

Outcomes in octogenarians undergoing percutaneous coronary intervention: nationwide data from the Netherlands Heart Registration

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ABSTRACT

Background In patients with coronary artery disease, age is of known significance in predicting outcomes. Data on clinical outcomes in patients ≥ 85 years undergoing percutaneous coronary intervention (PCI) remain scarce. The study aim was to determine clinical characteristics, risk of adverse cardiovascular events, and mortality in patients aged ≥ 85 years compared to those aged < 85 undergoing PCI.

Methods In this retrospective study, data were obtained from the nationwide Netherlands Heart Registration on patients undergoing PCI between January 1st, 2017 and January 1st, 2021. The primary endpoint was all-cause mortality at long-term follow-up.

Results A total of 155,683 patients underwent PCI, of which 100,209 (64.4%) acute coronary syndrome cases. Compared to patients aged < 85 years, patients aged ≥ 85 were more often female and showed a higher number of cardiovascular comorbidities, including impaired left ventricle ejection fraction and reduced kidney function. Mortality at short-term and long-term follow-up were significantly higher in those aged ≥ 85 ($P < 0.001$). Patients aged ≥ 85 were more likely to have a myocardial infarction within 30 days following the index intervention (0.9% vs. 0.7%; $P = 0.024$), though they less often underwent revascularization at long-term follow-up compared to patients aged < 85 ($P < 0.001$).

Conclusions The elderly (≥ 85 years) patient requiring PCI carries an extensive cardiovascular risk profile, translating in significant risk of recurrent cardiovascular events and increased mortality rate. Clinicians should carefully weigh perceived risks and potential benefits in the individual patient, considering the patients' age, cardiovascular risk profile, and associated risk of morbidity and mortality.

Advanced age is known to be one of the most predominant cardiovascular risk factors, with coronary artery disease (CAD) being the most common cause of death in patients above middle age.^[1] As advanced age is associated with accumulation of risk factors, co-morbidities, polypharmacy, and decreasing functional and neurocognitive functioning, the elderly patient is subjected to a significant risk of adverse events during hospitalization and any medical intervention.^[2]

Specifically following percutaneous coronary intervention (PCI), some studies report that angiographic success is less likely obtained in very elderly patient (≥ 85 years old), with higher rates of procedural complications and repeat myocardial infarction (MI).^[3–6] This, in turn, translates to mortality rates disproportionally higher in elderly patients.^[4–6] Data regarding clinical outcomes in very elderly patients are scarce, with most studies focusing on outcomes in patients below 80 or 85 years of age. Moreover, the few studies focusing on outcomes in octo-

genarians are mostly observational in nature and of relatively small sample size.^[2,4,7]

With a worldwide ageing population, the absolute number of people aged ≥ 80 years is expected to triple between 2020 and 2050.^[8] In the near future, physicians will be confronted with decision making regarding coronary angiography (CAG) and subsequent PCI in the very elderly patient on a regular basis. This study aimed to investigate clinical characteristics and long-term outcomes in elderly patients undergoing PCI, comparing those with ages < 85 and ≥ 85 years.

METHODS

The Netherlands Heart Registration (NHR) is a nationwide data registry which includes all cardiac invasive procedures, including PCIs as well as electrophysiological and surgical procedures.^[9] The aims of the NHR are to improve quality of care and provide transparency in procedural and clinical outcomes.^[10] Consultation of the NHR database for this study was approved by the local Medical Research Ethics Committee (reference number W19.270) and conducted in agreement with the principles of the Declaration of Helsinki. A waiver for informed consent for analysis of NHR data was obtained via NHRs scientific council. The legal basis is covered by the Healthcare Quality, Complaints and Disputes Act, which obligates healthcare providers to assess and improve their quality.^[10] Definitions of variables are recorded in the data dictionary.^[11]

In this multicenter retrospective cohort, data from patients who underwent a PCI between January 1st 2017 and October 1st 2021 were analyzed. Data were provided by all 29 medical centers in the Netherlands and stored in the NHR database. If a patient underwent more than one procedure in the studied timeframe, the first procedure was included and following procedures were considered part of clinical outcomes.

Study Population

All patients ≥ 18 years old undergoing a PCI in the aforementioned timeframe were included in the present study. Patients were divided into either one of two age groups: < 85 or ≥ 85 years old.

Endpoints

The primary endpoint was long-term all-cause mortality following the index PCI. Secondary endpoints in-

clude MI within 30 days and revascularization (PCI or coronary artery bypass grafting (CABG)) at long-term follow-up. Revascularization procedures were recorded until October 2021, resulting in varying follow-up times throughout the study population.

