

Does the subtype of acute coronary syndrome treated by percutaneous coronary intervention predict long-term clinical outcomes?

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Aims

The prognosis of patients undergoing percutaneous coronary intervention (PCI) for different subtypes of acute coronary syndromes (ACS) remains unclear. We compared short- and long-term mortality in patients undergoing PCI for unstable angina (UA), non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI).

Methods and results

This was a retrospective cohort study of 13 184 patients (5966 STEMI, 5307 NSTEMI, and 1911 UA) undergoing PCI between 1 January 2005 and 30 November 2013 in a multi-centre registry. Clinical and procedural characteristics, as well as outcomes, were compared by ACS subtype. Long-term all-cause mortality data were obtained via linkage to the National Death Index (NDI). Patients with STEMI compared with NSTEMI and UA were younger (62.9 ± 12.8 vs. 64.7 ± 12.5 vs. 65.5 ± 11.8 years; $P < 0.01$), had fewer comorbidities including diabetes, heart failure, and previous myocardial infarction (all $P < 0.01$). Procedural success was similar across all groups ($P = 0.54$). In-hospital, 30-day and 1-year all-cause mortality increased significantly from UA to NSTEMI to STEMI patients (1-year mortality 2.5% vs. 4.5% vs. 8.7%; $P < 0.01$). Kaplan–Meier survival estimates showed increased early mortality in the STEMI group (log-rank $P < 0.01$). However, after approximately 8.2 years, survival was similar across all groups. In a proportional-odds model using flexible parametric survival modelling, ACS subtype was not an independent predictor of NDI-linked mortality [UA: odds ratio (OR) 0.85, 95% CI 0.71–1.02; STEMI: OR 1.01, 95% confidence interval (CI) 0.88–1.16; NSTEMI as reference category].

Conclusion

Despite disparate baseline characteristics and differences in short-term mortality, long-term mortality was similar across the spectrum of ACS treated by PCI and contemporary medical therapy.

Keywords

Acute coronary syndrome • Percutaneous coronary intervention • Outcomes

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Introduction

Acute coronary syndromes (ACS) comprise a spectrum of clinical manifestations of coronary artery disease (CAD) ranging from unstable angina (UA), to non-ST-elevation myocardial infarction (NSTEMI) and finally to ST-elevation myocardial infarction (STEMI). Despite marked improvements in the prevention and management of CAD, ACS remains a major cause of morbidity and mortality in most countries.¹ Additionally, there remains significant uncertainty with respect to the long-term prognosis of the different subtypes of ACS particularly in the contemporary era of percutaneous coronary intervention (PCI) and adjunctive medical therapies. Previous studies comparing mortality following different subtypes of ACS have reported conflicting results. Several studies have shown that patients presenting with a STEMI experience a higher early mortality risk.^{2–4} However, different studies have reported both a higher, comparable or lower long-term mortality rate for patients presenting with a NSTEMI, compared with the STEMI group.^{2,4–8} Most of these studies have included a heterogeneous population of patients presenting with ACS, with varying proportions treated with an invasive strategy, with or without PCI. As increasing numbers of PCI are being performed for ACS indications these studies may not necessarily reflect contemporary clinical practice.⁹ Awareness regarding the importance of adherence to secondary prevention therapy in ACS has also increased which may positively impact on long-term outcomes in a contemporary cohort.¹⁰

In this study, we sought to evaluate short- and long-term clinical outcomes after PCI in patients enrolled in a multi-centre PCI registry across the spectrum of ACS.

Methods

This was a retrospective cohort study of patients undergoing PCI for ACS between 1 January 2005 and 30 November 2013 inclusive, enrolled prospectively in the Melbourne Interventional Group (MIG) registry. All consecutive adult patients undergoing PCI for ACS were eligible for inclusion. We excluded patients with a non-ACS or missing indication for PCI, and also patients in whom linkage to the Australian National Death Index (NDI) mortality database could not be considered due to incomplete case information at the time the registry data were sent for linkage, to derive our final study cohort (Figure 1). There were no differences in distribution of ACS subtype between the patients excluded from consideration for NDI linkage and the study cohort that was used ($P = 0.24$).

The MIG registry is a multicentre Australian PCI registry and has been previously described in detail.¹¹ Briefly, demographic, clinical, procedural and in-hospital outcome data are prospectively recorded on case-report forms using standardized definitions for all fields. Relevant information for 30-day and 12-month outcomes were obtained through telephone follow-up, and medical records were reviewed to verify events in patients who reported any events.¹² There are six participating hospitals located in metropolitan Melbourne and regional Victoria, that all have 24-h cardiac catheterization laboratory services. The primary ethics approval has been granted by the ethics committee at The Alfred Hospital (approval number 92/04), and also approved by each participating hospital, including the use of 'opt-out' consent as previously described.^{11,12}

Patients were divided into three groups according to the subtype of ACS (UA, NSTEMI, and STEMI) diagnosed on admission by the treating physician based on history, electrocardiography, and biochemical testing.

