include

heart failure or other high-risk features in the definition that do not necessarily create technical complexity.[21] Procedure-based criteria included multivessel PCI (≥3 vessels [including branches] or ≥2 vessels if including an unprotected left main coronary artery, or proximal left anterior descending artery), intervention on an unprotected left main coronary artery, saphenous vein graft, bifurcation (defined as at least 1 intervention [angioplasty or stenting] to each branch at a bifurcation; simple provisional wiring of the side branch did not qualify), or PCI involving atherectomy (including laser and lithotripsy). Lesion-based criteria included intervention on a lesion with severe calcification (as judged by the operator) or a chronic total occlusion. Cases referred for CABG, as mentioned in cardiology notes, where the patient refused or was deemed ineligible for CABG were also considered complex PCI. Noncomplex PCI was defined as any procedure that did not meet the definition for complex PCI.

There is no uniform definition of complex PCI in the literature.[12] Some authors have used a definition of complex PCI that relies heavily on the number and length of the lesions and stents.[18–20] For comparability, we performed a sensitivity analysis using an alternative definition of complex PCI defined as multivessel PCI, ≥3 stents implanted, ≥3 lesions treated, total stent length >60 mm, total lesion length >30 mm, or bifurcation or chronic total occlusion intervention.[18–20]

Study Covariates

We identified the following patient characteristics as possibly associated with complex PCI outcomes: (1) demographics (age, sex, race, marital status); (2) body mass index; (3) cardiovascular characteristics and risk factors (hypertension, hyperlipidemia, diabetes, smoking status [never, prior, or current smoker; smoking and marital status recorded as documented at time of data collection], prior MI, PCI, CABG, or cerebrovascular accident [including ischemic and hemorrhagic stroke and transient ischemic attack], history of heart failure [preserved, midrange, or reduced ejection fraction], peripheral artery disease, severe valvular disease, atrial fibrillation, or chronic kidney disease [with or without dialysis dependence]); (4) other comorbidities (chronic obstructive pulmonary disease, malignancy [excluding nonmelanoma skin cancer], cirrhosis, alcohol dependence, anemia, falls, gastrointestinal bleeding, depression); (5) complete guideline-directed medical therapy PCI (defined as prescriptions on discharge for 1 of each of the following drugs [any drug within the classes listed was acceptable]: aspirin [or anticoagulation], P2Y12 inhibitor, high-intensity statin, beta-blocker, renin-angiotensin system blocker [either angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, or angiotensin receptor–neprilysin inhibitor]); and (6) frailty variables (specifically the home functioning variables used in the National Cardiovascular Data Registry: gait [0=independent, 1=walks with assistance, 2=wheelchair bound], cognition [0=normal, 1=mild impairment, 2=dementia], and dependence for activities or instrumental activities of daily living [0=independent, 1=partially dependent, 2=fully dependent]; scores in each of the 3 domains were added into a cumulative frailty index ranging from 0 to 6).[22]

The following PCI-related covariates were also extracted: (1) intravascular imaging (intravascular ultrasound or optical coherence tomography), (2) fractional flow reserve (including instantaneous wave-free ratio; for lesions intervened upon), (3) brachytherapy, and (4) bivalirudin or glycoprotein IIb/IIIa inhibitor use.

Finally, the following physician and system covariates were extracted: (1) physician performing the PCI and (2) network-member hospital where the PCI was performed. Physician operators were classified according to their complex PCI volume, specifically as either high- or low-volume operators (high-volume=in the top 10% of complex PCI operators by volume). PCI procedures captured in this data set were performed at only 3 of the 5 network-member hospitals (designated as sites 1, 2, and 3).

Study Outcomes

The primary end point was event-free survival (EFS) at 12 months following index revascularization, defined as freedom from all-cause death, nonfatal MI, nonfatal stroke, and major bleeding (bleeding was defined according to the Bleeding Academic Research Consortium bleeding criteria[23]; all PCI periprocedural and post-PCI bleeding events were eligible; Bleeding Academic Research Consortium stage 3 or 5 was considered major bleeding[24]). Major bleeding was included in the EFS composite, as older adults are at particularly high risk for major bleeds following PCI, which carry a profound clinical impact in this population.[24] Secondary outcomes included 12-month all-cause death, TLR (defined as intervention on the lesion treated during the index PCI within the subsequent 12 months), and all bleeding events (Bleeding Academic Research Consortium 1–3 and 5). Nonfatal MI, nonfatal stroke, and cardiovascular death (defined as death from any cardiac cause, including cardiac arrest)[25] were also described separately from the EFS composite. Patients without a clearly documented cause of death were not included in the cardiovascular death analysis. Cause of death was determined by physician review of all clinical documentation around the time of death for any information relevant to the cause of death. All outcomes were manually extracted from physician notes and other documentation within the medical record and did not rely on billing codes.

