

ORIGINAL RESEARCH

Outcome of Percutaneous Coronary Intervention During Non–ST-Segment–Elevation Myocardial Infarction in Elderly Patients With Chronic Kidney Disease

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BACKGROUND: There is a paucity of data on the benefit of revascularization by percutaneous coronary intervention (PCI) during non–ST-segment–elevation myocardial infarction in patients aged >80 years with concurrent chronic kidney disease.

METHODS AND RESULTS: Patients aged >80 years with chronic kidney disease, defined as an estimated glomerular filtration rate (eGFR) <60 mL/min per 1.73 m² with non–ST-segment–elevation myocardial infarction, during 2011 to 2014 in Sweden retrieved from the SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) Registry. Cox regression was used to estimate adjusted hazard ratios with 95% CIs for all-cause mortality in patients with PCI versus no PCI treatment, stratified for eGFR. Logistic regression was used to evaluate adjusted odds for reinfarction and bleeding during hospitalization. Propensity score weighting analysis was also done as sensitivity analysis. In total, 12 821 patients were included, of whom 47%, 45%, and 8% had an eGFR of >60, 30 to 60, and 15 to <30 mL/min per 1.73 m², respectively. Patients with eGFR 30 to 60 and 15 to <30 mL/min per 1.73 m², 22%, and 10%, respectively, underwent PCI, compared with 36% among patients with eGFR >60 mL/min per 1.73 m². During a mean follow-up of 3.2 years, the absolute risk of death was 42%, 56%, and 76% in patients with eGFR >60, 30 to 60, and 15 to <30 mL/min per 1.73 m², respectively. Patients who underwent PCI had a lower risk of death in all groups of eGFR (0.47 [95% CI, 0.42–0.53], 0.50 [95% CI, 0.45–0.56], and 0.44 [95% CI, 0.33–0.59], respectively). Patients with eGFR 15 to <30 mL/min per 1.73 m² had a higher risk of bleeding with PCI. Propensity score weighting showed similar outcomes for mortality risk as the unweighted analysis in all the eGFR groups.

CONCLUSIONS: PCI is rarely used in non–ST-segment–elevation myocardial infarction elderly patients with chronic kidney disease, and it appears to offer a survival benefit.

Key Words: chronic kidney disease ■ elderly patients ■ estimated glomerular filtration rate ■ non–ST-segment–elevation myocardial infarction ■ percutaneous coronary intervention

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Chronic kidney disease (CKD) is a well-known risk factor for the development and progression of coronary artery disease. Moreover, CKD is associated with adverse outcomes in patients both with and without coronary artery disease.¹ An advanced age (>80 years) and CKD are often used as reasons

to withhold patients from cardiac revascularization. But data suggested that prognosis is similar with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) in patients with or without CKD during acute coronary syndrome or myocardial infarction.^{2–4} Interestingly, patients with CKD

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CLINICAL PERSPECTIVE

What Is New?

- In randomized studies, often elderly patients and patients with chronic kidney disease are excluded; therefore, there is little information on the outcomes on patients aged >80 years with chronic kidney disease who have non–ST-segment–elevation myocardial infarction.
- We found that elderly patients with chronic kidney disease have a survival benefit of being revascularized during a non–ST-segment–elevation myocardial infarction.

What Are the Clinical Implications?

- Our findings should lead to more elderly patients with chronic kidney disease being revascularized during non–ST-segment–elevation myocardial infarction.

Nonstandard Abbreviations and Acronyms

CABG	coronary artery bypass grafting
CKD	chronic kidney disease
eGFR	estimated glomerular filtration rate
NSTEMI	non–ST-segment–elevation myocardial infarction
PCI	percutaneous coronary intervention

are more likely to die from cardiovascular causes than from end-stage kidney failure.^{1,5} In addition, patients with CKD are frequently excluded from trials on revascularization of stable ischemic heart disease.⁶ It has been suggested that patients with stable coronary artery disease who undergo PCI get better symptom relief for angina and subsequent improvement of quality of life, irrespective of CKD stages, although no survival benefit is offered by PCI.⁷ In contrast, according to guidelines, CKD patients with non–ST-segment–elevation myocardial infarction (NSTEMI) or acute coronary syndrome should be treated with PCI, except for patients with end-stage CKD.⁵ There are significant risks of bleeding and cerebrovascular events and high rates of restenosis in CKD patients who undergo PCI.^{8,9} However, these data are relatively old considering the recent improvements in invasive techniques and newer antithrombotic medication in the era of new generations of drug-eluting stents.¹⁰ Because the aging population with CKD is growing and there is a paucity of data, we wanted to investigate if there are any advantages to revascularization by PCI during NSTEMI in patients aged

>80 years with concurrent CKD. We hypothesized that elderly patients with reduced estimated glomerular filtration rate (eGFR) can benefit from PCI after NSTEMI in terms of better survival.

METHODS

Patient and Public Involvement Statement

We report no direct patient or public involvement in this study.