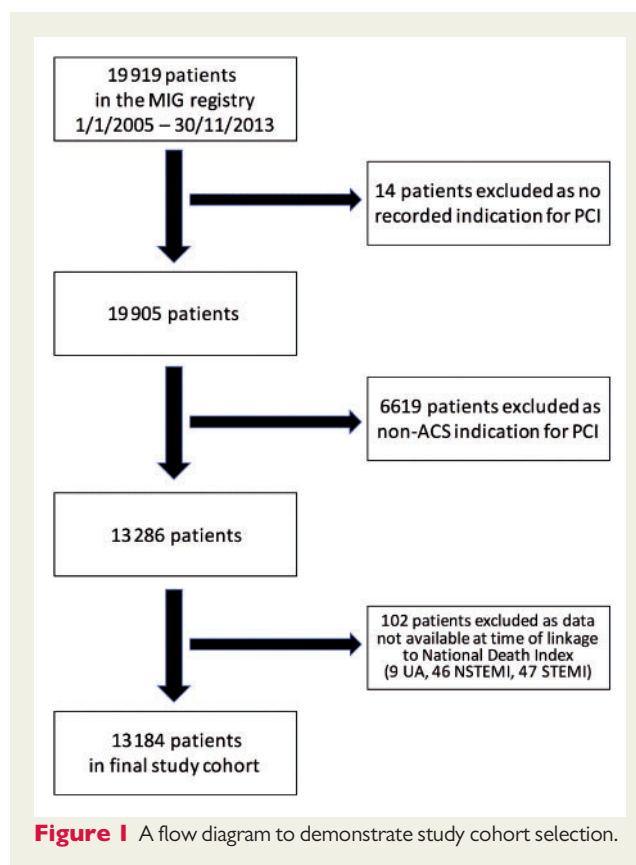


Figure 1 A flow diagram to demonstrate study cohort selection.

Baseline and procedural characteristics, as well as in-hospital, 30-day and 12-month clinical outcomes were compared across the groups (definitions shown in [Supplementary material online, Table S1](#)). Use of antiplatelet therapy, beta-blockers, angiotensin converting enzyme inhibitors (ACEi)/angiotensin receptor blockers (ARB), and cholesterol-lowering therapies (statins, fibrates, and ezetimibe) at 30 days and 12 months after the index, and PCI were also compared between the groups. Prescription of post-discharge medications was at the discretion of the treating physician according to contemporary guidelines.

Long-term mortality data were obtained by linkage to the Australian NDI, a database housed at the Australian Institute of Health and Welfare that contains records of all deaths occurring in Australia since 1980. The censoring date for linkage with the NDI in this study was 30 July 2014. Successful matching of patients through this linkage process was achieved in 99.4% of all patients in the MIG registry. The primary endpoint was NDI-linked mortality. Secondary endpoints included myocardial infarction (MI), target-vessel revascularization (TVR), and major adverse cardiovascular events (MACE). Major adverse cardiovascular event was defined as a composite of death, MI, and TVR.

Continuous variables are expressed as mean \pm standard deviation and were compared using Kruskal–Wallis equality-of-populations rank test. Categorical data are expressed as numbers and percentages, and were compared using Pearson's χ^2 test or Fisher's exact test as appropriate. The Kaplan–Meier method was used to estimate event-free survival rates and the log-rank test was used for survival comparisons. To determine whether ACS subtype was an independent predictor of the primary endpoint of NDI-linked mortality, in addition to ACS subtype, 28 other clinically relevant variables were considered. Those with a P -value of <0.1 on univariate analysis that were not co-linear were entered into a stepwise backwards selection modelling process for multivariable assessment ([Supplementary material online, Table S2](#)). Cox proportional hazard

Table 1 Baseline characteristics of patients by acute coronary syndrome subtype

	Total	UA	NSTEMI	STEMI	P-value
<i>n</i>	13 184	1911	5307	5966	
Age (years), mean \pm SD		65.5 \pm 11.8	64.7 \pm 12.5	62.9 \pm 12.8	<0.001
Male, <i>n</i> (%)	9949 (75.5)	1367 (71.5)	3968 (74.8)	4614 (77.3)	<0.001
BMI (kg/m ²), mean \pm SD		28.4 \pm 5.3	28.6 \pm 5.5	27.8 \pm 5.0	<0.001
BMI <20 (kg/m ²), <i>n</i> (%)	290 (2.7)	29 (1.9)	120 (2.7)	141 (2.9)	<0.001
BMI 20–24.9 (kg/m ²), <i>n</i> (%)	2776 (25.5)	373 (24.6)	1074 (23.8)	1329 (27.2)	
BMI 25–29.9 (kg/m ²), <i>n</i> (%)	4444 (40.7)	635 (41.9)	1761 (39.1)	2048 (41.9)	
BMI \geq 30 (kg/m ²), <i>n</i> (%)	3399 (31.2)	480 (31.6)	1554 (34.5)	1365 (28.0)	
Current smoker, <i>n</i> (%)	3964 (30.3)	348 (18.3)	1466 (27.7)	2150 (36.4)	<0.001
Ex-smoker, <i>n</i> (%)	4902 (37.4)	931 (48.9)	2147 (40.6)	1824 (30.9)	
Never smoked, <i>n</i> (%)	4233 (32.3)	626 (32.9)	1671 (31.6)	1936 (32.8)	
Chronic obstructive pulmonary disease, <i>n</i> (%)	1335 (10.2)	239 (12.6)	594 (11.3)	502 (8.4)	<0.001
Hypertension, <i>n</i> (%)	8139 (61.8)	1441 (75.4)	3533 (66.6)	3165 (53.1)	<0.001
Dyslipidaemia, <i>n</i> (%)	8397 (63.9)	1514 (79.4)	3764 (71.1)	3119 (52.5)	<0.001
Diabetes mellitus, <i>n</i> (%)	3010 (22.9)	565 (29.6)	1418 (26.7)	1027 (17.2)	<0.001
Diabetes, <i>n</i> (%)					
Not on insulin	2298 (17.4)	436 (22.8)	1058 (19.9)	804 (13.5)	<0.001
On insulin	712 (5.4)	129 (6.8)	360 (6.8)	223 (3.7)	
eGFR >60 mL/min/1.73 m ² , <i>n</i> (%)	9837 (76.6)	1438 (76.2)	4034 (76.7)	4365 (76.6)	<0.001
eGFR 30–60 mL/min/1.73 m ² , <i>n</i> (%)	2578 (20.1)	389 (20.6)	1006 (19.1)	1183 (20.8)	
eGFR <30 mL/min/1.73 m ² , <i>n</i> (%)	426 (3.3)	60 (3.2)	217 (4.1)	149 (2.6)	
Dialysis, <i>n</i> (%)	174 (1.3)	25 (1.3)	122 (2.3)	27 (0.5)	<0.001
Stroke, <i>n</i> (%)	821 (6.2)	149 (7.8)	377 (7.1)	295 (5.0)	<0.001
Peripheral vascular disease, <i>n</i> (%)	787 (6.0)	134 (7.0)	424 (8.0)	229 (3.9)	<0.001
Obstructive sleep apnoea, <i>n</i> (%)	432 (3.3)	79 (4.1)	212 (4.0)	141 (2.4)	<0.001
Previous MI, <i>n</i> (%)	2796 (21.2)	723 (37.9)	1276 (24.1)	797 (13.4)	<0.001
Previous PCI, <i>n</i> (%)	2368 (18.0)	677 (35.5)	965 (18.2)	726 (12.2)	<0.001
Previous CABG, <i>n</i> (%)	887 (6.7)	263 (13.8)	480 (9.0)	144 (2.4)	<0.001
Previous heart failure, <i>n</i> (%)	456 (3.5)	85 (4.5)	258 (4.9)	113 (1.9)	<0.001
Family history of CAD, <i>n</i> (%)	4920 (37.8)	751 (39.8)	2078 (39.5)	2091 (35.6)	<0.001