Statistical Analysis

Patients were divided into 2 groups: those receiving complex PCI and those receiving noncomplex PCI. We derived descriptive statistics for each study group. Patient characteristics between complex and noncomplex PCI groups were compared using the Mann–Whitney *U* test for numeric variables and the chi-square test for categorical variables.

For the primary EFS end point, we developed Kaplan–Meier curves for both the complex and noncomplex PCI groups. We then constructed multivariable Cox proportional hazards regression models using forward variable selection with EFS as the dependent. Forward selection criteria were based on optimizing the model according to the Akaike information criterion. Candidate variables for the forward selection were any covariates identified by the authors as possible confounders of the association between EFS and complex PCI group. The candidate independent variables for the forward selection procedure included the exposure (PCI group), baseline characteristics (patient demographics, comorbidities, frailty scores, complete guideline-directed medical therapy following PCI) and PCI features (use of any intravascular imaging, fractional flow reserve/instantaneous wave-free ratio, bivalirudin, glycoprotein IIb/IIIa inhibitor, or brachytherapy as well as operator volume and hospital network site). The factor levels used in the model can be found where these variables are displayed in Tables 1 and 2. Risk estimates for all-cause death were derived from the models for patients receiving complex PCI as compared with the reference noncomplex PCI group. We repeated these procedures for the other end points. Of note, forward selection was performed separately for each individual model.

We evaluated the association between the PCI group and the secondary outcome of any bleeding event within 1 year after PCI by constructing hierarchical binary logistic regression models with bleeding as the dependent variable and PCI group as the independent variable. Odds ratios were derived from the models. Anticoagulation, dual-antiplatelet therapy, triple therapy (aspirin, P2Y12 inhibitor, and anticoagulation), and access location (femoral or radial) were included as additional covariates in the forward selection procedure in models with bleeding events as an outcome (either alone or as part of a composite). We repeated the above procedures in a sensitivity analysis using the alternative definition of complex PCI.

Scaled Schoenfeld residuals were computed for each unadjusted Cox model to test the proportional hazards assumption, which was supported in every model. Residual plots for select outcomes are displayed in Figure S1.

The level of statistical significance was set at 0.05. All analyses were 2-sided and performed using R 4.0.3 (R Project for Statistical Computing, Vienna, Austria). The study was deemed exempt by the Yale University Institutional Review Board. Given the study's exempt status and retrospective nature, subjects were not contacted to obtain informed consent.

RESULTS

During the study period, 574 older adults received elective PCI for SIHD. After excluding 61 patients lost to follow-up, 513 patients (mean age, 81.3±4.6 years) were included in the final cohort, 56.1% (N=288) of whom underwent noncomplex PCI versus 43.9% (N=225) who underwent complex PCI. There was no difference in the indications for PCI between groups (*P*=0.5), with the most common indication being symptomatic control (66.1% of total cohort). A small minority of patients (3.7%; N=19) underwent elective PCI as a staged procedure to recent acute coronary syndrome intervention, which was not statistically different between groups (3.5 versus 4.1% for complex PCI; *P*=0.57), and 7.8% (N=40) underwent 2 elective PCI procedures as a staged revascularization. Nineteen patients (3.7%) had a failed or partially failed PCI in which ≥1 target lesions were not successfully revascularized, and only 7 (1.4%) patients received mechanical support during the procedure. There was a total of 39 operators performing PCI in older adults across the hospital network during the study period, only 4 of whom did not perform any complex PCI during the study period. Patients receiving complex versus noncomplex PCI were not statistically different across the vast majority of baseline (Table 1) and PCI characteristics (Table 2).

Event-Free Survival

The EFS at 12 months for the entire cohort was 84.0% (95% CI, 80.9–87.2%). Patients receiving noncomplex versus complex PCI had higher EFS (86.8% versus 80.4%, respectively; Figure 1); however, there was no statistically significant association between PCI group and EFS after adjustment for patient demographics, clinical characteristics, including frailty and pharmacotherapy, and PCI features (hazard ratio [HR], 1.38 [95% CI, 0.88–2.16]; Table 3).