Study Population

The study population included all patients aged >80 years with information on eGFRs at index NSTEMI during 2011 to 2014. Data were retrieved from the SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) Registry. A total of 17 935 patients with NSTEMI were included first. Thereafter, we excluded all patients with a history of other serious diseases, like cancer or dementia (n=4025), that led to treatment being withheld; patients with type 3, 4, and 5 myocardial infarction (n=56); and patients with known end-stage CKD, defined as eGFR <15 mL/min per 1.73 m² (n=1033), or missing information on eGFR. The final study population consisted of 12 821 patients with information on eGFR at index NSTEMI who were followed up for a median of 3.2 years. Baseline characteristics were assessed on the day of admission. Baseline medications were those that patients were using before admission, and medication used after discharge is what patients were using at the point of discharge. All the patients included in the present study were waived from informed consent, and the study was approved by the local ethics committee and adhered to the Declaration of Helsinki. The authors declare that all supporting data are available within the article.

Kidney Function

GFR was estimated using the CKD–Epidemiology Collaboration equation.¹¹ Serum creatinine was measured at admission with other relevant blood samples related to NSTEMI. The study population was categorized into the following categories of kidney function: >60 mL/min per 1.73 m² (normal), 30 to 60 mL/min per 1.73 m² (moderate CKD), and 15 to <30 mL/min per 1.73 m² (severe CKD).

Exposure and Outcome

Exposure was defined as treatment with PCI, and the reference was defined as no PCI treatment. Conservative treatment was defined as

guideline-recommended medical management of NSTEMI, except for PCI. Primary outcome was all-cause mortality, whereas secondary outcomes were bleeding and new myocardial infarction in hospital after the admission date for NSTEMI. Bleeding was defined as major when there was >50 g/dL decrease of hemoglobin or intracranial bleeding leading to death, whereas bleeding was defined as minor when there was >30 g/dL decrease of hemoglobin or bleeding requiring transfusion.^{12,13} New myocardial infarction or reinfarction was defined as new troponin increase of a minimum of >100% of reference level during admission or >50% increase of the previous maximum documented troponin level.

Follow-Up

Follow-up started at the admission date, and ended when the patient died or at the end of follow-up, which was March 10, 2016, whichever came first.

Statistical Analysis

Descriptive statistics were performed using means and SDs for summarizing numerical variables and frequencies and percentages for categorical variables. Bivariate analyses with χ^2 test were conducted to compare categorical variables with type of treatment and mortality, whereas *t* tests were used to compare numerical variables with type of treatment and mortality. We used the Kaplan-Meier method to estimate cumulative survival in relation to treatment with PCI or not in different strata of eGFR. Cox regression was used to estimate hazard ratios (HRs) for all-cause mortality in patients treated with PCI using patients receiving conservative treatment as referents and stratified for eGFR. HRs are reported with 95% CIs and estimated (1) crude, (2) adjusted for age, and (3) adjusted for age, sex, left ventricular ejection fraction, previous stroke, previous myocardial infarction, CABG, heart failure, prior PCI, diabetes mellitus, and hypertension and all the medications attributable to NSTEMI. All the variables were selected as they are recognized to be associated with cardiovascular mortality as primary outcome.³ In a similar way, logistic regression models have been used to estimate odds ratios (ORs) of new infarction and bleeding during hospital stay. As sensitivity analysis, we have estimated propensity score weighting considering the above mentioned variables in point 3 and then estimated the hazard and ORs mentioned above on the matched sample. For the propensity score weighting, we have used the Stata command *psmatch2* to create propensity scores and then used inverse probability weighting in the Cox and logistic regression models.

The collected data were analyzed with STATA version 15 software (Stata Corporation, College Station, TX).

RESULTS

Study Population

In total, 12 821 patients with NSTEMI were included and then followed up for a mean of 3.2 years. The mean age was 86 years, and sex was approximately equally distributed (Table 1). Approximately 65% of the study population had a history of hypertension, 25% had a history of diabetes mellitus, and 46% had a history of myocardial infarction. Less than half (47%) of the patients had an eGFR >60 mL/min per 1.73 m², and 45% and 8% had an eGFR of 30 to 60 and 15 to <30 mL/min per 1.73 m², respectively. Patients with eGFR 15 to <30 mL/min per 1.73 m² were more likely to have a history of myocardial infarction, heart failure, stroke, diabetes mellitus, and hypertension than patients with a higher eGFR (Table 1). Approximately 43% (n=6012) of total population went through coronary angiogram, whereas 67% of them were PCI treated during index NSTEMI. In patients with an eGFR of 30 to 60 and 15 to <30 mL/min per 1.73 m², only 22% and 10%, respectively, underwent PCI. A larger proportion of women than men were treated conservatively (55% versus 45%). Approximately 2.6% of patients with different stages of CKD with advanced multivessel disease were offered CABG.