Statistical Analysis

Categorical variables are expressed as frequencies and percentages and analyzed using the Chi-square test. Continuous variables are depicted as mean $\pm$ SD or median and interquartile range [IQR], depending on data distribution, and analyzed by the Student's *t*-test or Mann-Whitney *U* test. Survival curves were computed using Kaplan-Meier estimates and group comparisons were performed using the Log-rank test. A full-case Cox proportional hazard model was composed by incorporating all variables with significant differences across age groups in the univariable analyses. Cases with missing data points were omitted from analyses of affected parameters. In the Cox regression model, patients with any missing data points in the list of variables were excluded. A *P*-value < 0.05 was considered statistically significant. All statistical analyses were performed using Statistical Package for the Social Sciences (IBM SPSS Statistics, Version 28.0. Armonk, NY: IBM Corp.).

RESULTS

A total of 155,683 patients underwent PCI, of which 54,821 (35.2%) elective cases, and 100,209 (64.4%) acute coronary syndrome (ACS) cases. In the remaining 653 (0.4%), the indication remained unknown. Baseline characteristics are presented in Table 1. The ≥ 85 years group consisted of 7,375 (4.7%) patients, with a mean age of 87 ± 2 years, while the < 85 years group entailed 148,308 (95.3%) patients with a mean age of 66 ± 11 years ($P < 0.001$) (Figure 1). The ≥ 85 years group consisted of a significantly greater proportion of females (46.5% vs. 27.2%; $P < 0.001$) (Table 1). Patients ≥ 85 years were more likely to have worse renal function, decreased left ventricle ejection fraction (LVEF), and more often had a history of previous MI or revascularization procedures.

Angiographic Parameters

Angiographic parameters are presented in Table 2. Patients ≥ 85 years presented more often with ACS, were more likely to have multivessel disease, and less likely to have a chronic total occlusion (Table 2). Placement of an



Table 1 Baseline characteristics.

	Age < 85 yrs <i>n</i> = 148,308		Age ≥ 85 yrs <i>n</i> = 7,375		<i>P</i> -value group difference
	Data availability	Data	Data availability	Data	
Age, yrs	148,308 (100%)	65.6 ± 10.8	7,375 (100%)	87.4 ± 2.4	< 0.001
Female sex	148,306 (100%)	40,317 (27.2%)	7,375 (100%)	3,428 (46.5%)	< 0.001
Creatinin*	122,902 (82.9%)	83 [71-97]	6,137 (83.2%)	94 [76-117]	< 0.001
eGFR	13,880 (93.6%)	76 [62-90]	6,899 (93.5%)	58 [45-71]	< 0.001
Chronic dialysis	129,606 (87.4%)	729 (0.6%)	6,444 (87.4%)	22 (0.3%)	0.019
Diabetes mellitus	145,811 (98.3%)	31,237 (21.4%)	7,213 (97.8%)	1,530 (21.2%)	0.669
LVEF < 35%	59,748 (40.3%)	5,137 (8.6%)	2,981 (40.4%)	301 (10.1%)	0.005
Previous MI	145,702 (98.2%)	27,569 (18.9%)	7,226 (98.0%)	1,640 (22.7%)	< 0.001
Cardiogenic shock	148,006 (99.7%)	4,102 (2.8%)	7,355 (99.7%)	238 (3.2%)	0.018
OHCA	148,078 (99.8%)	5,315 (3.6%)	7,356 (99.7%)	156 (2.1%)	< 0.001
Previous PCI	136,070 (91.7%)	28,598 (21.0%)	6,777 (91.9%)	1,595 (23.5%)	< 0.001
Previous CABG	146,850 (99.0%)	12,138 (8.3%)	7,294 (98.9%)	668 (9.2%)	0.007

Values are depicted as mean ± SD, median [interquartile range], or *n* (%). *Creatinine values of patients on dialysis were not included in analysis. CABG: coronary artery bypass grafting; eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction; MI: myocardial infarction; OHCA: out of hospital cardiac arrest; PCI: percutaneous coronary intervention.