The 12-month risk of nonfatal MI was 1.4% (95% CI, 0.4–2.4%) and of nonfatal stroke was 2.7% (1.3%–4.1%) for the entire cohort. There was no statistically significant difference between PCI groups in the risk of nonfatal MI or nonfatal stroke (Table 3).

All-Cause Death

All-cause death for the entire cohort was 7.8% (95% CI, 5.4%–10.1%) at 12 months following index PCI.

Table 1. Baseline Characteristics

	Total cohort	Noncomplex PCI	Complex PCI	
	N=513	N=288	N=225	*P* value
Sociodemographics				
Age, y				0.42
Median (interquartile range)	81.0 (77.0–84.0)	81.1 (4.46)	80.0 (77.0–85.0)	
Sex, n (%)				0.01
Female	142 (27.7)	94 (32.6)	48 (21.3)	
Race, n (%)				0.39
Non-White	19 (3.70)	13 (4.5)	6 (2.7)	
Marital status, n (%)				0.01
Married	308 (60.0)	159 (55.2)	149 (66.2)	
Cardiovascular disease and risk factors				
Body mass index				0.81
Median (Interquartile range)	28.0 (25.0–32.0)	28.0 (25.0–32.0)	28.0 (25.0–31.0)	
Smoking status, n (%)				0.65
Prior or current	340 (66.3)	188 (65.3)	152 (67.6)	
Hypertension, n (%)				0.72
Yes	451 (87.9)	255 (88.5)	196 (87.1)	
Hyperlipidemia, n (%)				0.54
Yes	437 (86.7)	244 (85.6)	193 (88.1)	
Diabetes, n (%)				0.87
Yes	175 (34.7)	97 (34.0)	78 (35.6)	
Chronic kidney disease, n (%)				0.95
Yes	93 (18.1)	53 (18.4)	40 (17.8)	
Dialysis, n (%)				0.48
Yes	8 (1.6)	3 (1.0)	5 (2.2)	
Prior myocardial infarction, n (%)				0.13
Yes	102 (19.9)	50 (17.4)	52 (23.1)	
Prior PCI, n (%)				0.39
Yes	192 (37.4)	113 (39.2)	79 (35.1)	
Prior coronary bypass surgery, n (%)				<0.001
Yes	108 (21.4)	45 (15.8)	63 (28.8)	
Prior cerebrovascular accident, n (%)				0.54
Yes	68 (13.3)	41 (14.2)	27 (12.0)	
Peripheral artery disease, n (%)				0.50
Yes	139 (27.1)	74 (25.7)	65 (28.9)	
Heart failure, n (%)				0.09
Preserved, midrange, or reduced	148 (28.9)	74 (25.7)	74 (32.9)	
Severe valvular disease, n (%)				0.33
Yes	107 (20.9)	65 (22.6)	42 (18.7)	
Atrial fibrillation, n (%)				0.76
Yes	130 (25.3)	75 (26.0)	55 (24.4)	
Comorbidities				
Chronic obstructive lung disease, n (%)				0.81
Yes	63 (12.3)	34 (11.8)	29 (12.9)	
Cirrhosis, n (%)				0.37
Yes	2 (0.4)	0 (0.0)	2 (0.9)	

(*Continued*)

Table 1. Continued

	Total cohort	Noncomplex PCI	Complex PCI	
	N=513	N=288	N=225	*P* value
Malignancy, n (%)				0.25
Yes	112 (21.8)	57 (19.8)	55 (24.4)	
Anemia, n (%)				0.15
Yes	38 (7.4)	26 (9.0)	12 (5.3)	
Prior gastrointestinal bleed, n (%)				0.43
Yes	31 (6.0)	20 (6.9)	11 (4.9)	
Alcohol use disorder, n (%)				1.00
Yes	9 (1.8)	5 (1.7)	4 (1.8)	
Depression, n (%)				0.55
Yes	37 (7.2)	23 (8.0)	14 (6.2)	
Geriatric comorbidities				
Dementia, n (%)				0.24
Yes	5 (1.0)	1 (0.3)	4 (1.8)	
Frailty score, n (%)				0.88
0	365 (71.2)	204 (70.8)	161 (71.6)	
1	116 (22.6)	67 (23.3)	49 (21.8)	
2–6	32 (6.2)	17 (5.9)	15 (6.7)	
Pharmacotherapy following PCI, n (%)				
Full guideline-directed therapy				0.15
Yes	133 (26.0)	67 (23.3)	66 (29.3)	
Aspirin				0.49
Yes	425 (82.8)	242 (84.0)	183 (81.3)	
Anticoagulation				1.00
DOAC or warfarin	126 (24.6)	71 (24.7)	55 (24.4)	
High-intensity statin				0.60
Yes	284 (55.4)	156 (54.2)	128 (56.9)	
Renin system blockade				0.60
Yes	300 (58.5)	165 (57.3)	135 (60.0)	
Beta blocker				0.56
Yes	373 (72.7)	206 (71.5)	167 (74.2)	
P2Y12 inhibitor				0.06
Yes	490 (95.5)	280 (97.2)	210 (93.3)	
Dual antiplatelet therapy				0.64
Yes	360 (70.2)	205 (71.2)	155 (68.9)	
Triple therapy				0.30
Yes	55 (10.7)	35 (12.2)	20 (8.9)	