BMI, body mass index; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft surgery; CAD, coronary artery disease.

modelling was initially considered but it failed the proportional hazards assumption (global test $P < 0.001$). Of the other models considered, proportional-odds model using flexible parametric survival modelling with 10 degrees of freedom for spline function appeared to be the best model (log likelihood = -5770.5), and was therefore, used in this study (Supplementary material online, Table S3). Multivariable analysis and Kaplan–Meier analysis were performed for the whole patient cohort, as well as after exclusion of patients post out-of-hospital cardiac arrest (OHCA) or with cardiogenic shock, as it is recognized that this patient subgroup has high early mortality, which therefore, could skew the data. The proportion of missing data was <1% for all but 5 baseline variables: body mass index (17.3%), left ventricular ejection fraction (10.5%), estimated glomerular filtration rate (2.6%), family history of CAD (1.2%), and no-reflow (6.9%), as well as all 12-month outcomes (4.1%) (Supplementary material online, Table S4). Complete case analysis was performed for purposes of multivariable modelling (i.e. patients with missing values were excluded).

All statistical analyses were performed using Stata 13.1 software (StataCorp LP, College Station, TX, USA). P -values of <0.05 were considered to be statistically significant.

Results

In total, 13 184 patients undergoing PCI were included in this study, of which, 5966 patients presented with STEMI, 5307 patients with NSTEMI, and 1911 patients with UA.

Baseline characteristics

The baseline characteristics of the patients in this study are shown in Table 1. Patients in the STEMI group were younger (62.9 ± 12.8 vs. 64.7 ± 12.5 vs. 65.5 ± 11.8 years; $P < 0.01$) and included more males [4614 (77.3%) vs. 3968 (74.8%) vs. 1367 (71.5%); $P < 0.01$] than those in the NSTEMI and UA groups. However, patients with UA and NSTEMI had more comorbidities than patients with STEMI, such as diabetes mellitus, severe renal impairment, obstructive sleep apnoea, and peripheral vascular disease (all $P < 0.01$). A history of previous stroke, MI, PCI, or coronary artery bypass graft surgery (CABG), as well as a family history of CAD, were all more prevalent among patients with UA and NSTEMI than those with STEMI (all $P < 0.01$).

Table 2 Presentation and percutaneous coronary intervention characteristics by acute coronary syndrome subtype