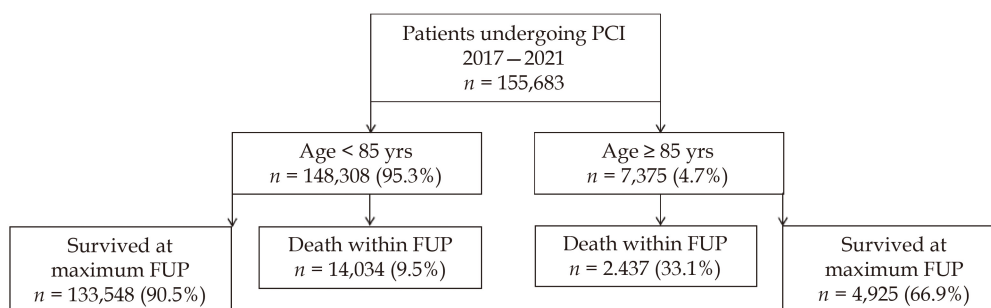


Figure 1 Study flowchart. FUP: follow-up; PCI: percutaneous coronary intervention.

Table 2 Angiographic parameters.

	Age < 85 yrs <i>n</i> = 148,308	Age ≥ 85 yrs <i>n</i> = 7,375	<i>P</i> -value
Elective	52,664 (35.7%)	2,157 (29.4%)	
STEMI	45,143 (30.6%)	2,347 (32.0%)	< 0.001
NSTEMI	49,892 (33.8%)	2,827 (38.6%)	
CTO	7,525 (5.1%)	184 (2.5%)	< 0.001
Multivessel disease	71,057 (49.0%)	4,424 (61.5%)	< 0.001
Radial approach	111,682 (85.8%)	5,320 (81.5%)	< 0.001
Treated vessels			
LM	5,512 (4.2%)	559 (8.5%)	< 0.001
LAD	64,881 (49.1%)	3,413 (52.0%)	< 0.001
RCx	33,214 (25.1%)	1,513 (23.1%)	< 0.001
RCA	47,094 (35.6%)	2,277 (34.7%)	0.131
Arterial/venous graft	2,617 (2.0%)	222 (3.4%)	< 0.001
Stent placement*	124,161 (94.3%)	6,123 (93.3%)	< 0.001

*Including bare metal stent, drug-eluting stent, and bioresorbable scaffold. Values are presented as *n* (%). Data availability is depicted in Supplemental Table 3. ACS: acute coronary syndrome; CTO: chronic total occlusion; LAD: left anterior descending; LM: left main; NSTEMI: non ST-elevation myocardial infarction; RCA: right coronary artery; RCx: ramus circumflex; STEMI: ST-elevation myocardial infarction.

intracoronary stent was less often performed in those ≥ 85 years.

Outcomes

Survival status was available for 154,944 patients (99.5%), with a mean follow-up duration of 870 ± 526 days. Patients ≥ 85 years clearly showed increased mortality rates at long-term follow-up compared to those aged < 85 , with similar differences found at 30 days and 1 year following the index PCI (Table 3, Figure 2). Data on repeat revascularization procedures (PCI or CABG) following the index procedure were available to October 2021, concerning 127,646 (82%) patients. A repeat revascularization procedure was more likely to be performed in those < 85 years (Table 3, Figure 3). When assessing mortality risk at long-term follow-up in a multivariable Cox regression model, age remained a significant contributing factor, together with reduced LVEF, decreased kidney function, presentation with ACS, cardiogenic

shock, and out of hospital cardiac arrest, amongst other factors (Table 4). Stent placement, as well as use of the radial approach (as opposed to any other access site), was associated with a lower mortality risk. Chronic dialysis was a strong predictor of mortality, showing an even higher hazard ratio compared to age (Table 4).

In the very elderly subpopulation (age ≥ 85), data on survival status was available for 7,362 patients (99.8%) with a mean follow-up time of 713 ± 510 days. Survivors were more often female, had better LVEF, and less likely to have suffered from a previous MI, have a history of revascularization, or present with cardiogenic shock (Table 5). Survivors showed lower serum creatinine levels and lower rates of diabetes. Non-survivors aged ≥ 85 years were more likely to suffer from a MI following the index PCI, though not statistically significant. Although myocardial infarction after the index procedure occurred more often in the ≥ 85 years group, revascularization procedures were less often performed (Table 3).

Table 3 Clinical outcomes.

	Age < 85 yrs $n = 148,308$	Age ≥ 85 yrs $n = 7,375$	P-value
Mortality within 30 days	3,651 (2.5%)	527 (7.2%)	< 0.001
Mortality within 1 year	7,415 (5.9%)	1,229 (19.4%)	< 0.001
MI within 30 days	728 (0.7%)	50 (0.9%)	0.024
Revascularization* within 30 days	12,899 (10.5%)	330 (6.3%)	< 0.001
Revascularization* within 1 year	24,564 (20.1%)	656 (12.5%)	< 0.001

Values are depicted as n (%). Data availability is depicted in Supplemental Table 4. *Revascularization included re-PCI or CABG following the index procedure. CABG: coronary artery bypass grafting; MI: myocardial infarction; PCI: percutaneous coronary intervention.