DOAC indicates direct oral anticoagulant; and PCI, percutaneous coronary intervention.

Patients receiving complex PCI had higher all-cause death at 12 months compared with patients receiving noncomplex PCI (10.2% versus 5.9%). We observed a higher risk of all-cause death for patients undergoing complex PCI in adjusted regression models (HR, 1.97 [95% CI, 1.02–3.79; Table 3). Kaplan–Meier curves are displayed in Figure 2 and demonstrate early divergence between the 2 groups.

There was no significant difference in the risk of cardiovascular death between patients receiving complex versus noncomplex PCI (1.7% versus 1.8%, respectively; Table 3). Five patients did not have a clearly documented cause of death.

Target Lesion Revascularization

Overall TLR was low at 2.9% (95% CI, 1.5%–4.4%) and not statistically different between the complex PCI and noncomplex PCI groups in unadjusted models (2.2% versus 3.5%, respectively; unadjusted HR, 0.64 [95% CI, 0.22–1.87]; Figure 2). However, complex PCI patients had a lower 12-month risk of TLR after adjusting

Table 2. PCI Characteristics

	Total cohort, n (%)	Noncomplex PCI, n (%)	Complex PCI, n (%)	
	N=504	N=285	N=219	*P* value
Indication				0.47
Symptomatic control	335 (66.1)	188 (65.7)	147 (66.5)	
Asymptomatic, noninvasive Findings	15 (3.0)	9 (3.1)	6 (2.7)	
Asymptomatic, before surgery	1 (0.2)	1 (0.4)	0 (0.0)	
Before valvular intervention	108 (21.3)	66 (23.1)	42 (19.0)	
Heart failure	29 (5.7)	12 (4.2)	17 (7.7)	
Recent acute coronary syndrome	19 (3.7)	10 (3.5)	9 (4.1)	
Complex PCI breakdown				
Unprotected left main	18 (3.5)	…	18 (8.0)	
Multivessel intervention	71 (13.8)	…	71 (31.6)	
Bifurcation intervention	59 (11.5)	…	59 (26.2)	
Saphenous vein graft intervention	35 (6.8)	…	35 (15.1)	
Atherectomy performed	42 (8.2)	…	42 (18.7)	
Severely calcified lesion	101 (19.7)	…	101 (44.9)	
Chronic total occlusion	38 (7.4)	…	38 (16.9)	
Declined for CABG	5 (1.0)	…	5 (2.2)	
Vessels				
Protected left main	15 (2.9)	5 (1.7)	10 (4.4)	0.12
Ramus intermedius	9 (1.8)	4 (1.4)	5 (2.2)	0.71
Left anterior descending	253 (49.3)	128 (44.4)	125 (55.6)	0.02
Proximal left anterior descending	135 (26.3)	58 (20.1)	77 (34.2)	<0.001
Diagonal branch	57 (11.1)	19 (6.6)	38 (16.9)	<0.001
Left circumflex	106 (20.6)	48 (16.7)	58 (25.8)	0.02
Obtuse marginal branch	53 (10.3)	25 (8.7)	28 (12.4)	0.21
Right coronary	156 (30.4)	88 (30.6)	68 (30.2)	1.00
Posterior descending	15 (2.9)	8 (2.8)	7 (3.1)	1.00
Posterolateral	6 (1.2)	4 (1.4)	2 (0.9)	0.91
Left internal mammary artery graft	2 (0.4)	2 (0.7)	0 (0.0)	0.59
PCI strategies				
Fractional flow reserve				0.04
Yes	77 (15.0)	52 (18.1)	25 (11.1)	
Any intravascular imaging				<0.001
Yes	125 (24.4)	47 (16.3)	78 (34.7)	
Brachytherapy				0.23
Yes	7 (1.4)	6 (2.1)	1 (0.4)	
Periprocedural medications				
Bivalirudin				0.06
Yes	31 (6.0)	23 (8.0)	8 (3.6)	
Glycoprotein IIb/IIIa Inhibitor				0.31
Yes	13 (2.5)	5 (1.7)	8 (3.6)	
Vascular access				0.06
Radial artery	323 (63.0)	197 (68.4)	126 (56.0)	
Femoral artery	190 (37.0)	91 (31.6)	99 (44.0)	
Operator and hospital site				
High-volume complex PCI operator				<0.001
Yes	150 (29.2)	63 (21.9)	87 (38.7)	