	Total	UA	NSTEMI	STEMI	P-value
<i>n</i>	13 184	1911	5307	5966	
Out-of-hospital cardiac arrest, <i>n</i> (%)	473 (3.6)	6 (0.3)	67 (1.3)	400 (6.7)	<0.001
Cardiogenic shock, <i>n</i> (%)	636 (4.8)	3 (0.2)	67 (1.3)	566 (9.5)	<0.001
Multi-vessel disease, <i>n</i> (%)	7508 (57.2)	1157 (61.0)	3084 (58.3)	3267 (54.9)	<0.001
Left main disease, <i>n</i> (%)	272 (7.4)	37 (7.5)	116 (7.6)	119 (7.2)	0.892
Left ventricular ejection fraction >45%, <i>n</i> (%)	8278 (70.1)	1312 (84.0)	3678 (77.6)	3288 (59.7)	<0.001
Left ventricular ejection fraction 30–45%, <i>n</i> (%)	3199 (27.1)	223 (14.3)	955 (20.2)	2021 (36.7)	
Left ventricular ejection fraction <30%, <i>n</i> (%)	327 (2.8)	27 (1.7)	105 (2.2)	195 (3.5)	
Total number of lesions treated	15 519	2279 (14.6)	6279 (40.5)	6970 (44.9)	
AHA/ACC B2/C lesion, <i>n</i> (%)	9153 (59.0)	1047 (46.1)	3262 (52.0)	4844 (69.5)	<0.001
Vessel treated					
Left main, <i>n</i> (%)	140 (0.9)	27 (1.2)	63 (1.0)	50 (0.7)	0.065
Left anterior descending, <i>n</i> (%)	5372 (34.6)	772 (34.0)	1991 (31.7)	2609 (37.4)	<0.001
Left circumflex, <i>n</i> (%)	2006 (12.9)	299 (13.2)	1037 (16.5)	670 (9.6)	<0.001
Right, <i>n</i> (%)	5177 (33.4)	665 (29.3)	1802 (28.7)	2710 (38.9)	<0.001
Chronic total occlusion, <i>n</i> (%)	339 (2.2)	57 (2.5)	187 (3.0)	95 (1.4)	<0.001
Bifurcation lesion, <i>n</i> (%)	1677 (10.8)	273 (12.0)	703 (11.2)	701 (10.1)	0.014
Pre-PCI TIMI flow 0–1, <i>n</i> (%)	5342 (34.6)	179 (8.0)	1038 (16.6)	4125 (59.4)	<0.001
Post-PCI TIMI flow 3, <i>n</i> (%)	14 774 (95.3)	2220 (97.9)	6059 (96.6)	6495 (93.3)	<0.001
PCI complications					
Acute closure, <i>n</i> (%)	128 (0.8)	15 (0.7)	49 (0.8)	64 (0.9)	0.439
Dissection, <i>n</i> (%)	34 (0.2)	4 (0.2)	15 (0.2)	15 (0.2)	0.857
Perforation, <i>n</i> (%)	34 (0.2)	3 (0.1)	18 (0.3)	13 (0.2)	0.296
Transient no reflow, <i>n</i> (%)	550 (3.8)	33 (1.7)	184 (3.1)	333 (5.1)	<0.001
Persistent no reflow, <i>n</i> (%)	135 (0.9)	8 (0.4)	33 (0.6)	94 (1.4)	
Drug-eluting stent, <i>n</i> (%)	5442 (41.3)	984 (51.5)	2507 (47.2)	1951 (32.7)	<0.001
Bare-metal stent, <i>n</i> (%)	6992 (53.0)	830 (43.4)	2545 (48.0)	3617 (60.6)	
Balloon angioplasty, <i>n</i> (%)	750 (5.7)	97 (5.1)	255 (4.8)	398 (6.7)	
Failed PCI, <i>n</i> (%)	33 (0.3)	7 (0.4)	12 (0.2)	14 (0.2)	0.543

PCI, percutaneous coronary intervention.

Procedural characteristics

A comparison of the PCI characteristics of the study patients is shown in Table 2. There were significantly more patients presenting following OHCA, with cardiogenic shock in the STEMI group, compared with the other two groups (all $P < 0.01$). Patients with UA were more likely to have multi-vessel disease, while more AHA/ACC B2/C class lesions were treated in the STEMI group (all $P < 0.01$). The proportion of failed PCI cases was <0.5% and similar across all groups ($P = 0.54$).

Outcomes

In-hospital, 30-day and 12-month outcomes for the three groups are shown in Table 3. In-hospital mortality and MACE were both significantly higher for the STEMI group compared with the NSTEMI and UA groups [327 (5.5%) vs. 71 (1.3%) vs. 5 (0.3%); $P < 0.01$ and 467 (7.8%) vs. 163 (3.1%) vs. 33 (1.7%); $P < 0.01$, respectively]. Of all deaths, the proportion of cardiac deaths was higher in the STEMI and UA groups, than the NSTEMI group (85.6% and 80.0%, respectively vs. 69.0%; $P < 0.01$). Other in-hospital complications such as stent thrombosis, heart failure, and stroke were all significantly more

common in the STEMI group compared with the other two groups (all $P < 0.01$).

Of the 12 781 patients discharged alive, 30-day follow-up was completed in 12 730 (99.6%) patients, while of the 12 715 patients alive at 30-days, 12-month follow-up was completed in 12 150 (95.6%) patients. At both 30-day and 12-month follow-up, there was a stepwise increase in all-cause mortality from patients in the UA, to the NSTEMI, to the STEMI group. However, between 30-day and 12-month follow-up, the rate of all-cause mortality increased by 257% [13 (0.7%)–47 (2.5%)] and 181% [87 (1.6%)–231 (4.5%)] in the UA and NSTEMI groups, respectively, but only increased by 40% [369 (6.2%)–497 (8.7%)] in the STEMI group. Patients in the STEMI group were more likely to have had a cardiac cause of death, than in the other two groups ($P < 0.01$). While heart failure was still more common in the STEMI patients at 30-day follow-up ($P < 0.01$), by 12 months, the incidence of complications like stroke, heart failure and TVR was similar across all three groups (all $P = \text{NS}$).

Long-term mortality

All-cause mortality data obtained using linkage with the NDI database showed a similar proportion of deaths in each of the three

Table 3 In-hospital, 30-day and 12-month outcomes by acute coronary syndrome subtype