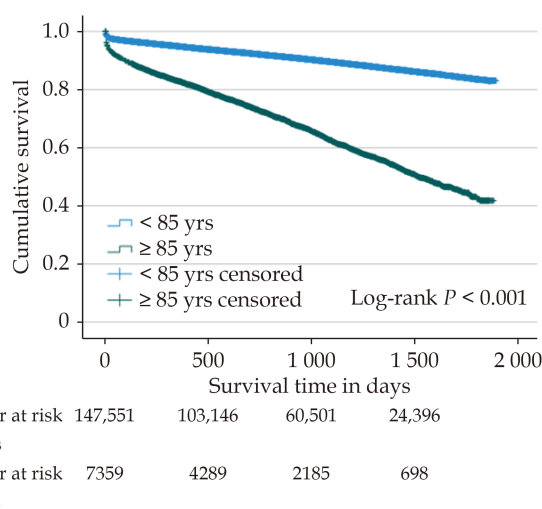


Figure 2 Kaplan-Meier curve depicting all-cause mortality at maximum follow-up. FUP: follow-up; PCI: percutaneous coronary intervention.

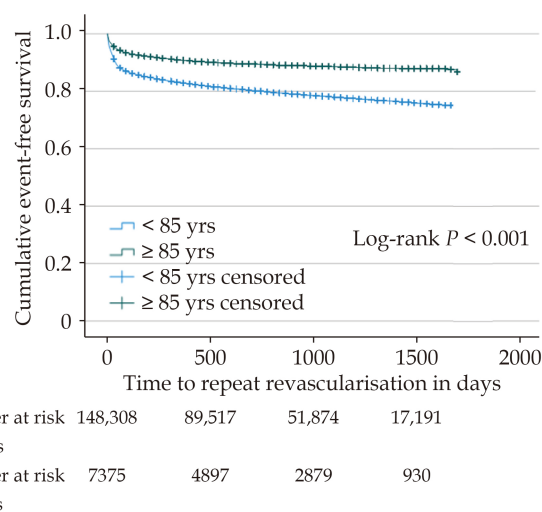


Figure 3 Kaplan-Meier curve depicting revascularization (PCI or CABG) following the index event at maximum follow-up. CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention.



Table 4 Cox proportional multivariable model of all-cause mortality at long-term follow-up.

	Hazard ratio (95% CI)
Age ≥ 85 yrs	3.332 (3.064–3.624)
Female sex	0.980 (0.918–1.045)
Chronic dialysis	4.377 (3.707–5.169)
LVEF < 35%	2.579 (2.400–2.772)
Previous MI	1.270 (1.185–1.362)
Previous PCI	1.034 (0.964–1.108)
Previous CABG	1.174 (1.077–1.279)
Cardiogenic shock	4.522 (3.999–5.114)
OHCA	1.887 (1.640–2.171)
CTO	0.897 (0.798–1.007)
Multivessel disease	1.515 (1.424–1.612)
PCI indication: ACS	1.250 (1.177–1.328)
Radial approach	0.673 (0.629–0.720)
Stent placement	0.721 (0.651–0.799)

Total number of cases included in full-case analysis: 49,857 (32.0%). Values are hazard ratios (95% CI). ACS: acute coronary syndrome; CABG: coronary artery bypass grafting; CTO: chronic total occlusion; MI: myocardial infarction; OHCA: out of hospital cardiac arrest; PCI: percutaneous coronary intervention.

Moreover, revascularization was performed at equal rates in those who did and did not survive. Comparing patients aged ≥ 85 years undergoing an elective PCI versus PCI in case of ACS showed increased mortality and higher repeat revascularization rates in ACS (Supplemental Tables 1 and 2).

DISCUSSION

The present cohort study entails over 150,000 patients who underwent a PCI for ACS or chronic CAD. Patients aged ≥ 85 years more often concerned females, and more frequently underwent PCI in case of ACS, particularly ST-elevation myocardial infarction (STEMI). Patients aged ≥ 85 years showed a more elaborate risk profile, including impaired LVEF, worse renal function, and a history of previous revascularization. Although patients ≥ 85 years were equally likely to suffer from MI within 30 days following the index PCI, they less often underwent a repeat revascularization procedure.