All-Cause Mortality

Mortality increased with decreasing eGFR, from 42% in patients with eGFR \geq 60 mL/min per 1.73 m² to 56% and 76% in patients with eGFR 30 to 60 and 15 to <30 mL/min per 1.73 m², respectively (Figure—Panel A through Panel C). Elderly patients who underwent PCI compared with patients who were treated conservatively had significantly lower adjusted risks of death in all strata of eGFR during follow-up: HR (95% CIs) in patients with eGFR \geq 60, 30 to 60, and 15 to <30 mL/min per 1.73 m² were 0.47 (0.42–0.53), 0.50 (0.45–0.56), and 0.44 (0.33–0.59), respectively (Table 2). Similar outcomes were observed on propensity score weighting sample among patients with eGFR \geq 60 mL/min per 1.73 m²: n=2072 treated with PCI, n=731 among treated with conservative treatment; among patients with eGFR 30 to 60 mL/min per 1.73 m²: n=1448 treated with PCI, n=727 among treated with conservative treatment; among patients with eGFR 15 to <30 mL/min per 1.73 m²: n=134 treated with PCI, n=108 among treated with conservative treatment in all the strata of eGFR.

Reinfarction and Bleeding

There was no significant association between treatment or not with PCI and reinfarction or all categories of bleeding in patients with eGFR >60 and eGFR 30 to 59 mL/min per 1.73 m² after adjusting by confounders. However, patients treated with PCI with eGFR 15 to

Table 1. Baseline Characteristics for Patients Aged >80 Years With NSTEMI in Sweden 2011 to 2014 in Relation to eGFRs and Treatment at Discharge With or Without PCI

Characteristic	All Patients		P Value	eGFR, mL/min per 1.73 m ²					
				>60		30–60		15–<30	
	No PCI	PCI		No PCI	PCI	No PCI	PCI	No PCI	PCI
No. of patients	8933 (69.7)	3888 (30.3)		3860 (63.7)	2200 (36.3)	4188 (73.1)	1542 (26.9)	885 (85.8)	146 (14.2)
Age, y	86.3 (4.2)	83.7 (3.1)	<0.001	85.6 (4.1)	83.3 (2.8)	86.8 (4.1)	84.1 (3.3)	87.4 (4.5)	84.2 (3.5)
Men, n (%)	4092 (45.8)	2232 (57.4)	<0.001	1794 (46.5)	1329 (60.4)	1916 (45.8)	823 (53.4)	382 (43.2)	80 (54.8)
Troponin (ng/mL)	508.8 (14.1)	674.2 (32.1)	<0.001	413.4 (17.9)	564.3 (40.3)	544.3 (21.0)	770.3 (52.8)	757.8 (64.8)	1345 (216.7)
Prior stroke, n (%)	1428 (16.1)	393 (10.1)	<0.001	589 (15.4)	199 (9.1)	688 (16.5)	163 (10.6)	151 (17.2)	31 (21.4)
Prior MI, n (%)	4288 (48.4)	1563 (40.5)	<0.001	1593 (41.6)	777 (36.6)	2214 (53.3)	697 (45.5)	481 (54.6)	89 (61.4)
Prior heart failure, n (%)	1924 (22.8)	530 (14.3)	<0.001	597 (16.1)	210 (10.0)	1053 (26.6)	268 (18.2)	274 (32.7)	52 (38.5)