	UA	NSTEMI	STEMI	P-value
In-hospital outcomes				
Death, <i>n</i> (%)	5 (0.3)	71 (1.3)	327 (5.5)	<0.001
Cardiac death, <i>n</i> (%)	4 (0.2)	49 (0.9)	280 (4.7)	0.003
MI, <i>n</i> (%)	24 (1.3)	48 (0.9)	69 (1.2)	0.306
Stent thrombosis, <i>n</i> (%)	3 (0.2)	10 (0.3)	48 (1.0)	<0.001
Heart failure, <i>n</i> (%)	18 (0.9)	143 (2.7)	523 (8.8)	<0.001
Stroke, <i>n</i> (%)	2 (0.1)	13 (0.3)	36 (0.6)	0.001
MACE, <i>n</i> (%)	33 (1.7)	163 (3.1)	467 (7.8)	<0.001
30-day outcomes				
Death, <i>n</i> (%)	13 (0.7)	87 (1.6)	369 (6.2)	<0.001
Cardiac death, <i>n</i> (%)	10 (0.5)	56 (1.1)	307 (5.2)	<0.001
Readmission for MI, <i>n</i> (%)	12 (0.6)	70 (1.3)	50 (0.8)	0.008
Readmission for heart failure, <i>n</i> (%)	15 (0.8)	34 (0.6)	76 (1.3)	0.002
Readmission for stroke, <i>n</i> (%)	0 (0.0)	12 (0.2)	11 (0.2)	0.123
Readmission for revascularization, <i>n</i> (%)	59 (3.1)	256 (4.8)	270 (4.6)	0.006
MACE, <i>n</i> (%)	58 (3.0)	267 (5.1)	583 (9.8)	<0.001
12-month outcomes				
Death, <i>n</i> (%)	47 (2.5)	231 (4.5)	497 (8.7)	<0.001
Cardiac death, <i>n</i> (%)	22 (1.2)	120 (2.4)	346 (6.1)	<0.001
Readmission for MI, <i>n</i> (%)	64 (3.5)	283 (5.6)	165 (2.9)	<0.001
Readmission for heart failure, <i>n</i> (%)	53 (2.9)	139 (2.7)	171 (3.0)	0.710
Readmission for stroke, <i>n</i> (%)	11 (0.6)	36 (0.7)	42 (0.7)	0.817
Readmission for revascularization, <i>n</i> (%)	251 (13.6)	621 (12.2)	717 (12.6)	0.320
MACE, <i>n</i> (%)	230 (12.4)	694 (13.6)	975 (17.1)	<0.001

MI, myocardial infarction; MACE, major adverse cardiovascular event (composite of death, MI, and revascularization).

groups [966 (16.2%) in STEMI vs. 813 (15.3%) in NSTEMI vs. 277 (14.5%) in UA; $P=0.16$]. Compared with NSTEMI as the reference group, unadjusted hazard ratios for UA and STEMI were 0.85 [95% confidence interval (CI) 0.74–0.97] and 1.09 (95% CI 1.00–1.20), respectively (Supplementary material online, Table S2). The Kaplan–Meier survival curves for the three groups are shown in Figure 2. Patients in the STEMI group had higher early mortality than the NSTEMI and UA groups (log-rank $P<0.01$). However, after approximately 8.2 years, survival was similar across all three groups with convergence and overlap of the curves. When these analyses were repeated after exclusion of patients with cardiogenic shock and post-OHCA, the STEMI group had the lowest long-term all-cause mortality, followed by UA and then the NSTEMI group [645 (12.4%) in STEMI vs. 755 (14.6%) in NSTEMI vs. 274 (14.4%) in UA; $P<0.01$]. Kaplan–Meier survival curves for these patients (Figure 3) showed that while patients presenting with STEMI without shock or post-OHCA still experience high early mortality, the STEMI and NSTEMI curves overlap much earlier at less than 2 years from the time of index PCI.

In a proportional-odds model using flexible parametric survival modelling analysis, the subtype of ACS was not found to be an independent predictor of long-term NDI-linked mortality [UA: odds ratio (OR) 0.85, 95% CI 0.71–1.02; STEMI: OR 1.01, 95% CI 0.88–1.16; NSTEMI as reference category] (Table 4). The three strongest predictors of long-term NDI-linked mortality were cardiogenic shock at

presentation, a history of Stage 4–5 chronic kidney disease (eGFR <30 mL/min/1.73 m²) and severe left ventricular systolic dysfunction (ejection fraction $<30\%$; OR 5.72, 5.58, and 4.63, respectively). Age (per year increase) was also shown to be a strong predictor of long-term mortality (OR 1.06, 95% CI 1.06–1.07). Even with patients with shock or post-OHCA excluded, the subtype of ACS was not an independent predictor of long-term mortality in our cohort (Supplementary material online, Table S5).

Secondary prevention therapy

Medication use by patients in each of the ACS subgroups at 30 days and 12 months is shown in Table 5. At 30 days post ACS, the use of dual antiplatelet therapy was lower in patients presenting with STEMI compared with those presenting with NSTEMI and UA [4567 (86.0%) vs. 4273 (87.9%) vs. 1623 (90.4%); $P<0.01$]. The use of other secondary prevention therapy such as beta-blockers, ACEi/ARBs, and statins were all significantly higher in patients with STEMI compared with patients with NSTEMI and UA (all $P<0.01$). At 12 months, the differences in dual antiplatelet therapy use across the ACS subgroups were no longer seen [2906 (60.7%) vs. 2680 (61.0%) vs. 1014 (62.6%); $P=0.39$] but the use of the other secondary prevention medications continued to be significantly greater in the STEMI group, compared with the NSTEMI and UA groups (all $P<0.01$).