All-cause mortality rates were significantly higher in patients ≥ 85 years compared to those < 85 years, and 19.4% of patients ≥ 85 years died before one-year follow-

Table 5 Characteristics of non-survivors vs. survivors ≥ 85 years.

	Non-survivors <i>n</i> = 2,437	Survivors <i>n</i> = 4,925	<i>P</i> -value
Age, yrs	87 [86–89]	87 [85–88]	< 0.001
Female sex	1,039 (42.6%)	2,384 (48.4%)	< 0.001
Chronic dialysis	16 (0.8%)	6 (0.1%)	< 0.001
Diabetes mellitus	601 (25.4%)	926 (19.2%)	< 0.001
LVEF < 35%	131 (13.5%)	169 (8.4%)	< 0.001
Previous MI	624 (26.2%)	1,011 (20.9%)	< 0.001
Cardiogenic shock	154 (6.4%)	84 (1.7%)	< 0.001
OHCA	77 (3.2%)	79 (1.6%)	< 0.001
Previous PCI	513 (24.1%)	1,079 (23.3%)	0.442
Previous CABG	276 (11.5%)	392 (8.0%)	< 0.001
PCI indication ACS	1,794 (74.0%)	3,370 (68.8%)	< 0.001
Multivessel disease	1,549 (64.5%)	2,863 (59.8%)	< 0.001
CTO	67 (2.8%)	117 (2.4%)	0.318
Radial approach	1,532 (76.8%)	3,777 (83.6%)	< 0.001
Stent placed	1,806 (90.0%)	4,304 (94.8%)	< 0.001
MI within 30 days	22 (1.2%)	28 (0.8%)	0.083
Revascularization* within 30 days	81 (6.4%)	249 (6.3%)	0.870
Revascularization* within 1 year	166 (13.1%)	490 (12.3%)	0.465

Values are depicted as mean ± SD or *n* (%). ACS: acute coronary syndrome; CABG: coronary artery bypass grafting; CTO: chronic total occlusion; LVEF: left ventricular ejection fraction; OHCA: out of hospital cardiac arrest; PCI: percutaneous coronary intervention.



up. Advanced age remained strongly associated with an increased risk of mortality in the multivariable Cox regression analysis.

Our results on distribution of patient demographics and risk factors are similar to the results from Appleby and colleagues, describing a larger proportion of female patients in those aged ≥ 85 years, as well as higher prevalence of renal insufficiency, and higher rate of presentation with ACS.^[4] Their study showed a more than tripled chance of in-hospital death and major adverse cardiac events (MACE) in the ≥ 85 group as compared to patients aged < 85 years, similar to the current results, showing close to a three- and nearly a four-fold risk of mortality in the ≥ 85 group at 30 days and 1 year, respectively. When focusing on the subgroup aged ≥ 85 , the current study showed a lower risk of mortality in those receiving stent placement during the index procedure. Survivors more often presented with stable CAD and in case of ACS, with non-ST-elevation myocardial infarction (NSTEMI).

Higher mortality rates in the advanced age group are expected due to two explanations. First, the all-cause mortality risk increases significantly with advancing age, in part due to the increased prevalence of risk factors and comorbidities. Second, elderly patients may be more likely to suffer from serious complications following interventions. The latter statement is supported by a recent study by Saada and colleagues, a large multi-center study comparing patients aged below and above 80 years undergoing PCI.^[12] Their results showed a higher rate of target lesion failure and target vessel related MI in patients aged > 80 , as well as a doubled risk of mortality after correcting for known confounders. On a similar note, very elderly patients are less likely considered good candidates for CABG due to more elaborate cardiovascular risk profiles and high complexity lesions.^[13] While surgical ineligibility on its own is associated with worse outcomes, complex lesions predispose the already frail patient to an increased risk of complications and death if revascularization is attempted.^[14] In a recent study by Kunadian, patients from a wider age range (75 years or older presenting with STEMI) were randomized to conservative or invasive management.^[14] They concluded that the invasive strategy, entailing to revascularization plus optimal medical therapy (OMT), did not result in differences in the composite endpoint of cardiovascular death and non-fatal MI when compared to OMT alone. Important to note, however, is that in Kunadian's study