Diabetes mellitus, n (%)	2301 (25.8)	944 (24.3)	0.070	844 (21.9)	476 (21.7)	1162 (27.8)	414 (26.9)	295 (33.5)	54 (37.0)
CABG, n (%)	318 (3.6)	25 (0.6)	<0.001	195 (5.1)	16 (0.7)	110 (2.6)	9 (0.6)	13 (1.5)	0 (0.0)
Aspirin, n (%)	7259 (81.4)	3625 (93.4)	<0.001	3219 (83.5)	2084 (94.8)	3377 (80.8)	1413 (92.0)	663 (74.9)	128 (87.7)
Other antiplatelet, n (%)	5180 (58.1)	3695 (95.2)	<0.001	2363 (61.8)	2108 (95.9)	2403 (57.4)	1453 (94.6)	414 (46.8)	134 (91.8)
Anticoagulant at discharge									
None, n (%)	7539 (84.4)	3370 (86.7)	<0.001	3254 (84.3)	1932 (87.8)	3552 (84.8)	1314 (85.3)	733 (82.8)	124 (84.9)
Warfarin, n (%)	1205 (13.5)	474 (12.2)		516 (13.4)	248 (11.3)	556 (13.3)	205 (13.3)	133 (15.0)	21 (14.4)
Dabigatran, n (%)	21 (0.2)	7 (0.2)		9 (0.2)	5 (0.2)	12 (0.3)	12 (0.1)	0 (0.0)	0 (0.0)
Rivaroxaban, n (%)	32 (0.4)	5 (0.1)		19 (0.5)	2 (0.1)	12 (0.3)	3 (0.2)	1 (0.1)	0 (0.0)
Apixaban, n (%)	32 (0.4)	8 (0.2)		12 (0.3)	4 (0.2)	17 (0.4)	4 (0.3)	3 (0.3)	0 (0.0)
Other, n (%)	90 (1.0)	16 (0.4)		43 (1.1)	7 (0.3)	32 (0.8)	8 (0.5)	15 (1.7)	1 (0.7)
Unknown, n (%)	14 (0.2)	7 (0.2)		7 (0.2)	2 (0.1)	7 (0.2)	5 (0.3)	0 (0.0)	0 (0.0)
β blockers, n (%)	7274 (81.4)	3395 (87.3)	<0.001	3182 (82.4)	1926 (87.6)	3390 (81.0)	1341 (87.0)	702 (79.3)	128 (87.7)
ACE inhibitors, n (%)	3971 (44.5)	2218 (57.1)	<0.001	1925 (49.9)	1338 (60.8)	1805 (43.1)	825 (53.5)	241 (27.2)	55 (36.7)
Statins, n (%)	5493 (61.5)	3471 (89.3)	<0.001	2521 (65.3)	2104 (91.6)	2567 (61.3)	1342 (87.1)	405 (45.8)	115 (78.8)
Previous PCI, n (%)	1657 (18.9)	1013 (26.3)	<0.001	660 (17.4)	519 (23.7)	836 (20.4)	451 (29.6)	161 (18.7)	43 (30.7)
Hypertension, n (%)	5621 (63.5)	2444 (63.2)	0.799	2301 (60.1)	1282 (58.6)	2727 (65.6)	1051 (68.6)	593 (68.0)	111 (76.6)
New infarction during hospital stay, n (%)	46 (0.5)	35 (0.9)	0.012	12 (0.3)	11 (0.5)	24 (0.6)	19 (1.2)	10 (1.1)	5 (3.5)
Cardiogenic shock, n (%)	88 (1.0)	41 (1.1)	0.720	23 (0.6)	14 (0.6)	47 (1.1)	22 (1.4)	18 (2.0)	5 (3.4)
Bleeding									
No	8806 (98.6)	3829 (98.5)		3824 (99.1)	2179 (99.1)	4117 (98.3)	1511 (98.0)	865 (97.7)	139 (95.2)
Deadly	4 (0.04)	0 (0.0)		1 (0.03)	0 (0.0)	2 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
Cerebral	8 (0.1)	4 (0.1)		5 (0.1)	2 (0.1)	3 (0.1)	2 (0.1)	0 (0.0)	0 (0.0)
Requiring transfusion	107 (1.2)	53 (1.4)		29 (0.8)	19 (0.9)	60 (1.4)	27 (1.8)	18 (2.0)	7 (4.8)
Unknown	8 (0.1)	2 (0.1)		1 (0.03)	0 (0.0)	6 (0.1)	2 (0.1)	1 (0.1)	0 (0.0)