(*Continued*)

Table 2. Continued

	Total cohort, n (%)	Noncomplex PCI, n (%)	Complex PCI, n (%)	
	N=504	N=285	N=219	*P* value
Hospital network site				0.01
Site 1	348 (67.8)	186 (64.6)	162 (72.0)	
Site 2	156 (30.4)	93 (32.3)	63 (28.0)	
Site 3	9 (1.8)	9 (3.1)	0 (0.0)	

CABG indicates coronary artery bypass graft; and PCI, percutaneous coronary intervention.

for relevant clinical characteristics (HR, 0.32 [95% CI, 0.11–0.93]; Table 3).

Bleeding

Patients receiving complex versus noncomplex PCI had a higher proportion of bleeding events at 1 year (25.3% versus 20.5%, respectively; Table 4). Adjusted logistic regression models constructed using forward selection were better optimized when excluding the PCI group as an independent variable; however, when included as an additional covariate in the forward-selected model, the PCI group was not sufficiently associated with bleeding events at 1 year (odds ratio, 1.26 [95% CI, 0.80–1.98]; Table 3).

Alternative Complex PCI Definition

In secondary analyses that used an alternative definition of complex PCI, there was no difference in EFS between patients receiving complex versus noncomplex PCI (84.0% for both). The differences in the risk of all-cause death or TLR did not reach statistical significance.

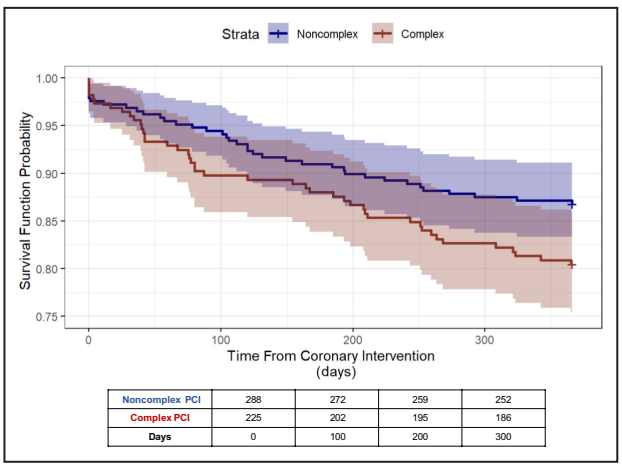

Figure 1. Kaplan–Meier curves for event-free survival.
Figure displays the Kaplan–Meier survival curves (survival function probability vs time from coronary intervention in days) for the event-free survival (freedom from all-cause death, nonfatal myocardial infarction/stroke, and target lesion revascularization) at 12 months from index percutaneous coronary intervention (PCI). The blue curve represents the group receiving noncomplex PCI, and the red curve represents the group receiving complex PCI.

DISCUSSION

In this investigation of complex PCI in older adults, we observed a 2-fold risk of all-cause death among older adults undergoing complex compared with noncomplex

Table 3. Regression Models

Outcome	Hazard ratio	95% CI	*P* value
Event-free survival (events=82)			
Unadjusted Cox regression	1.53	0.99–2.36	0.06
Adjusted Cox regression	1.38	0.88–2.16	0.16
Major events (unadjusted)			
Myocardial infarction (events=7)	0.96	0.21–4.28	0.96
Stroke (events=14)	1.28	0.45–3.64	0.65
Cardiovascular death (events=22)	1.09	0.47–2.53	0.84
All-cause death (N=40)			
Unadjusted Cox regression	1.78	0.95–3.33	0.07
Adjusted Cox regression	1.97	1.02–3.79	0.04
Target lesion revascularization (events=15)			
Unadjusted Cox regression	0.64	0.22–1.87	0.41
Adjusted Cox regression	0.32	0.11–0.93	0.04
Bleeding events (events=116)	**Odds ratio**	**95% CI**	***P* value**
Unadjusted logistic regression	1.32	0.87–2.00	0.19
Adjusted logistic regression	1.26	0.80–1.98	0.31

All displayed results represent the hazard or odds of the outcome at 12 months for complex PCI vs noncomplex PCI (reference). PCI indicates percutaneous coronary intervention.