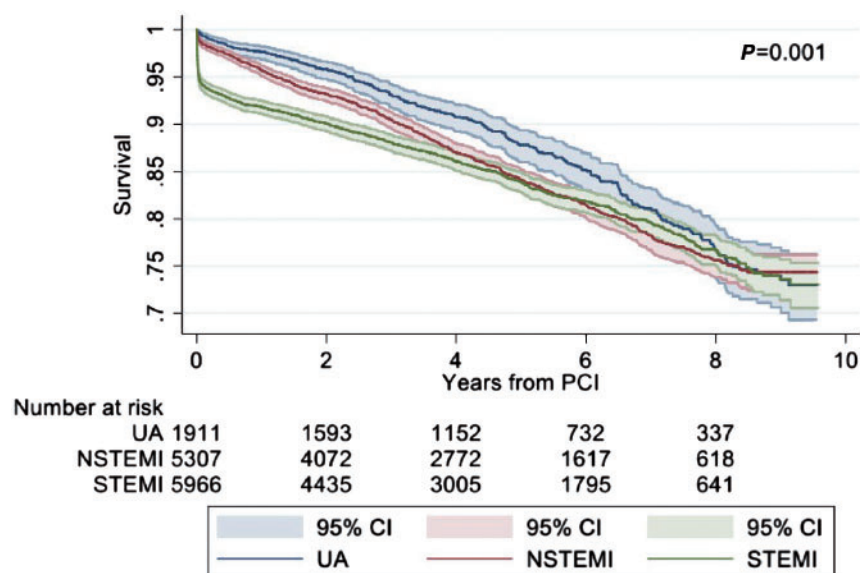


Figure 2 Unadjusted Kaplan-Meier survival analysis by subtype of acute coronary syndrome. PCI, percutaneous coronary intervention; NSTEMI, non-ST elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; UA, unstable angina.

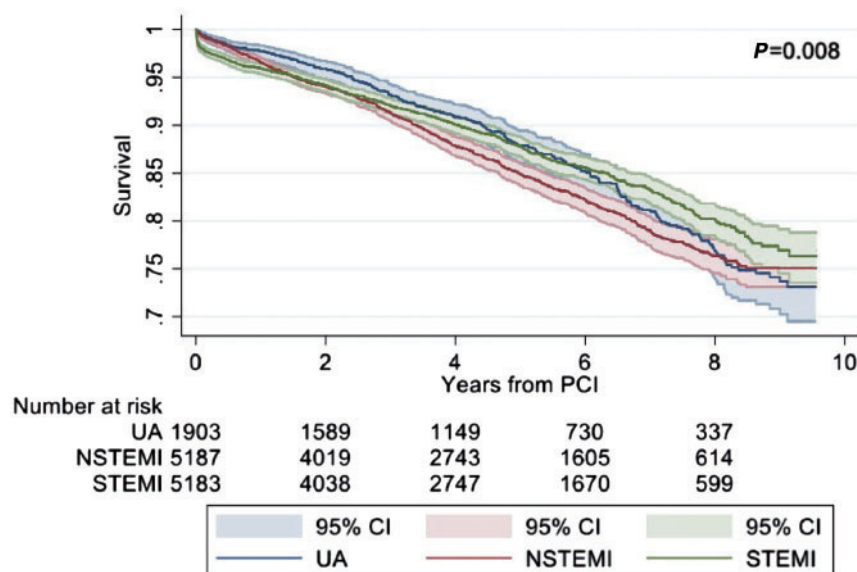


Figure 3 Unadjusted Kaplan-Meier survival analysis by subtype of acute coronary syndrome (excluding cardiogenic shock/post-cardiac arrest patients). PCI, percutaneous coronary intervention; UA, unstable angina; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction.

Discussion

This study evaluated clinical outcomes for different subtypes of ACS in a large multi-centre PCI population, at both short- and long-term follow-up. In this study, baseline characteristics differed significantly between the different subtypes of ACS but PCI success or

procedure-related complications were largely similar across the ACS subtypes. In the first year following PCI, the rate of mortality and MACE was highest in patients presenting with STEMI compared with those in the NSTEMI and UA groups. However, patients with NSTEMI and UA experienced a late catch-up in mortality risk such that there was no significant difference in survival between the three

Table 4 Flexible parametric survival modelling for National Death Index-linked mortality

	Odds ratio	95% CI	P-value
Cardiogenic shock	5.72	4.55–7.19	<0.001
eGFR			
eGFR >60 mL/min/1.73 m ²	1 (ref)		
eGFR 30–60 mL/min/1.73 m ²	1.86	1.63–2.12	<0.001
eGFR <30 mL/min/1.73 m ²	5.58	4.44–7.00	<0.001
Left ventricular ejection fraction			
Left ventricular ejection fraction >45%	1 (ref)		
Left ventricular ejection fraction 30–45%	1.57	1.38–1.78	<0.001
Left ventricular ejection fraction <30%	4.63	3.59–5.98	<0.001
Out-of-hospital cardiac arrest	3.02	2.27–4.03	<0.001
Chronic obstructive airways disease	1.81	1.54–2.13	<0.001
Peripheral vascular disease	1.72	1.43–2.08	<0.001
Diabetes mellitus	1.54	1.35–1.76	<0.001
Obstructive sleep apnoea	1.56	1.15–2.12	0.004
Previous stroke	1.39	1.15–1.68	0.001
Previous myocardial infarction	1.28	1.12–1.46	0.001
Age (per year increase)	1.06	1.06–1.07	<0.001
ACS subtype			
Non-ST-elevation myocardial infarction	1 (ref)		
ST-elevation myocardial infarction	1.01	0.88–1.16	0.871
Unstable angina	0.85	0.71–1.02	0.072
Drug-eluting stent use	0.84	0.74–0.95	0.004

eGFR, estimated glomerular filtration rate; ACS, acute coronary syndrome; ref, reference category.

groups with long-term survival analysis after approximately 8 years. Multivariable analysis also confirmed that the ACS subtype was not an independent predictor of long-term mortality. These findings emphasize that despite disparate baseline and procedural characteristics and differences in short-term mortality, long-term mortality was similar across the spectrum of ACS treated by PCI and contemporary medical therapy.