ACE indicates angiotensin-converting enzyme; CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; NSTEMI, non-ST-segment-elevation MI; and PCI, percutaneous coronary intervention.

<30 mL/min per 1.73 m² had a significantly higher risk of bleeding within 30 days of index date of NSTEMI (Tables 3 and 4). This result was not confirmed in the propensity scores weighting sample.

DISCUSSION

We report herein that PCI is rarely used in elderly patients aged >80 years in general, and even more

infrequently among patients with CKD during hospitalization for NSTEMI. Despite the anticipated high mortality and risk for complications, PCI was strongly associated with a lower mortality in our cohort of elderly patients with CKD. To the best of our knowledge, this study is the largest study to date that compares conservative treatment with PCI treatment following NSTEMI in patients aged >80 years with different stages of CKD.

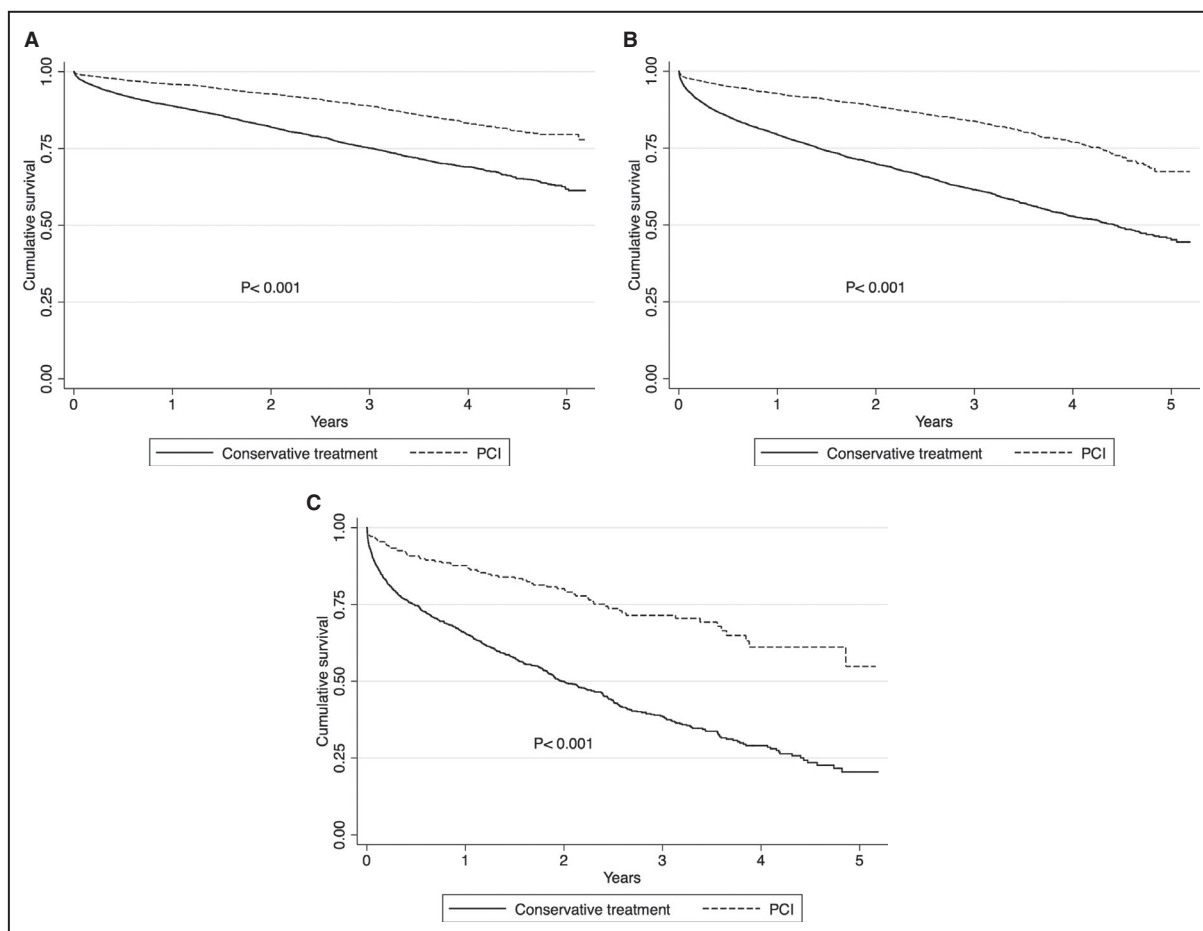


Figure. Cumulative survival in relation to percutaneous coronary intervention (PCI) vs. no PCI in patients >80 years of age estimated with the Kaplan Meier method.

(A) eGFR >60 ml/min/1.73 m²; (B) eGFR 30–60 ml/min/1.73 m² and (C) eGFR 15–<30 ml/min/1.73 m².

Elderly patients are underrepresented in available data in the contemporary era of PCI treatment with newer antiplatelet agents and stents. European Society of Cardiology/American Heart Association/American

College of Cardiology guidelines recommend appropriate revascularization intervention in patients with CKD during NSTEMI irrespective of age. However, in clinical practice, decisions about whether to perform

Table 2. HRs (95% CIs) for the Risk of All-Cause Mortality Associated With PCI Versus No PCI, Stratified for eGFR in Patients Aged >80 Years With NSTEMI

Variable	eGFR, mL/min per 1.73 m ²					
	>60 (No. Deaths=2186 [36.1%])		30–60 (No. Deaths=2947 [51.5%])		15–<30 (No. Deaths=749 [72.7%])	
	No PCI	PCI	No PCI	PCI	No PCI	PCI
Crude HR (95% CI)	Reference	0.39 (0.36–0.44)	Reference	0.41 (0.37–0.45)	Reference	0.38 (0.29–0.49)
HR (95% CI), adjusted for age	Reference	0.47 (0.42–0.52)	Reference	0.48 (0.43–0.53)	Reference	0.44 (0.34–0.57)
HR (95% CI), adjusted for confounders*	Reference	0.47 (0.42–0.53)	Reference	0.50 (0.45–0.56)	Reference	0.44 (0.33–0.59)
HR (95% CI) on the propensity score weighting sample†	Reference	0.66 (0.55–0.79)	Reference	0.63 (0.54–0.74)	Reference	0.54 (0.38–0.77)

eGFR indicates estimated glomerular filtration rate; HR, hazard ratio; NSTEMI, non–ST-segment–elevation myocardial infarction; and PCI, percutaneous coronary intervention.

*Full model was adjusted for all variables in Table 1.

†Propensity score weighting for treatment was estimated using all variables in Table 1.