After forward selection, the adjusted regressions included the following covariates:

1. Event-free survival: age, severe valvular disease, chronic kidney disease, peripheral artery disease, alcohol use disorder, chronic obstructive pulmonary disease, frailty score, full guideline-directed medical therapy, triple therapy, dual-antiplatelet therapy, anticoagulation
2. All-cause death: severe valvular disease, heart failure, dialysis, history of gastrointestinal bleeding, chronic obstructive pulmonary disease, glycoprotein IIb/IIIa inhibitor
3. Target lesion revascularization: age, race, hyperlipidemia, heart failure, prior cerebrovascular accident, anemia, frailty score, intravascular imaging
4. Bleeding events: age, hypertension, severe valvular disease, alcohol use disorder, chronic obstructive pulmonary disease, history of gastrointestinal bleeding, full guideline-directed medical therapy, anticoagulation, bivalirudin, intravascular imaging

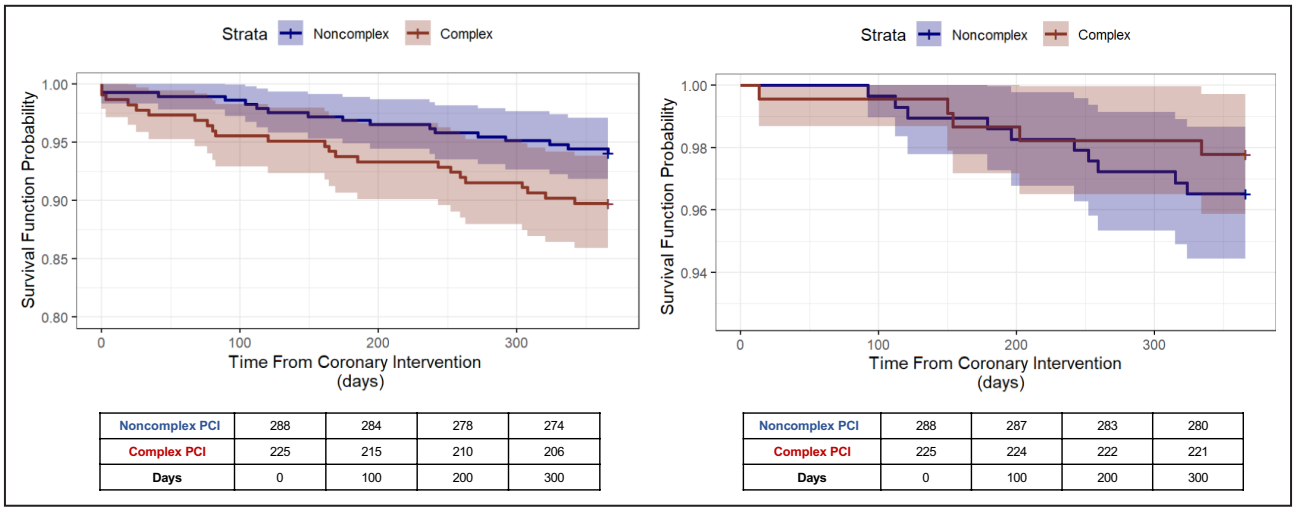

Figure 2. Kaplan–Meier curves for secondary outcomes.
Figure displays the Kaplan–Meier survival curves (survival function probability vs time from coronary intervention in days) for all-cause death (left) and target lesion revascularization (right) at 12 months from index percutaneous coronary intervention (PCI). At-risk tables are shown below each respective graph. The blue curves represent the group receiving noncomplex PCI, and the red curves represent the group receiving complex PCI.

PCI even after adjusting for patient and PCI characteristics. Given the dramatic difference in death risk for older adults receiving complex PCI, we suggest that such interventions in this exceptionally vulnerable population should be approached with additional caution and that further investigations are needed to define causality.