The risk of adverse events was particularly high during the index hospital admission and first 30 days after PCI among patients in the STEMI cohort. In-hospital and 30-day all-cause mortality for patients presenting with STEMI were approximately four times higher compared with patients with NSTEMI, and more than eight times higher when compared with patients with UA. This increased early mortality in patients with STEMI has been reported in multiple previous analyses.^{2,4} Our in-hospital and 30-day STEMI all-cause mortality rates of 5.5% and 6.2% respectively are comparable to unadjusted mortality rates from previous retrospective studies that have also analysed a PCI population rather than all-comers.^{2,13} This study also included a higher proportion of patients with cardiogenic shock in STEMI (9.5%) than some other studies, which may have contributed to the high

early mortality rate observed.^{13–15} Interestingly, the 30-day mortality rate for STEMI from multiple retrospective or registry-based studies including ours was substantially higher than the 30-day mortality rate of 2.2% found in a pooled analysis of five randomized controlled trials (RCTs) by Pilgrim et al.³ This is likely to reflect differences between the highly selected patients and care provided within the context of RCTs in contrast to an all-comer real world experience.

Similar to previous studies, baseline characteristics were significantly different between patients in the STEMI, NSTEMI, and UA groups in our cohort.^{2,13,16} Patients in the UA and NSTEMI groups were older and were more likely to have risk factors for CAD as well as prior MI, PCI or CABG, compared with patients in the STEMI group. Patients presenting with UA and NSTEMI were potentially more aware of their comorbidities due to previous contact with the healthcare system and cardiologists, whereas many patients presenting with STEMI may not have been aware of their risks until their index admission with MI. In addition, at the time of coronary angiography, patients with UA or NSTEMI were more likely to be diagnosed with multi-vessel disease than patients with STEMI, which may have contributed to the higher rates of MI at 12-month follow-up in the UA and NSTEMI groups. As STEMI tends to occur due to vulnerable plaque rupture than severe coronary stenosis, the higher early mortality seen in the STEMI group may also be due to the lack of ischaemic preconditioning that can occur with patients with NSTEMI and UA.^{17,18}

At 12-month follow-up after PCI, patients who had a STEMI continued to have the highest all-cause mortality of all three groups at 8.7%. However, between 30-day and 12-month follow-up, the increase in the all-cause mortality rates was significantly higher in the UA and NSTEMI groups (257% and 181%, respectively) compared with the STEMI group (40%). This late catch-up in mortality in the UA and NSTEMI groups could be, in part, explained by the higher prevalence of comorbidities and non-culprit CAD in these patients. Previous studies have shown that MACE during follow-up in patients who have presented with an ACS and undergone PCI, is equally attributable to culprit and non-culprit lesions.¹⁹ Age was also found to be a significant independent predictor of long-term mortality in this study. As patients in the UA and NSTEMI groups were older at the time of index PCI, their risk of death over time would also have increased more than in the STEMI group, which may have contributed to the late catch-up in mortality. The role of advanced comorbidities in our cohort is further demonstrated by the higher proportions of deaths occurring from non-cardiac causes at 12-month follow-up in the UA and NSTEMI groups compared with the STEMI group. Kaplan–Meier survival analysis showed overlapping of the survival curves underscoring that long-term mortality was similar across all three groups in this study. When cardiogenic shock and post-OHCA patients were excluded, patients presenting with STEMI who survived the initial period had lower late mortality whereas those presenting with NSTEMI tended to have higher late mortality. Strategies to aggressively lower the early hazard for mortality in patients with STEMI need to be investigated.

In addition to the disparities in baseline comorbidities, differences in use of guideline recommended therapy across the ACS subgroups may have contributed to the differences in clinical outcomes seen. Greater adherence to guideline-recommended medical therapy has been shown to improve survival in patients with CAD.²⁰ Beta-

Table 5 Medications at 30 days and 12 months by acute coronary syndrome subtype

	UA	NSTEMI	STEMI	P-value
30-day medications, n (%)				
Aspirin	1747 (97.1)	4766 (97.9)	5176 (97.2)	0.075
Clopidogrel/prasugrel/ticagrelor	1669 (92.9)	4360 (89.6)	4693 (88.3)	<0.001
Dual antiplatelet therapy	1623 (90.4)	4273 (87.9)	4567 (86.0)	<0.001
Beta-blocker	1317 (74.4)	3894 (81.0)	4603 (87.0)	<0.001
ACEi/ARB	1332 (75.3)	3933 (81.6)	4657 (88.0)	<0.001
Statin	1656 (93.5)	4590 (95.1)	5125 (96.8)	<0.001
Any cholesterol-lowering therapy	1682 (95.0)	4639 (96.1)	5154 (97.4)	<0.001
12-month medications, n (%)				
Aspirin	1539 (94.3)	4191 (94.7)	4593 (95.3)	0.185
Clopidogrel/prasugrel/ticagrelor	1080 (66.5)	2850 (64.7)	3054 (63.8)	0.139
Dual antiplatelet therapy	1014 (62.6)	2680 (61.0)	2906 (60.7)	0.388
Beta-blocker	1087 (67.6)	3213 (73.4)	3787 (79.7)	<0.001
ACEi/ARB	1186 (73.6)	3492 (79.8)	4027 (84.6)	<0.001
Statin	1479 (91.4)	4077 (92.8)	4499 (94.1)	<0.001
Any cholesterol-lowering therapy	1514 (93.5)	4145 (94.3)	4550 (95.2)	0.019

ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker.