Table 3. Logistic Regression for the Odds (95% CIs) of New Infarction During Hospital Stay Associated With PCI Versus No PCI in Patients Aged >80 Years With NSTEMI

Variable	eGFR, mL/min per 1.73 m ²					
	>60 (No. MIs=23 [0.4%])		30–60 (No. MIs=43 [0.8%])		15–<30 (No. MIs=15 [1.5%])	
	No PCI	PCI	No PCI	PCI	No PCI	PCI
Crude OR (95% CI)	Reference	1.61 (0.71–3.65)	Reference	2.15 (1.18–3.95)	Reference	3.11 (1.05–9.25)
OR (95% CI), adjusted for age	Reference	1.51 (0.64–3.55)	Reference	1.99 (1.05–3.77)	Reference	2.92 (0.92–9.21)
OR (95% CI), adjusted for confounders*	Reference	1.76 (0.71–4.37)	Reference	1.89 (0.95–3.76)	Reference	3.03 (0.90–10.22)
OR (95% CI) on the propensity score weighting sample†	Reference	...‡	Reference	1.48 (0.53–4.19)	Reference	3.78 (0.43–33.01)

eGFR indicates estimated glomerular filtration rate; MI, myocardial infarction; NSTEMI, non–ST-segment–elevation MI; OR, odds ratio; and PCI, percutaneous coronary intervention.

*Full model was adjusted for all variables in Table 1.

†Propensity score weighting for treatment was estimated using all variables in Table 1.

‡Omitted because of collinearity.

PCI in elderly patients are often taken at the discretion of the attending cardiologist or interventionalist.¹⁴ The proportion of patients with CKD is increasing constantly as elderly people are living longer, but also because of an increasing prevalence of hypertension and diabetes mellitus. Our study suggests that PCI should be encouraged in elderly patients with CKD instead of conservative treatment during NSTEMI. European Society of Cardiology/American College of Cardiology/American Heart Association guidelines and European Association for Cardio-Thoracic Surgery guidelines recommend CABG over PCI in patients with moderate to severe CKD with multivessel coronary disease provided patients comply with surgical risk profiles and life expectancy is >1 year.¹⁵ This recommendation is not based on any randomized controlled trial and dates back to the previous generation of stent and anti-thrombotic treatments. The work is based on reports that patients with CKD have a higher risk of procedural complications, such as major bleeding, new myocardial infarctions, or death.¹⁶ These studies of patients

with CKD were conducted when only bare metal stents or first-generation drug-eluting stents were available for PCI. However, some new data are available for the small number of patients with CKD, in whom better outcomes have been reported with the use of second-generation drug-eluting stents compared with bare metal stents.^{17,18} These studies have excluded elderly patients with CKD, and thus, to draw any conclusions about benefits with PCI, and additionally with the use of drug-eluting stents versus bare metal stents in elderly patients with CKD, is not possible. Our data do not indicate any procedural complications, but we have a finding of reduced mortality in the elderly patients with CKD who were treated by PCI compared with conservative medical treatment. The finding holds irrespective of stages of CKD. Our data contribute to existing information and suggest that PCI is well tolerated in elderly patients with CKD, with the exception of patients with severe CKD, in whom we found a higher risk of bleeding, although we could not reconfirm it by propensity score weighting analysis.^{19,20} Although characterization

Table 4. Logistic Regression for the Odds (95% CIs) of Bleeding During Hospital Stay Associated With PCI Versus No PCI in Patients Aged >80 Years With NSTEMI

Variable	eGFR, mL/min per 1.73 m ²					
	>60 (No. Bleeding Events=56 [0.9%])		30–60 (No. Bleeding Events=94 [1.6%])		15–<30 (No. Bleeding Events=26 [2.5%])	
	No PCI	PCI	No PCI	PCI	No PCI	PCI
Crude OR (95% CI)	Reference	1.05 (0.61–1.81)	Reference	1.22 (0.78–1.89)	Reference	2.29 (0.95–5.55)
OR (95% CI), adjusted for age	Reference	1.09 (0.62–1.93)	Reference	1.05 (0.66–1.66)	Reference	1.96 (0.78–4.94)
OR (95% CI), adjusted for confounders*	Reference	1.62 (0.86–3.08)	Reference	1.22 (0.73–2.03)	Reference	2.77 (1.03–7.49)
OR (95% CI) on the propensity score weighting sample†	Reference	1.84 (0.61–5.57)	Reference	1.77 (0.74–4.24)	Reference	1.14 (0.35–3.78)

eGFR indicates estimated glomerular filtration rate; NSTEMI, non–ST-segment–elevation myocardial infarction; OR, odds ratio; and PCI, percutaneous coronary intervention.

*Full model was adjusted for all variables in Table 1.

†Propensity score weighting for treatment was estimated using all variables in Table 1.

of post-PCI bleeding is heterogeneous, both mortality and major cardiovascular event rates are known to be higher in these categories of patients with CKD.²¹ This is probably because of the association between comorbidities and complex coronary lesions during NSTEMI, indicating that bleeding complications and reinfarctions are not unexpected in patients with severe CKD.²² Moreover, the atherosclerosis process is believed to be accelerating in patients with CKD and thus new onset of acute coronary syndrome or NSTEMI is not surprising. It has been stated that new-onset NSTEMI after PCI in patients with CKD is often related to a vessel other than the one at the index PCI during NSTEMI.²³ Patients with CKD have been considered at higher risk for procedural complications, like acute kidney injury, major bleeding, vessel dissection leading to new myocardial infarction, and death.^{1,24} This is certainly of high relevance in patients with end-stage kidney disease (eGFR <15 mL/min per 1.73 m²), and to the best of our knowledge, no study to date has found any benefit of PCI in this group of patients, even with the latest generation of stents. We found that only 2.6% of patient population went through CABG operation in our cohort. This may suggest that extreme age and high anticipated complications risk disqualified these elderly patients with CKD from CABG, considering no changes in long-term mortality compared with PCI.^{25,26} Our study indicates that elderly patients with CKD should be offered more PCI during NSTEMI as the complication rate is not higher as anticipated all the time. Selecting the right patients, radial access, and minimum contrast during PCI as well as shorter duration of antithrombotic medications are important aspects that cardiologists or attending physicians should consult and raise these issues to interventionist.