Complex PCI is becoming increasingly common in older adults.[9] We observed a substantial number of older

Table 4. Bleeding Events

	Total cohort, n (%)	Noncomplex PCI, n (%)	Complex PCI, n (%)	
	N=504	N=285	N=219	*P* value
Type of bleeding event				
All types	116 (22.6)	59 (20.5)	57 (25.3)	0.23
PCI periprocedural bleeding or hematoma	25 (4.9)	12 (4.2)	13 (5.8)	0.53
Gastrointestinal bleeding	27 (5.3)	13 (4.5)	14 (6.2)	0.51
Epistaxis	19 (3.7)	10 (3.5)	9 (4.0)	0.94
Hematuria	18 (3.5)	6 (2.1)	12 (5.3)	0.07
Intracranial hemorrhage	7 (1.4)	4 (1.4)	3 (1.3)	1.00
Dental procedure with excessive hemorrhage	3 (0.6)	3 (1.0)	0 (0.0)	0.34
Traumatic laceration with excessive hemorrhage	10 (1.9)	7 (2.4)	3 (1.3)	0.57
Spontaneous cutaneous hemorrhage	4 (0.8)	0 (0.0)	4 (1.8)	0.08
Surgical site rebleeding or hematoma	11 (2.1)	7 (2.4)	4 (1.8)	0.84
Hemoptysis	1 (0.2)	1 (0.3)	0 (0.0)	1.00
Noncranial internal hemorrhage	7 (1.4)	6 (2.1)	1 (0.2)	0.23
BARC staging*				0.09
1	9 (1.8)	3 (1.0)	6 (2.7)	
2	70 (13.6)	38 (13.2)	32 (14.2)	
3a	18 (3.5)	6 (2.1)	12 (5.3)	
3b	12 (2.3)	8 (2.8)	4 (1.8)	
3c	6 (1.2)	4 (1.4)	2 (0.9)	
5	3 (0.6)	0 (0.0)	3 (0.6)	

BARC indicates Bleeding Academic Research Consortium; and PCI percutaneous coronary intervention.
*Highest BARC staging in patients with multiple bleeding episodes.

adults receiving complex PCI (almost half of the cohort). Our work demonstrates that complex PCI may be associated with reliable target vessel patency in older adults, given a lower risk of TLR as compared with patients receiving noncomplex PCI. Superior TLR for patients receiving complex PCI may be due to higher usage of PCI adjuncts among patients receiving complex interventions. For instance, use of atherectomy would classify an intervention as complex, by definition, but a lesion that may have benefited from atherectomy without receiving it may be classified as noncomplex. Ultimately, the absolute difference in TLR between complex versus noncomplex PCI was small (1%) and complex PCI was at least as effective as noncomplex interventions at maintaining target vessel patency. Importantly, TLR has been identified as an independent predictor of worse outcomes, including death.[26] Thus, the lower rates of TLR observed in the complex PCI groups certainly provide reassurance that older adults undergoing more technically complex procedures can experience excellent midterm revascularization outcomes.

This analysis also highlights potential risk in older adults undergoing complex PCI, with a signal for higher death in older adults receiving complex interventions. It is difficult to hypothesize the role of selection bias in these findings. One may expect older adults selected for complex, high-risk procedures to have fewer comorbidities, or, alternatively, expect patients with more complex CAD to have more comorbidities and worse functional status. However, patients undergoing complex versus noncomplex PCI in this real-world cohort did not significantly differ across any of a host of clinical characteristics. Although the observational study design cannot account for unmeasured confounders, it is nonetheless notable that the study groups were not statistically different across predictors of poor PCI outcomes in older adults, including frailty.[27,28] Therefore, the baseline characteristics between PCI groups suggest that simple differences in comorbid disease burden are unlikely to be the culprit. Furthermore, the risk of all-cause death was actually amplified in adjusted analyses. Thus, we emphasize that the most notable observation from this analysis is the dramatic increase in adjusted death risk for older adults receiving complex PCI as compared with controls receiving noncomplex PCI. Five patients did not have a clearly documented cause of death. With an observational design, and without the benefit of adjudication as exists in prospective trials,[29] speculation about the root cause of the higher death risk is limited. The elevated risk of complex PCI, in the absence of other evidence, warrants, at a minimum, exceptional caution when electing older adults for complex PCI and should motivate further prospective investigations.