blockers and ACEi have been shown in numerous randomized trials to have a mortality benefit when used in patients who have survived an acute MI.^{21–23} Similarly, statins have been shown to reduce the risk of future fatal and non-fatal cardiovascular events in patients following an MI.²⁴ In this study, the use of secondary prevention therapy, particularly of beta-blockers, ACEi/ARB and statins were significantly higher in the STEMI group compared with the NSTEMI and UA groups, both at 30 days and 12 months post-ACS. While patients presenting with NSTEMI and UA were generally older with more comorbidities, and may have contraindications or experience adverse effects to these medications, underuse of optimal secondary prevention therapy could have partly contributed to the poorer long-term survival in these two subgroups. Similar differences in use of secondary prevention medical therapy, and mortality at 4-year follow-up between patients who had a STEMI and NSTEMI/UA were observed by van Leeuwen *et al.*⁴ in their registry, further emphasising the need for improvement in the use of guideline-recommended therapy in patients presenting with NSTEMI and UA.

Our results are also similar to those from the Swedish Coronary Angiography and Angioplasty registry (SCAAR) of PCI patients where 12-month mortality was also found to be higher in patients who had a STEMI compared with those who had NSTEMI, even when adjusted for baseline characteristics, while long-term adjusted mortality beyond 12 months was similar between the NSTEMI and STEMI groups.¹⁶ Interestingly however, the SCAAR registry showed a difference in long-term mortality between the UA and NSTEMI groups, which was not seen in this study. Our UA group included a substantially higher proportion of patients with diabetes (29.6% vs. 19.9%), previous MI (37.9% vs. 23.4%), multi-vessel disease (61.0% vs. 43.4%), and left main disease (7.5% vs. 4.7%) than the UA group in the SCAAR registry, and therefore, may have represented a higher risk cohort. Other retrospective analyses including PCI patients only have also shown that ACS subtype is not an independent predictor for long-term mortality on multivariable analysis, like in this study.^{2,4}

In contrast, a number of studies that have included a more heterogeneous cohort of ACS patients treated with either an invasive or conservative strategy have shown higher long-term mortality in patients who had NSTEMI compared with those who had a STEMI.^{6,8} This could be explained by selection bias in selecting patients with NSTEMI or UA who might have fewer comorbidities for revascularization, rather than medical therapy. Revascularization itself may also impart a prognostic benefit for NSTEMI and UA patients. Multiple randomized trials have shown that patients with NSTEMI or UA treated with an invasive strategy have better short- and long-term outcomes compared with those treated with medical therapy alone, which may also explain the overall better survival of our NSTEMI and UA cohorts.^{25–28}

Studies evaluating clinical outcomes between subtypes of ACS treated by PCI over time are limited and not directly comparable due to inclusion of different patient populations, variable periods of follow-up and different years of study. In the SCAAR registry between 1996 and 2010, 12-month mortality for patients treated with PCI for ACS fell for patients with STEMI (13.3%–9.4%, *P* for trend <0.001) while it showed a trend towards increasing for patients with NSTEMI/UA (3.1%–4.2%, *P* for trend = 0.70).⁹ This possibly reflects an increasing risk profile of patients with NSTEMI being treated invasively with PCI over time. In contrast, data on octogenarians from the Denmark Heart Registry showed no significant change in 30-day or 12-month mortality over the period 2002–08 for patients with STEMI or NSTEMI treated with PCI.²⁹ Compared with contemporary data from studies such as ours, older studies tend to show an earlier cross-over of the Kaplan–Meier survival curves for STEMI vs. NSTEMI/UA. A study by Chan *et al.*⁵ showed an initially higher mortality for STEMI patients treated with PCI between 1999 and 2005, but a cross-over of the curves at only 2 months after which, NSTEMI patients showed persistently higher mortality. Similarly, data from the British and Belgian cohorts of the GRACE registry of unselected ACS patients between 1999 and 2009 showed an overlap in the Kaplan–

Meier curves occurring much earlier than in this study at approximately 2.5 years.³⁰ This may be due to better contemporary medical therapy used in this study mitigating the hazard conferred by a higher baseline risk profile of patients with NSTEMI compared with STEMI, thereby resulting in better medium-term survival for patients with NSTEMI.

Limitations

This was a retrospective analysis of patients enrolled in a PCI registry, and therefore, we could not adjust for all possible clinically relevant factors, which might have confounded our results. Secondly, this study included patients over a time span of 10 years, and therefore, changes in clinical practice, PCI techniques, and adjunctive pharmacotherapy over the last decade could have influenced clinical outcomes—in particular, DES use in contemporary practice is much higher in the setting of STEMI than what was seen in this study. Thirdly, our analysis did not account for patients with missing data which, although applicable to only a small number of cases, might have affected our results. In addition, we did not have data on management of patients with multi-vessel disease, in particular whether complete revascularization was undertaken either at the index procedure or during the follow-up period. Finally, we only included patients who had undergone revascularization with PCI, and therefore, our results may not be generalizable to patients with ACS who receive medical management only or who do not have a culprit lesion requiring PCI.

Conclusion

In conclusion, patients presenting with STEMI tended to be younger and had fewer comorbidities than those with UA or NSTEMI, but had a significantly higher risk of early mortality and MACE, particularly during the initial hospital admission. Despite these disparate baseline characteristics and differences in short-term mortality, long-term mortality was similar across all ACS subtypes treated by PCI and contemporary medical therapy. Future efforts focusing on reducing the early mortality risk in STEMI patients, and improving the use of secondary prevention therapy may help to improve long-term mortality, especially for patients with non-ST-elevation ACS.

Supplementary material

Supplementary material is available at *European Heart Journal – Quality of Care and Clinical Outcomes* online.

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