LIMITATIONS AND STRENGTHS OF THE STUDY

The main limitation of our study, along with every observational study that compares 2 treatment strategies, is confounding by indication. Although we were able to control for the most important predictors of mortality, it is likely there were still patient characteristics that we had no information about, like frailty, an important reason to withhold invasive treatment from elderly patients. This was an observational cohort study so careful interpretations of data in the context of any clinical setting should be considered, mainly because of the inherent risk with residual confounding that we could not control for. However, the main strength of our study was the large cohort of patients aged >80 years and the long follow-up, which led to many events, and a high precision in our estimates. The SWEDEHEART Registry is monitored frequently, and the agreement

between the register and medical records is 95% to 97%.²⁷ Although the number of events in patients with severe CKD was small, we found a higher risk of bleeding. This should be addressed in future studies by using an appropriate pharmacological treatment strategy during PCI based on individual bleeding and ischemic profile.

In conclusion, traditionally advanced age (>80 years) and CKD are often used as reasons for denying patients cardiac revascularization. Our data suggest that elderly patients with CKD get the same survival benefit of PCI during NSTEMI.

ARTICLE INFORMATION

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Disclosures

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REFERENCES

- Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med*. 2004;351:1296–1305.
- Huang HD, Alam M, Hamzeh I, Virani S, Deswal A, Aguilar D, Rogers P, Kougias P, Birnbaum Y, Paniagua D, et al. Patients with severe chronic kidney disease benefit from early revascularization after acute coronary syndrome. *Int J Cardiol*. 2013;168:3741–3746.
- Holzmann M, Jernberg T, Szummer K, Sartipy U. Long-term cardiovascular outcomes in patients with chronic kidney disease undergoing coronary artery bypass graft surgery for acute coronary syndromes. *J Am Heart Assoc*. 2014;3:e000707. DOI: 10.1161/JAHA.113.000707.
- Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Cullerton B, Hamm LL, McCullough PA, Kasiske BL, Kelepouris E, Klag MJ, et al. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. *Circulation*. 2003;108:2154–2169.
- Shlipak MG, Heidenreich PA, Noguchi H, Chertow GM, Browner WS, McClellan MB. Association of renal insufficiency with treatment and outcomes after myocardial infarction in elderly patients. *Ann Intern Med*. 2002;137:555–562.
- Collins AJ, Li S, Gilbertson DT, Liu J, Chen SC, Herzog CA. Chronic kidney disease and cardiovascular disease in the Medicare population. *Kidney Int Suppl*. 2003;(87):S24–S31.
- Szummer K, Lundman P, Jacobson SH, Schön S, Lindbäck J, Stenström U, Wallentin L, Jernberg T. Influence of renal function on the effects of early revascularization in non-ST elevation myocardial infarction: data from the Swedish WebSystem for Enhancement and

- Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies (SWEDEHEART). *Circulation*. 2009;120:851–858.
8. Sedlis SP, Jurkovic CT, Hartigan PM, Goldfarb DS, Lorin JD, Dada M, Maron DJ, Spertus JA, Mancini GB, Teo KK, et al; COURAGE Study Investigators. Optimal medical therapy with or without percutaneous coronary intervention for patients with stable coronary artery disease and chronic kidney disease. *Am J Cardiol*. 2009;104:1647–1653.
 9. Ix JH, Mercado N, Shlipak MG, Lemos PA, Boersma E, Lindeboom W, O'Neill WW, Wijns W, Serruys PW. Association of chronic kidney disease with clinical outcomes after coronary revascularization: the Arterial Revascularization Therapies Study (ARTS). *Am Heart J*. 2005;149:512–519.
 10. Miao Y, Yu-Jie Z, Zhi-Jian W, Dong-Mei S, Yu-Yang L, Ying-Xin Z, Fei G, Shi-Wei Y, De-An J. Chronic kidney disease and the risk of stent thrombosis after percutaneous coronary intervention with drug-eluting stents. *Catheter Cardiovasc Interv*. 2012;80:361–367.
 11. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, Feldman HI, Kusek JW, Eggers P, Van Lente F, Greene T, Coresh J; CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150:604–612.
 12. Tonelli M, Wiebe N, Culleton B, House A, Rabbat C, Fok M, McAlister F, Garg AX. Chronic kidney disease and mortality risk: a systematic review. *J Am Soc Nephrol*. 2006;17:2034–2047.
 13. Rao SV, Eikelboom JA, Granger CB, Harrington RA, Califf RM, Bassand JP. Bleeding and blood transfusion issues in patients with non-ST-segment elevation acute coronary syndromes. *Eur Heart J*. 2007;28:1193–1204.
 14. Reinius P, Mellbin L, Holzmann MJ, Siddiqui AJ. Percutaneous coronary intervention versus conservative treatment for non ST-segment elevation myocardial infarction in patients above 80 years of age. *Int J Cardiol*. 2018;267:57–61.
 15. Foley RN, Murray AM, Li S, Herzog CA, McBean AM, Eggers PW, Collins AJ. Chronic kidney disease and the risk for cardiovascular disease, renal replacement, and death in the United States Medicare population, 1998 to 1999. *J Am Soc Nephrol*. 2005;16:489–495.
 16. Charytan D, Kuntz RE. The exclusion of patients with chronic kidney disease from clinical trials in coronary artery disease. *Kidney Int*. 2006;70:2021–2030.
 17. Lee JM, Kang J, Lee E, Hwang D, Rhee TM, Park J, Kim HL, Lee SE, Han JK, Yang HM, et al. Chronic kidney disease in the second-generation drug-eluting stent era: pooled analysis of the Korean multicenter drug-eluting stent registry. *JACC Cardiovasc Interv*. 2016;9:2097–2109.
 18. Tegn N, Abdelnoor M, Aaberge L, Endresen K, Smith P, Aakhus S, Gjertsen E, Dahl-Hofseth O, Ranhoff AH, Gullestad L, et al; After Eighty study investigators. Invasive versus conservative strategy in patients aged 80 years or older with non-ST-elevation myocardial infarction or unstable angina pectoris (After Eighty study): an open-label randomised controlled trial. *Lancet*. 2016;387:1057–1065.
 19. Varenne O, Cook S, Sideris G, Kedev S, Cuisset T, Carrié D, Hovasse T, Garot P, El Mahmoud R, Spaulding C, et al; SENIOR investigators. Drug-eluting stents in elderly patients with coronary artery disease (SENIOR): a randomised single-blind trial. *Lancet*. 2018;391:41–50.
 20. Sarno G, Garg S, Onuma Y, Gutierrez-Chico JL, van den Brand MJ, Rensing BJ, Morel MA, Serruys PW. Impact of completeness of revascularization on the five-year outcome in percutaneous coronary intervention and coronary artery bypass graft patients (from the ARTS-II study). *Am J Cardiol*. 2010;106:1369–1375.
 21. Hage FG, Venkataraman R, Zoghbi GJ, Perry GJ, DeMattos AM, Iskandrian AE. The scope of coronary heart disease in patients with chronic kidney disease. *J Am Coll Cardiol*. 2009;53:2129–2140.
 22. Bangalore S, Guo Y, Samadashvili Z, Blecker S, Xu J, Hannan EL. Revascularization in patients with multivessel coronary artery disease and chronic kidney disease: everolimus-eluting stents versus coronary artery bypass graft surgery. *J Am Coll Cardiol*. 2015;15:1209–1220.
 23. Hanna EB, Chen AY, Roe MT, Wiviott SD, Fox CS, Saucedo JF. Characteristics and inhospital outcomes of patients with non-ST-segment elevation myocardial infarction and chronic kidney disease undergoing percutaneous coronary intervention. *JACC Cardiovasc Interv*. 2011;4:1002–1008.
 24. Chhatrivala AK, Amin AP, Kennedy KF, House JA, Cohen DJ, Rao SV, Messenger JC, Marso SP; National Cardiovascular Data Registry. Association between bleeding events and in-hospital mortality after percutaneous coronary intervention. *JAMA*. 2013;309:1022–1029.
 25. Kappetein AP, Feldman TE, Mack MJ, Morice MC, Holmes DR, Stähle E, Dawkins KD, Mohr FW, Serruys PW, Colombo A. Comparison of coronary bypass surgery with drug-eluting stenting for the treatment of left main and/or three-vessel disease: 3-year follow-up of the SYNTAX trial. *Eur Heart J*. 2011;32:2125–2134.
 26. Alam M, Virani SS, Shahzad SA, Siddiqui S, Siddiqui KH, Mumtaz SA, Kleiman NS, Coselli JS, Lakkis NM, Jneid H. Comparison by meta-analysis of percutaneous coronary intervention versus coronary artery bypass grafting in patients with a mean age of ≥ 70 years. *Am J Cardiol*. 2013;112:615–622.
 27. Jernberg T, Attebring MF, Hambraeus K, Ivert T, James S, Jeppsson A, Lagerqvist B, Lindahl B, Stenström U, Wallentin L. The Swedish Web-system for enhancement and development of evidence-based care in heart disease evaluated according to recommended therapies (SWEDEHEART). *Heart*. 2010;96:1617–1621.