In contrast with the death signal observed in this older cohort, previous studies of complex PCI in younger populations have demonstrated mixed outcomes compared with noncomplex PCI. This includes some studies demonstrating no difference in all-cause or cardiovascular death,[30,31] though an analysis from the Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents study of a younger patient population did observe higher 2-year risk of major adverse cardiovascular events, MI, and stent thrombosis among individuals undergoing complex PCI.[30] This association was actually strongest among those with SIHD. Mohamed et al[18] identified a statistically significant death rate difference in a large, multicenter registry, though the absolute difference was relatively small (0.7%). Literature describing complex PCI outcomes in older adults are scarce.[8] An analysis of multinational registry data reported similar long-term outcomes in older adults undergoing unprotected left main coronary artery PCI versus older adults undergoing CABG.[32] Another prior study described trends toward improved outcomes in English older adults over time despite increasing rates of complex interventions.[9] Two studies of chronic total occlusion interventions in older adults reported no difference in adjusted analyses of periprocedural complications in older adults versus younger patients.[15,33] Postprocedural outcomes were not a focus of these latter studies. Complex PCI studies in older patients with somewhat younger chronologic age than the cohort analyzed here, in the 65- to 75-year range, are also uncommon. A recently published follow-up to the SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) trial described similar death rates and quality of life between older adults undergoing PCI versus CABG.[11] Therefore, the risk of certain complex interventions may be similar to the risk of CABG for certain outcomes in older adults, though the broader long-term risk of complex PCI in older adults remains unknown. It is worth mentioning that the survival benefit of CABG is less clear in older adults. A long follow-up duration, namely 10 years, was necessary to observe a survival benefit in the STICH (Surgical Treatment in Ischemic Heart Failure) trial, which may substantially shift the risk–benefit calculus for patients in their 9th or 10th decades of life.[34] Nonetheless, while the benefits of surgical revascularization are potentially high in patients with SIHD being considered for CABG, given the possible survival benefit with certain surgical coronary anatomy, these benefits are less clear in the majority of patients with SIHD undergoing PCI for stable angina who do not have surgical anatomy. Complex PCI is often performed on the basis of anatomic considerations and for symptomatic or quality-of-life benefits in older populations, without a clear survival benefit from revascularization. In these cases, the inherent risk is more relevant, further underscoring the need for investigations to precisely quantify the short- and long-term risks and benefits of complex PCI.

The lack of uniformity around defining complex PCI in the literature remains a barrier to future

investigations.[12] Moreover, some studies blur the distinction between complex and high-risk PCI.[21] We chose not to include numeric cutoffs (beyond multivessel PCI) in our primary definition of complex PCI, as such criteria only partially convey procedural complexity. For example, PCI with overlapping 38-mm and 26-mm stents deployed in the right coronary artery carries different technical risk from an unprotected left main trifurcation PCI or severely calcified chronic total occlusion PCI with atherectomy. Notably, stent length, specifically, no longer predicts worse outcomes in newer-generation stents.[35] In our sensitivity analysis, using a similar definition to the definitions used in several complex PCI investigations,[18–20] we did not observe a statistically significant death rate difference, underscoring the need for a uniform, clinically relevant definition that effectively predicts interventions with higher associated risk.

Bleeding events are of primary concern in older adults receiving drug-eluting stents. Many studies report higher bleeding risk in older adults on dual antiplatelet therapy.[8] The risk of bleeding was high in both groups, with almost one-quarter of the total cohort experiencing a bleeding event within 1 year of index PCI. However, although the absolute difference was about 5%, we observed no statistically significant difference between patients receiving complex PCI versus noncomplex PCI. This may be considered clinically significant and may have reached statistical significance with a larger sample size.

The findings of this study should be viewed in light of the following limitations: as an observational study, we cannot infer causality, and unmeasured confounding may contribute to differences seen between treatment groups. We may be limited by sample size for some outcomes, although the number of patients is offset by the high level of granularity possible with a manual chart review that is not available with larger registry studies. Some patients were lost to follow-up, though we did extract data from outside hospital records to limit the number of patients who were counted as lost to follow-up and to ensure capture of all outcomes. The lack of definition around complex PCI limits comparison across other studies. This is balanced by our sensitivity analysis, which examines a previously used alternative complex PCI definition. Chart data extraction often involves some interpretation that may lead to imprecision, though we expect this limitation to be mitigated in this study as compared with studies without manual extraction or where nonphysician extractors record the data. Moreover, manual extraction by physicians is likely more accurate than the use of billing codes, which are often incorrect.[36,37] The study is limited to a single health system with multiple sites and so validation of these data across other centers will be needed. Finally, given the nature of the data set, we used the date of the health care encounter as a proxy for the date of the initial PCI procedure; however, these dates almost always coincide or fall within a few days of each other and we do not expect the difference to influence the study findings.

CONCLUSIONS

Older adults without substantial statistical differences in baseline characteristics undergoing elective complex versus noncomplex PCI for SIHD had lower TLR but higher risk of all-cause death 12 months from the index intervention. Further investigation into the outcomes following complex PCI in older adults is needed.

ARTICLE INFORMATION

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Supplemental Material

Figure S1

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