revascularization was performed rather late following the event (3-7 days), and details on the exact indication for revascularization (based on which extent of stenosis and how this was assessed) were not described. In a recent systematic review and meta-analysis, patients aged ≥ 75 years old whom presented with NSTEMI and were subjected to an invasive management strategy showed a reduced risk of repeat MI.^[15] All-cause mortality and cardiovascular mortality rates, however, did not differ from patients who were conservatively managed. In the narrative review by Verardi and colleagues, the authors elaborate that the contribution of primary PCI to survival, even in very elderly patients, is clearly established for STEMI cases.^[16] The benefit of PCI in NSTEMI cases, on the other hand, is less evident. Thus, although the current results demonstrate a survival benefit associated with stent placement—at least during the index event—this benefit may be at least partially attributable to its interaction with the indication for revascularization. This is supported by the obvious worse outcomes in ACS patients versus elective PCI in the current data. The results from previous studies, even though descending from studies using different age groups, propose a critical view on the added benefit of invasive management in elderly patients presenting with MI, and suggest that the main benefit of PCI may not be found in terms of improved survival. One may conclude that these findings, together with the current results, advocate for careful decision making and pose a rather reluctant attitude towards invasive procedures performed in the very elderly. Moreover, when using the term “elderly patients”, one should be aware that each age subgroup may show a different composition of patient characteristics and concomitant risk of complications and mortality, and indices of frailty should be taken into account when weighing risks and benefits in the individual patient.

Clinicians will continue to face the challenge of decision-making in the growing elderly patient population presenting with an indication for PCI. When estimating the risk of complications in an individual patient, advanced age should obviously not be considered the single factor driving the decision to subject a patient to or withhold from a PCI. The current study showed that, besides advanced age, presentation with cardiogenic shock, reduced LVEF, and a previous MI, amongst other factors, are also associated with worse chances of survival. Presentation with cardiogenic shock showed a haz-



ard ratio of 4.52 in a multivariable regression model including aforementioned covariates, suggesting a strong association with mortality risk. The 2021 AHA guidelines on coronary artery revascularization recommend to consult the Heart team to carefully weigh risks and benefits for patients with advanced age (≥ 75 years), taking patients' preferences into account and employ shared decision-making.^[17] While these general propositions remain valid, the guidelines are mostly based on outdated studies^[7,18,19] and studies comparing stent placement with CABG.^[20–22] Moreover, while knowledge on the interactions between cardiovascular risk factors increase over time, prevalence of known risk factors may vary significantly throughout the years, affecting morbidity and mortality in short- and long-term.^[23]

Limitations

When interpreting the current study results, a few limitations should be considered. Due to the nature of the study, a retrospective analysis of prospectively collected data, the presence of bias cannot be excluded, and association does not indicate the presence of a causal relationship. For example, selection bias could have occurred in the decision to subject a patient to PCI or to opt for conservative treatment instead. The absence of a conservatively managed patient group omitted analysis on the added benefit of invasive management in the (very) elderly. A potential source of bias to consider is limited data availability in some variables. This includes myocardial infarction following the index event, which might remain undetected if diagnosed in a hospital different from the index event. In the Cox regression model specifically, patients with any missing data points in the list of variables were excluded which resulted in a relatively small proportion of the total population included in the model, thereby potentially introducing selection bias.

Moreover, a limited set of variables was recorded in this national registry. For example, data on the presence of hypertension and hypercholesterolemia, and a history of stroke or transient ischemic attack were unavailable. In addition, variables related to complications related to the index PCI, such as coronary embolism, stent malapposition, and coronary artery dissection, were not registered.

Besides data availability of predefined variables, the presence of unmeasured confounders may have affected the current study results. For example, indices of physical and cognitive functioning, or frailty, were not available. Frailty, defined as a state of increased vulnerability

resulting from ageing-associated decline in physiologic reserve and functioning, is associated with an increased risk of procedural complications and mortality.^[24,25] Outcomes in a conservatively managed elderly patient group and comparison to those undergoing PCI should be performed while taking these frailty indices into account. Future studies should aim for a holistic approach, incorporating indices of frailty as part of patient characteristics to improve insight in procedural and mortality risk.

In conclusion, the elderly (≥ 85 years) patient undergoing PCI for either stable CAD or ACS carries an extensive cardiovascular risk profile, translating in significant risk of future cardiovascular events and mortality. Clinicians should carefully weigh perceived risks and potential benefits in the individual patient, considering the patients' age and associated risk of morbidity and mortality.

DISCLOSURE

Conflict of Interest

A.W.J. van 't Hof has received unrestricted grants from AstraZeneca, Medtronic, Abbott Vascular and Boehringer Ingelheim and is an associate editor of the Netherlands Heart Journal. The other authors report no competing interests or disclosures.

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